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2021 WCHRI Research Day website content & abstracts

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Research Day 2021

Attendee user guide | Program | Presentation schedule | Abstracts | Keynote speaker

WCHRI Research Day 2021 will be November 3 and 4!

WCHRI will host its annual Research Day on the afternoon of **November 3** and the morning of **November 4**. This year our format will be again entirely online, scheduled over two half days.

WCHRI Research Day brings our members and stakeholders together to share common interests and research outputs on women and children's health and is a great venue for our trainees to communicate their recent work, discuss their research and network with colleagues. Presentations for Research Day will be combined into themed sessions and presented in moderated virtual sessions. As well, participants are invited to take part in virtual networking activities!

We are delighted to welcome **Janet Smylie** as our keynote speaker! Janet is the director of the Well Living House Action Research Centre for Indigenous Infant, Child, and Family Health and Wellbeing in Toronto and the Tier 1 Canada Research Chair in Advancing Generative Health Services for Indigenous Populations in Canada.

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Important dates:

Registration and abstract submission opens	**July 28**
Learning Session: How to prepare your abstract for WCHRI Research Day Zoom video replay & presentation slides	**July 28**
Abstract submission closes	**September 15 (4 p.m.)**
Learning Session: How to prepare your presentation for WCHRI Research Day Zoom replay	**October 6**
Registration closes	**October 31 (4 p.m.)**

See you November 3 and 4!

WCHRI Research Day is an open event where photographs of presenters and attendees are taken.

Questions? Contact wcgrants@ualberta.ca.

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Program

This year's program takes place on November 3 (afternoon) and November 4 (morning).

Day #1 – 12:45 to 5:15 p.m. (4.5 hours)

Time						
12:45	1:00	**Participants gather**				
1:00	1:15	**Welcome/opening remarks**				
1:15	2:05	**3MT-style (3 min presentation, 3 min questions, 2 min transition)**				
		Pregnancy and developmental	*Children's health and wellbeing:*	*Children's health and*	*Children's health and wellbeing:*	*Lifelong women's health*

1:15	2:05	**3MT-style (3 min presentation, 3 min questions, 2 min transition)** *Pregnancy and developmental trajectories* | *Children's health and wellbeing: Development* | *Children's health and wellbeing: Genetics* | *Children's health and wellbeing: Musculoskeletal health* | *Lifelong women's health*
2:05	3:35	**Keynote presentation**
3:35	4:05	**Break / sponsor rooms / networking**
4:05	5:05	**5 min poster (5 min presentation, 3 min questions, 2 min transition)** *Pregnancy and developmental trajectories* | *Children's health and wellbeing: Cardiac health* | *Children's health and wellbeing: Infection* | *Children's health and wellbeing: Critical care* | *Children's health and wellbeing: Mental health and addiction* | *Children's health and wellbeing: Respiratory health* | *Lifelong women's health*
5:05	5:15	**Wrap up and thank you**

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Day #2 – 7:45 a.m. to noon (4.25 hours)

Time		
7:45	8:00	**Participants gather**
8:00	8:15	**Welcome**
8:15	10:00	**10 min orals (10 min presentation, 5 min questions, 2 min transition)** *Pregnancy and developmental trajectories* | *Children's health and wellbeing: Critical care* | *Children's health and wellbeing: Genetics* | *Children's health and wellbeing: Musculoskeletal health* | *Lifelong women's health*
10:00	10:15	**Break**
10:15	11:35	**5 min poster (5 min presentation, 3 min questions, 2 min transition)** *Pregnancy and developmental trajectories* | *Children's health and wellbeing: Development* | *Children's health and wellbeing: Musculoskeletal health* | *Nutrition and gastrointestinal health* | *Children's health and wellbeing: Critical care* | *Children's health and wellbeing: Cancer and genetics* | *Lifelong women's health*
11:35	12:00	**Wrap up and thank you** *Award winners to be announced separately the next day via our website*

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Presentation schedule

Day one (November 3—afternoon)

Three-minute thesis (3MT) style presentations: 1:15–2:05 p.m.

Five-minute poster presentations: 4:05–5:05 p.m.

Day two (November 4—morning)

10-minute oral presentations: 8:15–10 a.m.

Five-minute poster presentations: 10:15–11:35 a.m.

Abstracts

Presenters, please use a laptop or desktop when giving your presentation, not a tablet (e.g. iPad, Galaxy Tab, etc.) or mobile device. These devices are fine for attendees but not for presenters.

All abstracts are included below and listed alphabetically. Click on the "presenters" or "supervisors" button to narrow down your search and then choose from the drop-down menu to filter by abstract theme, presentation type and keyword. When you have found the abstract you want to view, click on the "+" symbol to view the full abstract.

A B C D E F G H J K L M

Click here for Research Day 2020 abstracts.

Every effort to report the abstract as submitted has been made. Questions may be addressed to wcgrants@ualberta.ca.

Presenters | Supervisors

Abstract theme | Presentation type | Abstract keyword

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Keynote Speaker

Join internationally renowned Indigenous health researcher Dr. Janet Smylie for our keynote lecture entitled “Advancing generative health services for First Nations, Inuit and Metis peoples”.

Photo: Samuel Engelking

Health and social services such as hospitals, family services, and policing are commonly of limited social value for First Nations, Inuit and Metis (FNIM) peoples. In this presentation, Janet Smylie will discuss the root causes of this failure and how to overcome them. She will share evidence and examples of successful FNIM health service innovations and open a conversation on change leadership.

By the end of the session participants will:

- Have witnessed and participated in self-location;
- Be able to provide one concrete example of how existing health service systems are failing FNIM peoples and one underlying driver of this failure;
- Be able to describe an example of a successful FNIM community-led health service innovation and one underlying driver of this success;
- Identify one or more change leadership strategies and one more change leadership pitfalls.

Dr. Smylie is the Director of the Well Living House Action Research Centre for Indigenous Infant, Child, and Family Health and Wellbeing, Tier 1 Canada Research Chair in Advancing Generative Health Services for Indigenous Populations in Canada and a professor in the Dalla Lana School of Public Health at the University of Toronto.

By the end of the session participants will:

Photo: Samuel Engelking

- Have witnessed and participated in self-location;
- Be able to provide one concrete example of how existing health service systems are failing FNIM peoples and one underlying driver of this failure;
- Be able to describe an example of a successful FNIM community-led health service innovation and one underlying driver of this success;
- Identify one or more change leadership strategies and one more change leadership pitfalls.

Dr. Smylie is the Director of the Well Living House Action Research Centre for Indigenous Infant, Child, and Family Health and Wellbeing, Tier 1 Canada Research Chair in Advancing Generative Health Services for Indigenous Populations in Canada and a professor in the Dalla Lana School of Public Health at the University of Toronto.

Dr. Smylie's research focuses on addressing Indigenous health inequities in partnership with Indigenous communities. She is particularly focused on ensuring all First Nations, Inuit, and Métis peoples are counted into health policy and planning wherever they live in ways that make sense to them; addressing anti-Indigenous racism in health services; and advancing community-rooted innovations in health services for Indigenous populations. She maintains a part-time clinical practice at Seventh Generation Midwives Toronto and has practiced and taught family medicine in a variety of Indigenous communities both urban and rural. A Métis woman, she acknowledges her family, traditional teachers, and ceremonial lodge.

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Promote your research—virtually!

WCHRI Research Day offers trainees under the supervision of WCHRI academic members the opportunity to showcase their research progress. This year, we look forward to interacting virtually with our academic members, their trainees and our funders, the Stollery Children's Hospital Foundation and the Alberta Women's Health Foundation!

WCHRI is hosting Research Day virtually this year using PheedLoop, an interactive event platform.

Please access the Abstract Submission and Registration Form to register and/or submit your abstract.

All attendees must register even if you are not submitting an abstract. **Please register if you plan to attend.**

Click on the topics below for additional information on how to present your research this year.

Program opportunity

Abstracts and presentations are scientific and should be accessible to a broad audience.

- Abstract submissions will be allocated to either a:
  - three-minute thesis (3MT-style) presentation,
  - 5-minute poster presentation, or
  - 10-minute oral presentation.
- Only abstracts that evidence alignment with WCHRI Research Day abstract relevance criteria are eligible for publication and presentation.
- Presentation format is recommended by the WCHRI Research Day abstract review committee and based on reviewer impression of the abstract and commensurate with trainee level:
  - undergraduate
  - graduate
  - fellows
  - residents
- Presentations are representative of WCHRI's three research themes:
  - children's health and well-being
  - pregnancy and developmental trajectories and
  - lifelong women's health.

Submission of an abstract to WCHRI constitutes confirmation of the trainee's availability to present on either November 3 or November 4.

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Abstract preparation outline

Before you start your registration and abstract submission, review the submission and completion requirements. Most trainees develop their abstract in a Word document and copy and paste the abstract into the abstract submission form.

The purpose of your abstract is to:

- present a large amount of information in a concise manner.
- engage and promote your work with a broad audience.

Why it's important:

- This will determine the format you are invited to present on Research Day.
- Abstracts will be posted on our website, so it will be a chance to build your professional portfolio.

Structure

For the abstract itself, key components include:

- a title
- an introduction
- methods
- results
- conclusion

Abstract submission

- Abstracts must be complete and submitted to WCHRI on or before **September 15 (4 p.m.)**.
- Abstract submission is open to undergraduate, graduate, fellows and residents under the direct supervision of a current WCHRI academic member.
- One abstract submission per trainee maximum.
  - Where the presenter submits more than one abstract, the abstract submission received closest to the deadline date will be accepted.
- Information submitted in the form is not subject to amendment.
- Presentation in the virtual platform is "live" and delivered by the trainee invited to present.

Trainees are encouraged to download their abstract details from the submission confirmation page. This is confirmation of abstract and registration form submission.

Abstract review process

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Abstract review process

The abstract review process is as follows:

- The WCHRI Research Day abstract review committee is composed of WCHRI academic members.
- Abstracts will first be evaluated for relevance by the committee.
- The committee, composed of WCHRI postdoctoral fellows and academic members, will recommend each abstract to one of the following presentation types/ opportunities:
  - 3MT-style presentation,
  - (5-minute) poster presentation, or
  - (10-minute) oral presentation.
- Feedback from the committee is not provided.
- Abstracts that meet WCHRI relevance criteria will be published on our website on **October 5**.
- WCHRI will provide notification to all trainees of the outcome of their abstract submission by **October 5**.

Research Day presentation types/opportunity

Please note: iPads and mobile devices are fine for attendees but not for presenters! Presenters, please use a laptop or desktop when giving your presentation.

WCHRI offers the following opportunities to trainees to support and network their research. All presentation types are to support promotion and networking of scientific research with a broad audience composed of trainees, academic faculty, research staff and funding partners and their donors. Each trainee will be assigned a time to start and end their presentation to judges.

3MT-style presentation

Each trainee will be assigned to a presentation space with up to five other presenters. One static, non-animated slide may be used. Trainees have three minutes to present their research followed by three minutes for questions from judges and/or the moderator. Judges may be WCHRI postdoctoral fellows, academic members and/or Stollery Children's Hospital Foundation and/or Alberta Women's Health Foundation representatives.

5-minute poster presentation

Each trainee will be assigned to a poster space with up to three other poster presenters. One dynamic slide may be used to support the presentation. Trainees have five minutes to present their research followed by up to three minutes of questions from poster judges. Poster judges may be WCHRI postdoctoral fellows or academic members.

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10-minute oral presentation

Each trainee will be assigned to an oral presentation space with up to five other presenters. Dynamic slides may be used to support the presentation. Trainees have 10 minutes to present their research followed by up to five minutes of questions from presentation participants (judges, moderators and/or audience members, including Stollery Children's Hospital Foundation and/or Alberta Women's Health Foundation representatives). Oral presentation judges and moderators may be WCHRI postdoctoral fellows or academic members.

Learning Sessions

WCHRI hosts two learning sessions to help trainees navigate requirements and expectations for Research Day. The first session is to help you prepare your abstract and the second session offers specific details about the components required to deliver an effective presentation.

How to prepare your abstract for WCHRI Research Day

- Event date: July 28, 11:30 a.m.–1 p.m.
- Zoom video replay and presentation slides

How to prepare your presentation for WCHRI Research Day

- Event date: October 6, 11:30 a.m.–1 p.m.
- Zoom replay

Deadlines

- Abstract submission for WCHRI Research Day closes **September 15** at **4 p.m.**
- Registration for WCHRI Research Day closes **October 31** at **4 p.m.**

Applications must be submitted to WCHRI using the Research Day Abstract Submission/ Registration Form. Late submissions are not accepted.

Access to Research Day registration will be closed from **September 15** at **4:01 p.m.** through to **September 16** at **9 a.m.**

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Acknowledgement

WCHRI is supported by the Stollery Children's Hospital Foundation and the Alberta Women's Health Foundation. Without their generous support, our institute would be unable to continue to support the research done by you and your colleagues.

You are required to acknowledge the funding sources that contributed to your research. All research is supported in some way by a financial commitment. If you are unsure of the funding source(s) for your project, please ask your supervisor. All research projects funded by or receiving subsidized research services from WCHRI must acknowledge the support of WCHRI and the appropriate Foundation, including using logo(s) on your presentation slides.

Further information on acknowledgement requirements and logo files can be found on WCHRI's acknowledgements and logos webpage.

Access the abstract submission and registration form

Access the WCHRI 2021 Research Day Abstract Submission/ Registration Form.

Questions? Contact WCHRI grants administration at wcgrants@ualberta.ca.

Registrations are open until **October 31 at 4 p.m.**

Please use this link to register.

Please register if you plan to attend.

Abstract submissions were closed on September 15.

Participant #: 101
Presenter: Reyhaneh Ababzadeh
Supervisor: Lou, Edmond HM
Title: Applying Machine Learning Algorithms to Predict Curve Progression in Children with Adolescent Idiopathic Scoliosis
Authors: Reyhaneh Ababzadeh, Nastaran Gholizadeh, Mahdieh Khodaei, Edmond Lou

Theme: Children's health and well-being

Introduction
Adolescent Idiopathic Scoliosis (AIS) is an unusual curving and twisting of the spine which affects 1-3% of adolescents. Radiographs are taken on all children who attend scoliosis clinics. Although the progression cases are approximately 20%, radiographs taken for the non-progressive cases are, in retrospect, unnecessary. Hence accurately predicting the progression of scoliosis is crucial because it can reduce the radiation exposure to children who have non-progressive scoliosis. There are many machine learning (ML) algorithms that can be applied to predict curve progression for children with AIS. The best algorithm reported in literature was 81% accurate. The objective of this study was to test 6 common ML algorithms and determine which one provided the most accurate model to predict curve progression.
Methods
154 adolescent females with AIS (aged 14.5±11.3 yrs, X-ray Cobb angle 25.0°±9.3°) were consented and recruited. Among those, 32 cases had curve progression >5 degrees. Full spine ultrasound (US) scans were obtained in a standing position at the baseline and follow-up visits. Five parameters including the baseline a) X-ray Cobb, b) US apical axial vertebral rotation (AVR), c) US torsion, d) RC value as an index of the bone quality measured of the reflected US signals from the L5 lamina area and e) US Cobb change were investigated as input parameters for prediction model development.
To determine which features would be used for prediction, a heatmap using Pearson correlation was created. Under the heatmap, the AVR had a strong correlation with the torsion (r=0.9) and the variance of torsion was higher than AVR. Therefore, AVR was dropped from the input. As there were more non-progress cases in the dataset, the ML result would bias toward detecting non-progress cases. Therefore, before training the algorithm, the SMOTEENN method was used to balance the dataset, which combined oversampling and under-sampling using SMOTE and Edited Nearest Neighbors. To develop the ML algorithms, the dataset was split into 80% training and 20% testing. The performances of six classification algorithms, including Logistic Regression, Decision Tree, Naive Bayes, Support Vector Machine, K-Nearest Neighbors (KNN), and Random Forest were tested and compared. To determine the best model, test accuracy, train accuracy, sensitivity, specificity, and ROC area, were compared.
Results
Based on the balanced dataset, logistic regression and KNN methods performed the same and better than others. Among the 5 tested parameters, only the train accuracy for the logistic regression and KNN were different, 0.869 versus 0.978. The test accuracy, sensitivity, specificity, and ROC were 0.961, 1.0, 0.928, and 0.964 respectively. There was no significant difference between these two ML algorithms.
Conclusion
Using logistic regression and KNN machine learning algorithms with 4 input parameters, provided 96% accuracy to predict curve progression. Implementing these two artificial intelligence methods can assist decision-making in clinical environments and reduce the number of X-rays required for children with scoliosis.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 186
Presenter: Maryam Adesunkanmi
Supervisor: Ospina, Maria
Title: Social Determinants of Health and Adverse Outcomes in Adolescent Pregnancies: Implications for Policy and Practice
Authors: Sana Amjad, MBBS MSC; Maryam Adesunkanmi, BSc (Hons); Jasna Twynstra, PhD; Jamie Seabrook, PhD; Maria Ospina MB, PhD.

Theme: Pregnancy and developmental trajectories

Introduction: The association between adolescent childbearing and adverse maternal and birth outcomes has been well documented. Adverse adolescent pregnancy outcomes are associated with a substantial risk of long-term morbidities for the young mothers and their newborns. Multiple levels of social disadvantage have been linked to adverse pregnancy outcomes among adolescent mothers.
Methods: Using the PROGRESS-PLUS equity framework as a conceptual model, we conducted an overview of the current scientific evidence on SDOH aspects that have clinical and practical implications in the context of adolescent pregnancies.
Results: Patterns of cumulative social adversity define the most marginalized group of adolescents at the highest risk of experiencing adverse maternal and birth outcomes. A multi-sectorial approach to adolescent perinatal health is recommended to improve the perinatal and long-term well-being of pregnant adolescents and their children.
Conclusion: The intersectional nature of multiple SDOH should be taken into account when formulating clinical and societal interventions to address the needs of the most marginalized pregnant adolescents. Understanding the mechanisms and pathways from structural SDOH to disadvantage in adolescent maternal and birth outcomes should be a priority for future adolescent perinatal researchers.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 48
Presenter: Usman Ahmed
Supervisor: Hawkes, Michael
Title: An emerging biomarker predicts childhood pneumonia severity and mortality in a resource-limited setting
Authors: Usman Ahmed; Jeremy Soo; Andrea L. Conroy; Sophie Namasopo; Robert O. Opoka; Ravi Bhargava; Michael T. Hawkes

Theme: Children's health and well-being

Introduction: Pneumonia is the world's leading infectious cause of death for children under five years old with more than three-quarters occurring in the African and South-East Asian regions. Accurate patient triage in low resource settings is essential and various host biomarkers have been suggested as indicators of pneumonia severity. Soluble T cell immunoglobulin and mucin-domain containing protein 3 (sTIM-3) has not been explored to our knowledge, although it has a role in inflammatory pathology of several disease states. The aim of this study was to determine the potential prognostic value of sTIM-3 in childhood pneumonia. Methods: We conducted a prospective cohort study at two hospitals in Uganda among children < 13 years old with severe pneumonia. We assessed sTIM-3 levels at hospital admission and their association with pneumonia severity and subsequent mortality. Pneumonia severity was determined by the composite clinical severity score, Respiratory Index of Severity in Children (RISC). sTIM-3 and C-reactive protein (CRP) levels were collected at hospital admission and quantified using enzyme-linked immunosorbent assays. Child demographics, history and physical, and radiographic and laboratory investigations were collected prospectively. Results: A total of 77 children (median age 1.1 years) were included. The median sTIM-3 level was 2.9 ng/ml (IQR 1.7-4.8) with 51 (66%) patients having measurements <4.0 ng/ml (lower 2 tertiles, group 1) as compared to 26 (34%) patients with measurements ≥ to 4.0 ng/ml (upper tertile, group 2). sTIM-3 levels were positively correlated with the RISC (ρ=0.35, p=0.0017). In contrast, CRP was not significantly correlated with the RISC (ρ=0.17, p=0.13) in our cohort. Hypoxemia (67% in group 1 vs 92% in group 2, p = 0.014) and intercostal retractions (59% in group 1 vs 88% in group 2, p = 0.017) were more common in group 2. Transfer to a tertiary hospital (2% in group 1 vs 15% in group 2, p = 0.042) was more common in group 2. There were no deaths in group 1 as compared to 4 (15%) deaths in group 2 (p = 0.011). sTIM-3 levels were higher in fatal than non-fatal cases (5.8 ng/ml (IQR 4.5-7.3) vs 2.9 ng/ml (IQR 1.7-4.5), p = 0.032). Conclusion: Taken together, higher sTIM-3 levels at admission were associated with disease severity and were predictive of mortality in childhood pneumonia in a resource-limited setting. Thus, sTIM-3 could potentially be translated as a point-of-care triage tool in low resource settings with the goal of improving outcomes in childhood pneumonia.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 164
Presenter: Amber Ali
Supervisor: Newton, Amanda (Mandi) S.
Title: Assessing the use of experience-based co-design in mental health studies: A scoping review

Authors: Amber Z. Ali, Bruce Wright, Amanda S. Newton

Theme: Children's health and well-being,Lifelong women's health

Introduction: Experience-based co-design (EBCD) is an approach to health care service design that involves patients and clinicians working in partnership to develop and improve health care services. EBCD has been primarily used in clinical settings for quality improvement initiatives, but more recently has been incorporated into research studies involving intervention design and evaluation. The aim of this scoping review is to examine the use and reporting of EBCD in mental health studies that involved patients.

Methods: Electronic databases (MEDLINE, Embase, PsycInfo, CINAHL, Scopus, and Pro-Quest) were systematically searched for variations of 'mental health', 'experience-based co-design', 'participatory research', and 'patient engagement' to identify English language, peer-reviewed articles published from January 2005 to March 2021. Studies of any design related to pediatric and/or adult mental health services that involved a co-design approach or patient engagement were eligible for inclusion. Identified studies underwent independent abstract and title screening by three reviewers; full text review is currently being conducted to identify which studies will be included in the review. From included studies, the team will extract data on how EBCD was used (e.g., approach to setting up the project and team, methods for gathering experience data, methods used for co-design) and organize the data according to the six-stage EBCD framework. Study quality will be assessed by examining the report of patient involvement and using the Guidance for Reporting Involvement of Patients and the Public 2 (GRIPP2) checklist.

Results: The search identified 2,471 articles; of these, 203 full-text articles were screened for eligibility. To date, 50% of 203 studies have been screened with 39 being eligible thus far. Results will be presented in a tabular form, and include how each project team followed the stages of the EBCD framework. Adherence to EBCD stages and activities will be calculated and presented in a chart. Barriers, constraints, and facilitators to EBCD as reported in studies will also be presented in a tabular form, possibly grouped separately for pediatric and adult studies, depending on the extent of data available. A narrative summary will accompany the tabulated and charted results and describe how the results relate to the scoping review objective. Recommendations for future co-design mental health studies with patients will be based on the review's findings.

Conclusion: Findings from this scoping review will lead to a better understanding of how mental health studies involving co-design are being conducted with patients and identify trends and gaps in EBCD activities in these studies. The recommendations from this review may result in a more informed approach among health services researchers for using EBCD to collaborate with patients and families to improve mental health care and services.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 124
Presenter: Sarah Almas
Supervisor: Ospina, Maria
Title: Evaluation of an air-quality sensor to monitor indoor pollution for asthma control in childhood
Authors: Sarah Almas, Ariel Delorme, Linn Moore, Ran Zhao, Elizabeth Hicks, and Maria-Beatriz Ospina

Theme: Children's health and well-being

Introduction
Asthma is the most common chronic disease of childhood and is a major cause of pediatric emergency departments visits in Canada. Despite advances in pharmacological therapies for asthma, the symptomatic control in children remains an unmet goal. With the current pandemic, air pollutants in households are expected to increasingly impact asthma control. Measuring indoor air quality using novel technologies holds potential as an efficient strategy for controlling symptoms. However, the acceptability of implementing an indoor air quality sensor has yet to be discovered. Here, we hypothesize that families will be receptive to installing an indoor air quality sensor after understanding its health benefits.

Methods
For this cross-sectional study, we recruited 7 caretakers of children aged 5-17 years with an asthma diagnosis through contactless QR codes at the Stollery Hospital Pediatric Respirology Clinic and social media. After electronic consent was obtained, participants were randomized to either read an infographic or watch a brief video illustrating the characteristics of a novel air quality sensor. Participants completed a questionnaire on sociodemographic information, household living conditions, time spent at home, familiarity with smart home technologies, perceived air quality in the household, acceptability of a sensor, and perceived barriers for implementation.

Results
6/7 respondents found the information provided on the functionality and purpose of an indoor air quality sensor to be informative, with a nearly even split between preference of a video or infographic. Most respondents (5/7) were either likely or very likely to use the sensor out of personal interest, and all respondents were either likely or very likely to use the sensor for research purposes. Barriers to use included cost (5/7), intrusiveness and value (3/7), as well as availability, effectiveness, noisiness, and data sharing (2/7). Features that would make the sensor more acceptable included a small size and mobility (5/7). When asked for input, respondents indicated they would use the sensor for curiosity or to monitor air quality levels. Additionally, respondents averaged a score of 7.5/10 for familiarity with smart-home technologies, indicating the ease to which this novel sensor technology could be employed.

Conclusion
This pilot study evaluates the acceptability of a digital health solution to inform preventive health management solutions for asthmatic children. Identifying modifiable indoor determinants of asthma control during a crucial window of development would improve the quality of life of young asthmatics and prevent progression to chronic respiratory conditions.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 156
Presenter: Anastasia Ambrose
Supervisor: Andrews, Saadet
Title: Mitochondrial long chain fatty acid oxidation and carnitine defects in a single Canadian metabolic genetics clinic
Authors: Anastasia Ambrose, Melissa Sheehan, Taryn Athey, Shailly Ghai-Jain, Alyssa Lyn Ostlund, Angela Schinkinger, Komudi Siriwardena, Alicia Chan, Saadet Mercimek-Andrews

Theme: Children's health and well-being,Lifelong women's health

Mitochondrial long chain fatty acid oxidation (LCFAOD) and carnitine defects are inherited metabolic disorders. Their estimated incidence is 1 in 5,000-10,000 births. We performed a retrospective cohort study in our Metabolic Genetics Clinic (REB-ID#Pro00108842). All patients with LCFAOD and carnitine defects were included. We reviewed patient charts. Thirty-nine patients included (21 children (<18 years) and 18 adults): carnitine uptake defect (CUD) (n=15), carnitine palmitoyltransferase I (CPTI) (n=10) and II (CPTII) (n=3) deficiencies, carnitine-acylcarnitine translocase (CACT) (n=3), very long-chain acyl-CoA dehydrogenase (VLCAD) (n=4), long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) (n=3), and multiple acyl-CoA dehydrogenase (MAD) (n=1) deficiencies. All patients were diagnosed by biochemical and/or molecular genetic investigations of candidate genes. Mean age was 20.4±17.6 years (range 3 months- 55 years). Seven patients had hypoglycemia: CPTI (n=3), VLCAD (n=1), CACT (n=2) and MAD (n=1) deficiencies. Six patients had episodes of rhabdomyolysis including CPTII (n=3), and LCHAD (n=3) deficiencies. History of myalgia was reported in 5 patients including CPTII (n=2), CUD (n=1) and VLCAD (n=3) deficiencies. Fatigue was reported in five patients with CUD. Retinopathy was present in two patients and peripheral neuropathy was present in one patient with LCHAD deficiency. One patient with VLCAD deficiency had cardiomyopathy. One patient with CACT deficiency died due to cardiac arrest at the age of five days. There were 10 patients who had long-chain fat restricted diet including CPTII (n=2), LCHAD (n=3), VLCAD (n=4), MAD (n=1) deficiencies. In diet patients, long chain fat intake ranged between 6-44% of daily caloric intake while restriction ranged between 10-35%. In conclusion, newborn screening allowed us to diagnose 41% of the patients to initiate early treatment. The prevalence of LCFAOD and carnitine defects was 4.75% in our clinic. This is the first study in Alberta with a large number of patients from a single center.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 200
Presenter: Sana Amjad
Supervisor: Ospina, Maria
Title: The impact of COVID-19 on the socioeconomic well-being of Métis children in Alberta
Authors: Sana Amjad, Reagan Bartel, Ian Colman, Maria B. Ospina

Theme: Children's health and well-being

Background: The COVID-19 pandemic and the resulting public health measures have caused major socioeconomic disruptions and impacted the health of families worldwide. In collaboration with the Métis Nation of Alberta (MNA), we explored the impact of the COVID-19 pandemic on socioeconomic well-being of Métis children in Alberta.

Methods: We analyzed data from two waves of a COVID-19 survey conducted among Métis people in Alberta between December 2020-January 2021 (W1; n=1,508 Métis people) and March-April 2021 (W2; n=749). Respondents were recruited through a multi-modal strategy using social media and MNA newsletters. Survey responses were entered on a Research Electronic Data Capture (REDCap) database held at a secure server at the University of Alberta. We compared parental reporting of changes in quality of life, school attendance, family financial situation, food security, social interaction, and overall mental health of Métis children.

Results: A total of 572 respondents in W1 were Métis parents/guardians of children aged <18 years, of which 26% (n=150) had children aged < 4 years, while 284 respondents in W2 were Métis parents/guardians of children aged <18 years, of which 25% (n=70) had children aged < 4 years. The majority of parents indicated an overall reduction in quality of life (69% in W1 and 62% in W2). The proportion of parents will full time employment remained unchanged (43% in W1 and 42% in W2). There was an increase in the proportion of parents reporting being worse off financially (46% in W1 to 64% in W2) and experiencing challenges affording food at least once during the pandemic (26% in W1 to 34% in W2). The number of children attending K12 schools in person increased from 35% in W1 to 72% in W2. About 30% of parents experienced some gaps in child care which increased to 36% in W2. The proportion of children experiencing difficulties accessing laptop, computer or internet necessary for schooling activities remained unchanged (33% in W1 and 32% in W2). The majority of parents reported an increase in their children's screen time (80% in W1 and 79% in W2). The proportion of children experiencing reduced socialization with friends increased from 60% in W1 to 67% in W2 while the frequency of mood changes such as feeling down, depressed, or upset decreased from 60% in W1 to 52% in W2.

Conclusion: The ongoing COVID-19 pandemic continues to negatively impact the material and social well-being of Métis families exposing children to financial insecurity, poor nutrition, decreased social interaction, and ill mental health. The long-term sequelae of the pandemic on Métis children's social development and mental well-being are yet to be seen.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 94
Presenter: Nicole Anderson
Supervisor: Hicks, Matt
Title: Single centre 10-year experience with HIE: Risk factors for poor outcome
Authors: Nicole Anderson, Matt Hicks, Po-Yin Cheung, Maria Ospina

Theme: Children's health and well-being,Pregnancy and developmental trajectories

Introduction: Total body cooling (TBC) has become the standard of care for infants with moderate to severe hypoxic-ischemic encephalopathy (HIE). Randomized control trials completed over 10 years ago displayed improved short and long-term outcomes. This has led to further exploration of clinical risk factors that predispose children to have neurodevelopmental impairment after completion of TBC and subsequent discharge from hospital. A number of risk factors have been considered including but not limited to severity of HIE, hypercarbia, amplitude electroencephalogram (EEG) findings, pattern of injury on MRI, presence of seizure, and use of anticonvulsants medication.

Given the multiple risk factors present in cooled neonates, in addition to substantial clinical variability, prognostication remains difficult. There are limited prognostic tools since the advent of TBC as a treatment standard for HIE which makes discussion with families about their child's future difficult. Prior to the use of TBC, the Thompson score utilized 9 clinical signs to estimate long term outcomes. This score has been used in neonates who underwent TBC but does not include other important risk factors. A tool for prognostication is necessary, not only for management discussions in the acute setting but for provision of appropriate developmental follow-up.

Methods: Using data from neonates with moderate to severe HIE in Edmonton, Canada who underwent TBC since its introduction over ten years ago, the primary objective is to identify risk factors for neurodevelopmental impairment. Risk factors will include baseline characteristics, laboratory markers, resuscitative needs and neurological examination prior to total body cooling and on Day 7. Neurodevelopmental assessment at 18 months and 3 years old will be used. Neurodevelopmental impairment will be defined as cerebral palsy (gross motor functional classification system level 2 to 5), developmental delay (Bayley III or equivalent, mental developmental index less than 70), blindness and/or sensorineural deafness. The secondary objective will be to develop a prediction tool for neurodevelopmental impairment using identified risk factors.

Results: Since 2007, 464 babies have undergone total body cooling for a diagnosis of HIE. This is an average of 33 infants per year, ranging from a minimum of 9 (in 2007) and maximum of 49 (in 2018). An average of ~4 infants with HIE have died per year prior to hospital discharge in the last 5 years. Of those who survive past hospital discharge we will link their hospital data to developmental data from the Glenrose Neonatal Follow-up Clinic. Statistical analysis by means of regression and classification and regression (CART) model development are ongoing.

Conclusion: In neonates with moderate to severe HIE, we have identified baseline laboratory, resuscitative and neurological examination variables associated with neurodevelopmental impairment. These prognostic factors will be used to build a CART model for prognostication.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 181
Presenter: Saeed Anwar
Supervisor: Yokota, Toshifumi
Title: Antisense oligonucleotide-mediated exon 27 skipping of dysferlin for the treatment of dysferlinopathy
Authors: Saeed Anwar, Rika Maruyama, Toshifumi Yokota

Theme: Children's health and well-being

Introduction: Dysferlinopathies are a family of disabling muscular dystrophies caused by mutations in the DYSF gene, which encodes dysferlin protein. Dysferlin is a key player in sarcolemmal homeostasis and plasma-membrane resealing. It is a modular protein with multiple calcium-dependent C2 lipid binding (C2) domains. Based on reports of patients with very mild and late-onset phenotypes, dysferlin lacking one or more of the repetitive domains retain (at least partial) functionality. This provides the rationale for the development of exon skipping therapies for dysferlinopathies. Exon skipping therapy uses DNA-like synthetic molecules called antisense oligonucleotides (AOs) to modulate splicing, allowing exons harboring or near genetic mutations to be removed and the open reading frame corrected. Previous investigations have suggested that skipping single or multiple exons is a promising therapeutic approach for dysferlinopathies. In this study, we are developing exon 27 skipping therapy for patients with dysferlinopathies.
Methods: Using a computational tool, we designed three AOs targeting exon 27 of DYSF to be tested in a patient muscle cell line with a splice site mutation that leads to exon 26 deletion. We then evaluated the efficiency of the AOs in immortalized myoblasts and myotubes. Exon skipping efficiency of the AOs and restoration of in-frame gene transcripts with a deletion of exons 26-27 were evaluated by reverse transcriptase-PCR. We analyzed the rescue of dysferlin protein using western blotting. We utilized a membrane-wounding assay to evaluate the ability for membrane resealing of the AO-treated patient cells.
Results: Analysis of the mutation status of the patient-derived cells suggested that exon skipping of exon 27 would restore the reading frame. As measured by RT-PCR, all three AOs efficiently skipped DYSF exon 27 at 10 μM dose, with a skipping efficiency of up to 90% in both myoblasts and myotubes. Western blotting analysis of the AO-treated myoblasts and myotubes revealed that the treatment with AOs rescued nearly 50% of normal dysferlin expression levels in these cells. Membrane wounding assay showed functional recovery of membrane wounding in the myotubes with exon 27 skipping.
Conclusions: This study showed that skipping of DYSF exon 27 and restoration of in-frame transcripts with exons 26-27 deletion rescues expression of dysferlin and membrane resealing ability in patient-derived cells. This study paves the way for future in vivo work that would help establish a foundation for the future clinical implementation of antisense-mediated exon skipping for dysferlinopathy.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 169
Presenter: Tejal Aslesh
Supervisor: Yokota, Toshifumi
Title: A novel peptide-conjugated morpholino oligomer DG9-PMO crosses the blood-brain barrier and improves bodywide symptoms in a mouse model of spinal muscular atrophy
Authors: Tejal Aslesh, Rika Maruyama, Esra Erkut, Toshifumi Yokota

Theme: Children's health and well-being

Introduction: Spinal muscular atrophy (SMA), is the most frequent genetic cause of infant mortality worldwide. It is caused by the deletion of the survival of motor neuron 1 (SMN1) gene. SMN2, an SMN1 paralog can produce only 10% functional SMN because of a mutation that produces unstable transcripts. Antisense therapy is a promising strategy to treat SMA. Splice-switching oligonucleotides (SSOs) that bind to a silencer region in the SMN2 gene can restore the production of full-length SMN2 (FL-SMN2) mRNA. Spinraza, the first approved drug for SMA, is an 18-mer SSO. Significant problems persist with Spinraza treatment, including injection-site adverse effects, treatment costs, and repeated invasive intrathecal injections. Recent findings also revealed that SMA is a multi-organ disorder affecting the heart, liver, thymus, and spleen; however, Spinraza is injected intrathecally to avoid renal toxicity and therefore can treat only motor neurons. As such, a compound providing effective yet safe delivery of SSO to the central nervous system (CNS) and body-wide organs is needed to prevent SMA-related morbidity and death.

Methods: To improve uptake of SSOs in vivo, a novel cell-penetrating peptide called DG9 was identified from screening several peptides in zebrafish. With a 10-to-100-fold efficiency in cellular uptake compared to other peptides, DG9 was conjugated to an SSO called phosphorodiamidate morpholino oligomer (PMO) targeting SMN2. We subcutaneously injected SMA mice with DG9-PMO on postnatal day 0 (PD0). SMN2 expression was evaluated using quantitative PCR and Western blots. We assessed the functional improvement with tests such as rotarod, forelimb grip strength and righting reflex. To establish the superiority of the peptide in blood-brain barrier (BBB) penetration, mice were injected with fluorescently tagged DG9-PMO at PD5 when the BBB is highly developed.

Results: A single administration of DG9-PMO increased median survival to 58 days (d) compared to 8d for non-treated (NT) and 14d for naked PMO-treated mice. DG9-PMO treated mice exhibited up to 10-fold and a 5-fold higher expression of FL-SMN2 gene compared to NT control and naked PMO treatments respectively in the CNS and body-wide tissues. These mice showed significantly increased body weights and improved motor function, accompanied by increased muscle fibre size and innervation at the neuromuscular junction. No apparent toxicity was observed. We also observed the localization of DG9 peptide in the brain and spinal cord when administered even after injection at PD5.

Conclusion: DG9-PMO is a promising therapeutic option to treat SMA, overcoming the necessity for invasive injections with a single peripheral administration and treating body-wide tissues without apparent toxicity.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 103
Presenter: Beimnet Ayalew
Supervisor: Tan, Qiumin
Title: 3-D Imaging of Transient Neurons in the Mouse Brain
Authors: Beimnet Ayalew, Qiumin Tan

Theme: Children's health and well-being

Cajal Retzius (CR) cells are a heterogeneous population of cells that are critical for early brain development. They are described as transient neurons because they effectively disappear from the postnatal brain, except for a small population of CR cells that persists in the hippocampus throughout adulthood in both mice and humans. Incomplete CR cell removal has been thought to play a role in brain pathologies, including brain malformation and epilepsy, opening the possibility that CR cell death itself is regulated to play a constructive role in sculpting the maturing brain. Therefore, the project's goal was to decipher the temporal and regulatory code of CR cell death in the developing mouse brain. To visualize CR cells, a technique known as CUBIC was used. CUBIC is a method that visualizes whole tissues by making the tissue optically transparent while labelling the cells of interest with fluorescence. Using this technique, it was possible to see where the CRs were located throughout the brains of mice. We aim to apply the procedure to a knockout mouse model with abnormal hippocampal CR cell persistence and increased seizure susceptibility. Comparing the distribution of CR cells between control and knockout mice throughout brain development may give greater insight into the pathogenesis of epilepsy.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 137
Presenter: Tara Azimi
Supervisor: Montesanti, Stephanie
Title: Exploring the experiences and support needs of mothers of children with type 1 diabetes: A qualitative descriptive analysis.
Authors: Azimi, T.

Theme: Children's health and well-being,Lifelong women's health

Type 1 diabetes (T1D) is an incurable and life-threatening chronic condition that is on the rise globally. Canada is sixth among countries with the highest rates of T1D in children under the age of 15. T1D can be difficult to control, requiring constant vigilance to reduce the risk of complications and improve long-term health outcomes. The management of T1D primarily lies with the parent- especially mothers, who report performing 70% of all blood glucose checks and 79% of insulin administrations. Caregivers report the management of T1D as being intensive, stressful, and never- ending, and these daily strains often lead to depression, fatigue, anxiety, and burnout. These outcomes are reported to be more severe and prevalent among mothers, compared to fathers, of children with T1D. Anxiety levels in some mothers post diagnosis, even five years afterward, meet the diagnostic criteria for PTSD. Although studies have reported on psychological consequences of caring for children with T1D, no qualitative study has focused on the experience of mothers in Canada. Furthermore, there is little recent evidence on the supports that are most important to mothers, such as financial and emotional assistance. Understanding the unique experiences and needs of mothers caring for children with T1D is necessary for planning, improving, and advocating for services for this population. Enhanced support for mothers also translates to better caregiving, diabetes management, and health outcomes in their affected children.

[Research Question]: What are the experiences and support needs of mothers in Edmonton, Alberta, caregiving for children with T1D under the age of 18?

[Objective(s)]: (1) To understand the experiences of maternal caregiving for children with T1 diabetes and (2) to identify the support needs of these mothers to improve their health and mental well-being.

[Methods]: I will use a qualitative approach to examine the experience of caring for a child with T1D. Utilizing an integrated KT approach, this research study will be developed and carried out collaboratively with an advisory committee comprising mothers of children with T1D. To address my research objectives, I will conduct two inter-related studies. Study 1: Semi-structured interviews with mothers in Edmonton caring for children with T1D under the age of 18. Participants will be recruited using a convenience sampling approach through The Stollery Pediatric Diabetes Education Centre (PDEC) in Edmonton, Alberta. I will use a qualitative descriptive method to interpret the personal experience of caring for a child with T1D, as depicted by participants, and the specific meaning they place on providing this care. Study 2: Three focus groups with participants in study 2 to identify and prioritize support needs for mothers of children with T1D. Specific strategies prioritised during the focus groups will be validated in a follow-up debriefing meeting where participants will rank the most important strategies to be implemented by health planning stakeholders. All data will be audio- recorded and analysed using thematic analysis. Advisory members will be involved in tasks such as informing the interview guide, reviewing themes post data analysis and assisting with KT and dissemination of findings.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 138
Presenter: Katherine Babyn
Supervisor: Yuksel, Nese
Title: Cannabis use in menopause: A survey on usage patterns and perceptions
Authors: Katherine Babyn, Sue Ross, Nese Yuksel

Theme: Lifelong women's health

Introduction: Use of cannabis has increased in Canada since recreational cannabis legalization in 2018, with growing interest to manage health issues. Midlife women may be using cannabis to help with symptoms overlapping with menopause. As part of a mixed methods study, the purpose of the survey was to characterize cannabis use patterns and perceptions in a population of midlife women living in Alberta, Canada.

Methods: A cross-sectional, web-based survey was designed by the research team and hosted on Qualtrics. Survey questions included demographics, clinical data used to categorize menopause stage, cannabis characteristics, information sources, and overall perceptions. Inclusion criteria for participation was women, ages 35 and over, and living in Alberta. Recruitment was done from October to December 2020 via social media platforms (Facebook, Instagram, and Twitter) using post-sharing and targeted-ad campaigns. The survey link was publicly available and screening questions identified eligible participants who then completed the survey in English-only. Descriptive statistics, between-group comparative analysis, and logistic regression analysis were used to analyze the quantitative data collected.

Results: Of the 1,761 responses collected, 1,485 were included for analysis. Respondents' median age was 49 years (IQR=43.0-55.0), were predominantly white (93%), and 8% were current tobacco smokers, while 35% were past smokers. Women were categorized into menopause stages: 18% pre-menopause, 33% perimenopause, and 35% post-menopause. Overall, 13% had a hysterectomy and 4% had a bilateral oophorectomy. Most reported menopause symptoms were sleep issues (65%), concentration difficulties (49%), and anxiety (49%). One-third of women (34%) indicated using cannabis within the last 30 days, and 65% indicated ever using cannabis. Of the 499 current cannabis users, 75% reported use for medical purposes, 43% used at least once daily, most common forms were edibles (52%) and oils (47%), and use rates were similar between menopause stages. Most common symptoms for current use were sleep issues (65%), anxiety (45%), muscle/joint achiness (33%), irritability (29%), and depression (25%). Three-quarters of current users found cannabis helpful for symptoms. Compared to current non-users, current users were more likely to report sleep issues, mood issues (including depression, irritability, mood swings, and anxiety) difficulty concentrating, muscle/joint achiness, and painful intercourse. Common sources of cannabis information were internet searches (46%) or family/friends (34%). Poor health status and history of smoking were found to be significant predictors of current cannabis use.

Conclusion: Midlife women are using cannabis for symptoms which overlap with menopause. Women who currently use cannabis reported more symptoms than women who do not use cannabis. Information about cannabis was more frequently accessed through online searches and personal contacts rather than healthcare providers. Further research is required to assess the safety and efficacy of cannabis for menopausal symptoms and develop clinical resources for women.

This research has been facilitated by WCHRI through the generosity of the supporters of the Lois Hole Hospital for Women.

Participant #: 34
Presenter: Yasaman Bahojb Habibyan
Supervisor: Elahi, Shokrollah
Title: Deciphering how CD71+ erythroid cells influence the microbiome and enteric nervous system in newborns

Authors: Yasaman Bahojb Habibyan, Petya Koleva, Purvi Dhaliwal, Shokrollah Elahi

Theme: Children's health and well-being

Introduction: Mounting preclinical and clinical evidence strongly supports a crucial role for the gut microbiota in health. Dysbiosis of the microbiome is associated with a spectrum of disorders, including inflammatory bowel disease (IBD) and necrotizing enterocolitis. We have found that CD71+ erythroid cells (CECs) are abundant in the gut of newborns. The removal of CECs from the intestinal tissues by the anti-CD71 antibody disrupts immune homeostasis and results in inflammation. This suggests an essential role for CECs in the adaptation of newborns to colonization with microbial communities.
Additionally, we have observed that CECs secrete artemin, a neurotrophic factor. Artemin acts on neurons by binding to the tyrosine kinase membrane receptor (RET) and GDNF receptor-α 3 (GFRα3) complex. Notably, we have observed a lower frequency of CECs in the cord blood of C-Section compared to vaginally delivered twins. Similarly, preterm deliveries have a lower frequency of CECs in their cord blood. These observations may, in part, explain the underlying mechanisms associated with dysbiosis and other GI tract complications in these infants. Our objective is to explore the short and long-term effects of CECs on establishing the microbiome, whether the microbiome determines the generation of CECs, and the role of CEC-derived artemin on the development of the enteric nervous system (ENS).

Methods: CECs were depleted using the anti-CD71 antibody in Balb/c mice (3-6 days old); control mice were treated with the isotype control antibody. To examine the short-term effects of CECs on the microbiome, mice were sacrificed two days post-treatment; for long-term effects, the mice were sacrificed two weeks post weening. Bacterial genomic DNA was isolated for 16S rRNA gene amplicon sequencing. The small intestinal and colonic tissue were collected separately and subjected to RNA isolation. RNA samples were submitted for RNAseq analysis and qRT-PCR to evaluate the pattern of gene expression profile in the absence/presence of CECs in the gut. The 2-ΔΔCt method was used to calculate the relative fold gene expression of samples.

Results: At day 3, germ-free mice had significantly reduced levels of CECs in the small and large intestines when compared to the wild-type counterpart ($p < 0.005$). Moreover, there was a higher frequency of CECs in the gut of neonatal mice compared to adults ($p < 0.05$). Depletion of CECs resulted in a significant downregulation of SOX10, FOXP3, and PHOX2b, which are involved in the ENS development at day 4 and day 22 ($p < 0.05$). Interestingly, depletion of CECs at day 4 did not cause downregulation of RET, however, at day 22 RET expression was significantly downregulated ($p < 0.005$).

Conclusion: The frequency of CECs are elevated in the gut of neonatal mice. Furthermore, preliminary data suggests a role for CECs in relation to the proper development of the ENS through differential expression of transcriptional factors. We anticipate that these proposed studies provide a comprehensive understanding of the role of CECs in the health of the GI tract in the newborn. Despite the complexity of the cellular biology of the gut, our data will provide a novel role for CECs in the dialogue between the microbiota, immune system, and the ENS.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 106
Presenter: Emma Bedard
Supervisor: Yuksel, Nese
Title: Long-acting reversible contraception services by pharmacists and other healthcare professionals: a scoping review
Authors: Emma Bedard, Nicole Kremer, Janice Kung, Nese Yuksel

Theme: Lifelong women's health

Introduction: Long-acting reversible contraception (LARC), including intrauterine contraception (IUC), implants, and injections, is the most effective form of reversible contraception. Increasing access to and use of LARC is a strategy for reducing unintended pregnancies. Several studies have looked at ways to increase LARC use, but a review of the existing literature has not been published. Our objective is to describe LARC services that have been provided by healthcare professionals including pharmacists, physicians, nurses, and other providers.
Methods: We conducted a scoping review based on the Joanna Briggs Institute Manual for Evidence Synthesis and the PRISMA Extension for Scoping Reviews. A comprehensive search was run on MEDLINE, Embase, CINAHL, Cochrane Library, and Google Scholar databases (from inception to January 6, 2021). Search terms encompassed LARC methods, provider types, and programs or services. Bibliographies of included studies and excluded review articles were hand-searched for relevant articles. Title, abstract and full text screening was completed by two reviewers using Covidence. Data extraction was completed by two reviewers using Microsoft Excel. Discrepancies were resolved by consensus or a third reviewer. Studies were included if they described healthcare professional-led LARC services for contraception and included an evaluation of the service, with or without patient outcomes.
Results: After removal of duplicates, a total of 1561 articles were found. After screening, 63 articles relating to 59 studies were eligible for inclusion. Articles were primarily experimental design (78%) and took place in a community setting (71%). Overall, 41% of articles looked at IUC and implants, 32% at IUC only, 19% at injectable contraception, 5% at only implants, and 3% at all LARC methods. Provider types included physicians, nurses, nurse practitioners, midwives, pharmacists, community health workers, and others. A multidisciplinary team approach was utilized in 33 articles (52%). The most common interventions were provider education or training (53 articles), LARC provision or placement (45 articles), and patient counselling (46 articles). Other interventions included patient screening, referrals, provider resources, demand creation, and program supervision. An increase in LARC use was reported in 34 articles. The effect size varied: one article reported increased LARC use from 0.1% to 0.4% and another article saw an increase from <1% to 37.4%. LARC use was reported in 15 articles ranging from 4.4% to 82% of participants without comparison to baseline usage rates. The interventions reported reaching users new to family planning in 13 articles.
Conclusions: This review identified many healthcare provider-led services for LARC therapy. While varied in their interventions, providers, and outcome measures, these services appear to increase rates of LARC use and reach women who are new to family planning methods. Future interventions around LARC therapy could adopt methods identified in this review to have impact at the patient-level.

This research has been facilitated by WCHRI through the generosity of the supporters of the Lois Hole Hospital for Women.

Participant #: 187
Presenter: James Benoit
Supervisor: Scott, Shannon
Title: Parent priorities and perceptions of impact: co-design of an mHealth app with parents for managing their child's illness.
Authors: James Benoit
Lisa Hartling
Carlos Jarquin
Shannon Scott

Theme: Children's health and well-being

Introduction
Patients under 18 have more than 150% as many avoidable visits to the emergency department as other age groups. Parent education has been identified as a key factor in decreasing avoidable hospital visits. While conventional means of parent education have been ineffective, apps have been shown to increase engagement, improve health outcomes, reduce health disparities, and reach diverse populations. In this study, we translated findings from two parent co-design studies, a survey and focus group, into app development priorities. Our aims were to (1) rxplore which app attributes influence parents' perceptions of an app's potential for real-world impact, and (2) identify app development priorities by understanding how different app attributes are valued and perceived by parents.

Methods
We carried out a survey and focus group. In the survey, parents (n=26) were asked to evaluate a commercially available app, Baby and Child First Aid, for parents managing children's illnesses and injuries, and answer a set of six questions to share their perceptions of the types of impact generated from using the app. In the focus group (n=9), parents were asked about their app use experiences and preferences. The survey and focus group were analyzed separately using thematic analyses. The results of these two analyses were compared, synthesized, and approached through the lens of the User Experience Honeycomb to suggest an initial set of prioritized app features for development.

Results
Parents perceived the app as most impactful to their knowledge of appropriately treating child illnesses (Mean 4.2/5, SD 1.1), and least impactful to attitudes (Mean 3.5/5, SD 1.12). Paired t-tests between parents' perceptions of impact type showed parents perceived the app to impact knowledge significantly more than it impacted awareness (P=0.031), help seeking (P=0.008), intention to change (P<0.001) and attitudes (P<0.001), but not significantly different from behaviour change (P=0.057). Qualitative thematic analysis of the survey identified six themes to increase perceived impact including concise and actionable information, knowledge quizzes, and app visibility. Five focus group themes examining parent priorities for app development identified that parents were embedded in communities of trust, suggested the app focus on actionable information, and highlighted widgets as a means of expediting care. Three development priorities were identified from examining these findings using the User Experience Honeycomb: usefulness, accessibility, and findability.

Conclusion
Parents prioritized app usefulness, accessibility, and findability. Usefulness involved presenting all KT tools as core elements of the app, and designing the app with features to make use of the KT tool information. Accessibility prioritized enabling parents to communicate symptoms without an underlying literacy requirement. Findability translated to a dissemination strategy that presented parents with the app in multiple contexts. Taken together, this app will help parents find the right health information, engage effectively with the KT tools, and take evidence-supported steps for their children's health.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 91
Presenter: Amrita Bhattacharjee
Supervisor: Turner, Justine M
Title: Clinical features of children with serology negative, biopsy positive celiac disease
Authors: Bhattacharjee A, Houlder K, Migliarese Isaac D, Turner J

Theme: Children's health and well-being

Introduction
Celiac Disease (CD) is a common autoimmune enteropathy, caused by gluten sensitivity in genetically susceptible individuals [1]. The North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) recommends serology followed by intestinal biopsy for the diagnosis of CD [2]. However, a subset of patients may have negative serology and can be diagnosed only by intestinal biopsy. The most common reasons for serological negative celiac disease (SNCD) include IgA deficiency or reduced-gluten intake [3]. The prevalence of SNCD in children is poorly described, given they are difficult to diagnose. Understanding clinical features of SNCD will enable better case detection and guide the timing of endoscopy, thereby preventing unnecessary morbidity.

Methods
A retrospective chart review of CD patients diagnosed at the Stollery Children's Hospital between January 2013 and December 2016 was undertaken. Patients with a positive biopsy and negative serology were identified, with careful exclusion of any alternate diagnosis and use of rigorous inclusion criteria, based on genetic and endoscopy findings. SNCD patients were compared to a random subset of sero-positive CD (SPCD) patients diagnosed within the same timeframe.

Results
Of 879 charts screened between January 2013 and December 2016, 27 patients were identified as SNCD and 417 patients as SPCD. Comparing SNCD and SPCD patients (n=86), there was no difference in mean age at diagnosis (8.6[5.1] vs 9.7[4.2]; p 0.27), gender (56% vs 60% female; p 0.70) or ethnic group (92% vs 87% Caucasian; p 0.098). There was also no significant difference in Marsh scores between the two study groups ($p = 0.22$). All of the SPCD patients were IgA sufficient, whereas 9/27 in the SNCD group were IgA insufficient ($p < 0.001$). 18/26 (69%) of the SNCD patients had a family history of CD, compared to the 75/86 (28%) of the SPCD group.

Conclusion
In our health region, 6% of children were identified as SNCD, which compares to reported rates in the adult population of 5%. Patients with SNCD appear very similar to those with SPCD. The main difference were higher frequency of IgA insufficiency or a family history of celiac disease, likely reflecting a case finding bias. Of note, IgA deficiency was not uniform amongst the SNCD group, and should therefore not be the only reason to consider SNCD. Our next step is to compare time to diagnosis and symptom presentations to determine if other clinical features can help better identify children with SNCD.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 105
Presenter: Harneet Bhullar
Supervisor: Alexander, R Todd
Title: Cldn2-Trpv6 Double Knockout Mice Provide Evidence of a Novel Vitamin- D Mediated Colonic Calcium Absorption Pathway
Authors: Harneet Bhullar and R. Todd Alexander

Theme: Lifelong women's health

Introduction: Vitamin D is a significant regulator of bone health, with both insufficient and too much contributing to diseases such as osteoporosis. The prevalence of osteoporosis increases with age and is more commonly seen in women. In 2015-2016, about 2.2 million Canadians were living with osteoporosis and 80% of those affected were women. Calcium and phosphate are the major components of bone and insufficient calcium absorption is the primary risk factor for developing osteoporosis. Dietary calcium is absorbed from the intestine via either a transcellular or a paracellular pathway, yet the interrelatedness of these pathways is unknown. The majority of absorption occurs via the paracellular pathway when dietary calcium is sufficient. In contrast, the transcellular pathway predominates when dietary calcium is low. The transcellular pathway relies on the calcium channel Trpv6, whereas paracellular movement is facilitated through claudin tight junction proteins, including claudin-2. Calcium is reabsorbed along the renal tubule primarily through claudin tight junction proteins including claudin-2.
Methods: To study the interaction between transcellular and paracellular intestinal calcium absorption we first confirmed the absence of a significant calcium phenotype in Trpv6 mutant mice harboring an inactive mutation (TRPV6D541A/D541A). This was done by performing metabolic cage studies and collection urine and fecal samples for ion chromatography analysis. We hypothesized this was due to significant paracellular intestinal calcium absorption. To test this hypothesis, we generated a Cldn-2/Trpv6 double knockout (dko) mouse.
Results: Metabolic cage studies of the dko mouse model revealed hypocalcaemia and significant hypercalciuria, compensated by increased intestinal calcium absorption in the dKO mice. In contrast to the single claudin-2 KO mice and Trpv6 mutant animals the dko mice had elevated 1,25 (OH)2 D3 and PTH. RT-qPCR of intestinal segments and whole kidney revealed increased calbindin-D9k expression in the proximal colon (but not duodenum) and calbindin-D28k in the kidneys.
Conclusion: Together these results infer a vitamin D sensitive transcellular calcium absorption pathway in the proximal colon, the identity of which remains to be determined. Ultimately, delineation of this novel pathway will provide much needed insight into how intestinal calcium absorption occurs, a prerequisite to improved treatment of women with osteoporosis.

This research has been facilitated by WCHRI through the generosity of the supporters of the Lois Hole Hospital for Women.

Participant #: 184
Presenter: Nadia Browne
Supervisor: Ball, Geoff DC
Title: Using readiness to change rulers to assess motivation to change healthy lifestyle behaviours in pediatric obesity management: An environmental scan
Authors: Sela Scott, Marcus O'Neill, Nadia Browne, Geoff D.C. Ball

Theme: Children's health and well-being

Introduction: Motivation is an important component of behaviour change, but it can be difficult to quantify. The Readiness to Change Ruler is a simple tool that can be used to assess the motivation to change behaviour by visually having individuals rank, often using a scale of 0 to 10, their motivation to change their behaviour. The objectives of this study were to: 1) conduct an environmental scan of the literature to determine how and for which behaviours Readiness to Change Rulers have been used to assess motivation to change in managing pediatric obesity and 2) determine if the psychometric properties (e.g., validity, reliability) of Readiness to Change Rulers were measured in these studies.

Methods: Research activities occurred from June to September, 2021. Multiple databases, including PubMed, Google Scholar, and the UAlberta Library were searched. Keywords used in our search included 'readiness to change', 'motivation to change', 'readiness', 'motivation', 'ruler', 'ladder', 'overweight', 'obesity', 'child' and 'pediatric'. Search terms were derived from a scoping review we completed recently on motivation and managing pediatric obesity. No limitations on study type or publication date were applied.

Results: Upon screening >2,000 articles, our environmental scan revealed 4 independent articles that applied Readiness to Change Rulers in managing pediatric obesity. All articles were published between 2009 and 2020. Research occurred in a variety of clinical and community settings, with most (n=3) studies completed in the US. Readiness to Change Rulers were used in the context of several lifestyle behaviours, including diet (n=4 articles), physical activity (n=3 articles), and sedentary activity (n=2 articles). Psychometric properties of the Readiness to Change Rulers were not reported in any of the articles.

Conclusions: Our environmental scan showed that Readiness to Change Rulers have been used infrequently in pediatric obesity research. The lack of published data on the psychometric properties of Readiness to Change Rulers highlights an important evidence gap that future research should address.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 98
Presenter: Silvia Cardani
Supervisor: Pagliardini, Silvia
Title: Etonogestrel, a potent progestin drug, alters gene and protein expression in the solitary tract nucleus of female rats
Authors: Silvia Cardani, Tara A. Janes, Roberta Benfante, Diego Fornasari, Silvia Pagliardini

Theme: Children's health and well-being

Introduction: Phox2b is a transcription factor essential for the development of the Autonomic Nervous System (ANS). Heterozygous mutations in the coding region of Phox2b gene are responsible for Congenital Central Hypoventilation Syndrome (CCHS), a rare neurological disorder characterized by inadequate respiratory response to hypercapnia and hypoxia and life-threatening hypoventilation during sleep, that is present since birth. Although no pharmacological intervention is currently available for treating the disease or its symptoms, it has been shown that hormonal treatment (progestin drug) may provide partial recovery of chemoreflex impairment in CCHS patients, opening the possibility for a relief of the respiratory symptoms and improved survival. Moreover, progesterone and its progestin analogues are powerful respiratory stimulants that may be useful for treating adult sleep apneas, and apneas in pre-term neonates.
Our previous in vitro data in cell lines showed a direct molecular link between PHOX2B expression and progestins. However, the exact mechanism through which these drugs ameliorate respiratory symptoms in vivo remains unknown. In this study we investigated the effects of a potent progestin, Etonogestrel (ETO) in adult female rats to better understand its mechanism of action.
Materials and methods: We treated rats with ETO for 4 weeks and assessed respiratory function with whole body plethysmography. We also used complementary approaches of RT-PCR, western blot immunofluorescence and RNAScope to determine changes in gene and protein expression driven by ETO in different brain regions important for respiratory control.
Results: ETO treatment has modest effects on baseline breathing and chemoreflex responses in healthy female rats. Nonetheless, qRT-PCR and WB analyses of ETO-treated brain tissue show a reduced mRNA and protein expression of Phox2b and its target genes Phox2a, Th and DBH selectively in the area of the dorsal medulla, comprising of the dorsal motor nucleus of the vagus (X) and the solitary tract nucleus (NTS), a brain region crucial for breathing control, while other brain areas that express both progesterone receptor and Phox2b were not affected.
Conclusions: Our data suggest that NTS, a key integrative area for chemoreception, rich in both progesterone receptors and Phox2b, is a good candidate for ETO-induced respiratory modulation.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 81
Presenter: Palehswan Chitrakar
Supervisor: Davidge, Sandra
Title: Advanced maternal age in rats impairs main uterine artery structural adaptations in pregnancy
Authors: Palehswan Chitrakar, Amy L Wooldridge, Mazhar Pasha, Raven Kirschenman, Anita Quon, Floor Spaans, Tamara Sáez, Christy-Lynn M Cooke, Sandra T Davidge

Theme: Pregnancy and developmental trajectories

Introduction: An increasing number of pregnancies occur at an advanced maternal age (≥ 35 years), which is associated with pregnancy complications. While the causes of these complications are largely unknown, impaired pregnancy adaptations may contribute to the poorer outcomes seen in aged mothers. Specifically, uterine artery adaptations during pregnancy are essential to accommodate a large blood volume to the fetoplacental unit. Previously, we showed that main uterine artery compliance increases with pregnancy in young rats, but to a lesser extent in aged rats. However, the mechanisms are unknown. Structural proteins in the vascular wall, such as elastin and collagen, are associated with vessel compliance, and expression of these proteins changes during pregnancy to facilitate uterine artery remodeling. For instance, a lower collagen to elastin ratio indicates an increase in vessel compliance. Therefore, we hypothesize that advanced maternal age impairs uterine artery structural remodelling such that the collagen to elastin ratio reduction during pregnancy is less in aged compared to young dams.

Methods: Pregnant young (~4 months) and aged (~9.5 months; ~35 years in humans) Sprague-Dawley rats were studied on gestational day 20 of 22 and compared to age-matched non-pregnant rats (n=3 per group). Rats were euthanized, and main uterine arteries were isolated, frozen in Optimal Cutting Temperature (OCT) compound and sectioned at 8 µm. Collagen and elastin were visualized by Masson's Trichrome and Verhoff's stains, respectively, and imaged by light microscopy. Immunofluorescence staining was performed for collagen I and collagen III and imaged by fluorescence microscopy. Image data (mean ± SEM) were acquired using ImageJ software and analyzed by two-way ANOVA with Sidak's post hoc comparisons using GraphPad Prism software. $p<0.05$ was considered significant.

Results: No differences in the percent positive area of collagen or elastin were found in uterine arteries between the groups. However, the collagen to elastin ratio was reduced in arteries from young pregnant rats compared to young non-pregnant rats (young non-pregnant 1.97±0.23 vs. young pregnant 0.97±0.17; $p=0.0107$). Moreover, the same pregnancy-induced change was not found in arteries from aged rats, as their collagen to elastin ratios were similar to aged non-pregnant rats, and to young pregnant rats. Expression of collagen I and III in the uterine arteries did not differ between the groups.

Conclusion: In support of our hypothesis, the decrease in the collagen to elastin ratio with pregnancy in the young, but not the aged rats, indicates an impaired pregnancy adaptation in the uterine arteries. This may explain the aged-related differences in vessel compliance. Thus, impaired structural arterial wall remodelling may contribute to the increased complications associated with aged pregnancies in humans. Future research should study proteins in the molecular pathways related to collagen and elastin levels to help develop new therapeutics to prevent pregnancy complications in aged mothers.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 209
Presenter: Thomas Corsiatto
Supervisor: Tyrrell, Gregory
Title: Epidemiological characterization of the neonatal pathogen group B Streptococcus in Alberta, Canada
Authors: Thomas Corsiatto, Angela Ma, L. Alexa Thompson, Donna Hurteau, and Gregory J. Tyrrell

Theme: Children's health and well-being

Introduction:
Group B Streptococcus (GBS) is a leading cause of invasive neonatal disease. Neonatal acquisition of GBS is primarily a result of vertical transmission from mothers colonized with GBS in the gastrointestinal or urinogenital tracts to neonates during pregnancy or birth. GBS related disease in neonates is generally classified as either being early onset disease (EOD) that occurs within the first 7 days after birth or late onset disease (LOD) arising between 8 to 90 days later after birth. Severe disease in neonates such as pneumonia, sepsis, and meningitis can result due to GBS infection. GBS possess an exterior capsular polysaccharide (CPS) that has traditionally been used to classify GBS into 10 different serotypes which is important as virulence and pathogenesis of GBS has been associated with certain CPS types. Epidemiological surveillance of GBS is an important initiative in order to determine cumulative incidence, antimicrobial resistance rates, and enhance maternal and neonatal disease prevention.

Methods:
This study presents an update on the epidemiology of invasive GBS in Alberta, Canada from 2014 to 2020 in comparison to a previous survey from 2003-2013. 1556 invasive GBS isolates were submitted to the Alberta Public Health Laboratory for capsular polysaccharide (CPS) typing and antimicrobial susceptibility testing using disk diffusion from 2014 to 2020. The incidences of EOD and LOD in the province were also tabulated over this time.

Results:
The percent distribution of CPS types in Alberta were CPS types III (23.6%), Ia (16.0%), Ib (14.8%), II (13.3%), V (12.7%), IV (12.5%), and VI (2.38%) with less than 1% of CPS types being VII, VIII, and IX. Cumulative incidences of invasive GBS cases per 100,000 population and LOD per 1000 live births increased from 4.43 to 5.36 and 0.38 to 0.41, respectively. However, the incidence of EOD decreased during the 7-year period from 0.2 to 0.07. All GBS isolates were found to be susceptible to vancomycin and penicillin. Conversely, erythromycin nonsusceptibility significantly increased from 36.9% to 50.8%. Clindamycin nonsusceptibility also significantly increased from 21.0% to 45.8% over time from 2014 to 2020.

Conclusion:
Compared to data from 2003-2013, the overall rates of invasive GBS disease from 2014 to 2020 have increased along with antimicrobial resistance. In addition, the prevalence of CPS types have varied as well over this time period. The significant decrease in the incidence of EOD is suggestive of successful intrapartum antibiotic chemoprophylaxis treatment programs. However, the increase in LOD is of noteworthy concern in the province.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 202
Presenter: Chentel Cunningham
Supervisor: Scott, Shannon
Title: Understanding What Web-based Knowledge Translation Tools Exist for Parents Who have a Child with Heart Failure: An Environmental Scan
Authors: Chentel Cunningham, MN PhD(c) NP; Hyelin Sung, BScN Student; James Benoit, PhD; Jennifer Conway, MD MSc; Shannon D. Scott, PhD RN

Theme: Children's health and well-being

Introduction: Childhood heart failure is a factor in many admissions each year. Successful discharge of a child with heart failure involves effective parents' education as they must become proficient in understanding a suite of new, complex knowledge. Inadequate knowledge acquisition by parents can result in numerous unnecessary accesses to the health care system, less parental participation in health care decision-making, along with overall heightened familial anxiety and potentially harm. Environmental scans (ES) are a newer methodology used to understand what tools or resources are available for specific contexts and audiences, while also evaluating their quality. Within the literature, no environmental scan exists in the pediatric heart failure context. To date, there is no documented understanding of what educational resources exist for parents who have a child with heart failure.

Methods: We conducted a comprehensive search of web-based educational tools about pediatric heart failure that targeted parent audiences. A two-step search process included searching the internet (Google) and application (app) stores (Apple and Google Play) in Canada and the US. Inclusion criteria were: 1) content that focused solely on childhood heart failure, 2) tools developed in either Canada or the USA, 3) information targeting parent/caregiver audiences, and 3) tools written in English language. Each relevant tool was appraised for health literacy using the Suitability of Assessment Measures. Key informants who developed each tool were invited for a semi-structured qualitative interview about the development process. Descriptive statistics included frequencies and means, and thematic analysis highlighted key themes.

Results: The search occurred in June 2020. No applications met inclusion criteria and 16 relevant tools were identified. One additional tool was included after consultation with a substantive expert. Our appraisal revealed that most tools scored in the adequate range (n=15) and the rest as non-suitable (n=2). The lowest scores were in the domains of graphics and highest scores in the domain of layout. Four organizations agreed to participate in interviews. Two major themes were identified.

Conclusion: Our ES has identified that there are currently no educational apps and a modest amount of education web-based tools for parents about their child's heart failure. While the majority of tools scored in the suitable range, improvements to graphics would help the overall delivery of content to parent audiences. Key informant interviews suggest a focused be made on better, more effective knowledge translation strategies and more in-depth knowledge.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 37
Presenter: Karina da Costa Silveira
Supervisor: Kannu, Peter
Title: Expanding clinical and molecular evidence of CYP26B1 involvement in retinoic acid catabolism defects
Authors: Karina da Costa Silveira, Inara Chacon Fonseca, Oswaldo Artigalas, Aline Iacovone, Eric Campos, Denise Pontes Cavalcanti, Peter Kannu

Theme: Pregnancy and developmental trajectories

Introduction: Homozygous missense variants in CYP26B1 have been described in very few individuals with skeletal abnormalities. The P450 cytochrome CYP26B1 metabolizes retinoic acid (RA) in the developing embryo to tightly control RA levels and locally regulates signaling. The CYP26B1 mutation phenotype ranges from a lethal presentation with skull defects, craniosynostosis, encephalocele, radiohumeral fusion, oligodactyly and a narrow thorax to a milder presentation with craniosynostosis, radiohumeral joint limitation, hearing loss and intellectual disability. Here, we describe three new patients and novel CYB26B1 variants in order to further clarify the spectrum of clinical disease caused by mutations in CYP26B1.
Methods: Molecular diagnosis was performed using whole exome sequencing (WES) and Sanger sequencing (SS) in 3 patients from two non-related families. A minigene assay was performed to access the pathogenicity in one of the mutations found.
Results: We identified two siblings affected by arachnodactyly, reduced radio-ulnar joint movement, conductive hearing loss and a mild to moderate learning disability. Craniosynostosis was not present in either sibling. In a second family, a lethal presentation in a female stillbirth with large hydrocephalus associated with generalized spina bifida occulta and poor mineralization of the whole skeleton and limb defects including oligodactyly was found. WES of family 1 revealed two novel CYP26B1 gene variants in trans: c.353C>T (p.Pro118Leu) and c.701G>A (p. Arg234Gln). In family 2, a novel homozygous point variant (c.1083C>A) was identified through SS of CYP26B1. In silico analysis suggested that the variant activates a cryptic splice site altering splicing. A minigene assay showed the variant leads to a deletion of part of exon 5 generating mRNA with a deletion of 21 amino acids (p.[Val361_Asp382del]).
Discussion: Here we demonstrate the utility of WES to establish the etiology of rare genetic disorders. A precise diagnosis is important to provide accurate reproductive risk counselling, guide management and inform prognosis. We hypothesize that variants found in family 1 generate a protein with reduced enzyme activity and the degree of retained enzymatic activity drives phenotypic severity. However, further studies are still necessary to prove the pathogenicity of these variants. The siblings affected by the CYP26B1 compound heterozygous variants represent a milder phenotype when compared to previously described cases. The deletion found in family 2 includes the ExxR motif and SRS-5 region, which are related to the stabilization of the meander loop and the maintenance of the CYP tertiary structure and the orientation of the substrate near the heme center, respectively. This deletion leads to the severest clinical presentation so far.
Conclusion: Taken together, we propose the phenotype associated with CYP26B1 varies depending on the type of variant, although all are inherited in a recessive matter. Furthermore, we describe here the first patient associated with a splicing variant resulting in a severe and lethal phenotype. With their description, we add to the genotypic and phenotypic spectrum seen with defects of the catabolism of RA.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 79
Presenter: Rana Dahlan
Supervisor: Sharifzadeh-Amin, Maryam
Title: Parental Acculturation and Oral Health of Children among Immigrants
Authors: Rana Dahlan, Humam Saltaji, Bukola Salami, Babak Bohlouli, Maryam Amin

Theme: Children's health and well-being

Introduction: Global immigration has been rapidly growing over the past few decades. Although Canada is one of the most welcoming immigrant destinations, immigrants still face numerous challenges that would consequently affect their general and oral health. Children of immigrants have higher rate of dental caries and lower rate of dental visits. Therefore, the aim of this study was to examine the impact of mother's acculturation level and strategies on their children's caries experience and oral health (OH) behaviors among immigrants.

Methods: Using a targeting nonprobability snowball sampling technique, first-generation immigrant parents and their children aged 2-12 years were recruited in this cross-sectional study. Multilingual community workers helped with recruitment of participants and data collection. Parents completed a validated questionnaire gathering information on socio-demographics, child's OH behaviors, and parental acculturation. Dental examinations determined child's caries experience using the total number of decayed (unrestored), missing due to caries, and filled (restored) (i.e., DMFT/dmft). Univariate and multivariate regression analyses were used.

Results: A total dyad of 336 parents and their children was included in the study. Children's mean (SD) age was 6.2 ± 2.8 years, 50.6% were female, and 60.7% were born in Canada. The mean (SD) age of mothers was 37 ± 6.3 years, and 67% had college or university education. The monthly household income of 42% of the participants was $2000-$4000 and over 90% were Canadian citizens or permanent residents with an average of 8 years of living in Canada. Length of residency (B= 0.103; 95% CI 0.064, 0.141) parental education (B= 1.691; 95% CI 1.228, 2.155), and household income (B= -0.959; 95% CI -1.566, -0.352) significantly predicted parental acculturation level. Parents with high Canadian culture knowledge reported higher frequency of children's toothbrushing (P-value =0.015). Parents of children who consumed sugar >1/day had higher mean score of acculturation to Canadian culture (P-value =0.016), English language proficiency (P-value =0.024), and Canadian food adoption (P-value =0.046). Parents of children who visited the dentist within the last 12 months had significantly higher assimilation and lower separation mean scores. Parents of children who visited the dentist because of dental problems had higher marginalization mean scores than those who went for check-ups (P-value=0.046). Parental acculturation was not significantly associated with their children's dmft/DMFT level.

Conclusions: Parental acculturation to Canadian culture improved toothbrushing, but not dietary habits of their children. Assimilated parents reported more and marginalized parents reported less favorable OH behaviors than integrated and separated parents. Parental acculturation level or strategy was not associated with children's caries experience.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 167
Presenter: Pieter de Vos
Supervisor: Gokiert, Rebecca J
Title: Journeys through Early Learning and Child Care - The Experiences of Cultural Minority Families in Edmonton
Authors: Pieter de Vos
Rebecca Gokiert
Yvonne Chiu
Heather Raymond

Theme: Children's health and well-being

INTRODUCTION: Early childhood experiences play a critical role in shaping learning and behaviour, and physical and mental health. A growth-promoting environment (i.e., adequate housing, nutrition, supportive caregiving, and exposure to appropriate social and emotional experiences) can lay the foundation for healthy functioning throughout the lifespan; conversely, an adverse environment can impede development (Center on the Developing Child at Harvard University, 2016).

In Edmonton, cultural minority women and families have experienced challenges in accessing affordable, appropriate, and culturally-relevant child care. This participatory action research project will explore the needs, aspirations, and experiences of cultural minority women and families with young children (0 to 5 years) in community-based early learning and child care in Edmonton.

Key research questions include: (1) What are the lived experiences of cultural minority women and families as they attempt to access and receive child care in Edmonton? (2) What assets, cultural resources, and ways of knowing can be harnessed to improve the system? (3) What opportunities exist to bridge the gap between cultural minorities and mainstream systems to shift approaches and practices? (4) What opportunities exist to catalyze positive change in child care policies and practices in order to better meet the needs of cultural minority families?

METHODS: The Journeys Project is a partnership with the Multicultural Health Brokers (MCHB), the Edmonton Council for Early Learning and Care (Council), and the Evaluation Capacity Network (ECN). The research project is intended to be collaborative, inquiry-based, and action-focused. The aim is to produce useful results to inform decision-making and collective action. A participatory research approach (Minkler & Wallerstein, 2008; Janzen et al., 2016) will be used throughout all phases of this project from the design to analysis, interpretation and mobilization of research findings.

The research will involve five main forms of engagement, data collection, analysis, and mobilization:
1) Semi-structured interviews with cultural minority families about their experiences with child care in Edmonton; 2) Focus groups on lived experience to develop rich case studies and to explore emerging themes; 3) Journey-mapping workshops to visualize the emotional, mental and social experiences of cultural minority families as they interact with child care services; 4) Joint meetings between the Multicultural Health Brokers and members of the Edmonton Council for Early Learning and Care (Council) to explore emerging themes and identify systemic factors. Follow-up conversations may also be arranged with Council members if further clarification or systems insight is needed; and 5) A Strategic Planning session with the Multicultural Health Brokers and with members of the Council to identify opportunities for collective action.

RESULTS: The research is underway. A collaborative governance model has been developed and community members are being trained to help facilitate the research process. Learning Teams have been established to support dialogue, sense-making and theme-weaving.

CONCLUSION: Research results and supporting resources will be shared in March 2022.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 157
Presenter: Olena Didenko
Supervisor: Pagliardini, Silvia
Title: Etonogestrel implantation as a potential cure of CCHS
Authors: Olena Didenko, Tara A Janes, Silvia Cardani, Silvia Pagliardini

Theme: Lifelong women's health

Introduction
Congenital central hypoventilation syndrome (CCHS) is a rare life-threatening genetic disorder, which affects respiration and develops as a result of PHOX2B gene mutation. This disorder is mainly characterized by impairment in autonomic control that causes reduced and shallow breathing, which is associated with inability to respond to changes in carbon dioxide levels in the blood. Moreover, PHOX2B gene mutation leads to the broad range of additional symptoms, due to its effect on nervous system development, such as dysregulation of heart rate, blood pressure, decreased perception of pain, low body temperature, and occasional episodes of heavy sweating. With the exception of supporting ventilation, no other treatment or intervention is available to CCHS patients. Previous work suggests that female sex hormones, such as estrogen and progesterone, modulated breathing in human and animal models. Interestingly, a serendipitous study indicates respiratory recovery in women affected by CCHS after the administration of desogestrel, a potent progestin drug. In order to have a better understanding of the mechanisms of action of desogestrel and its active metabolite, Etonogestrel (ETO) we tested respiratory function and gene and protein expression in female rats.

Methods
The experiment was conducted on adult female rats in the proestrus phase of the cycle. We measured breathing in freely-behaving rats using whole body plethysmography in different conditions: room air, hypercapnia (5% and 7% CO2) and hypoxia (10% O2). All breathing measurements were done before (baseline) and 28 days following subcutaneous etonogestrel implantation (250ug/ml plasma levels). Controls received sham surgery. Data were analyzed to determine tidal volume, breathing frequency, minute ventilation and oxygen consumption. Data on gene and protein expression are presented in a separate abstract (Cardani et al).

Results
We found no significant changes in tidal volume, breathing frequency and minute ventilation values in all three breathing air compositions in both ETO and SHAM groups. This indicates that ETO does not have an impact on breathing, which contradicts with its known respiratory stimuli properties. However, we have also detected a significant increase in Ve/VO2 and Ve/VCO2 in both room air and hypercapnia groups. Ve/VO2 was 28% and 29% higher in ETO treated rats compare to SHAMs in room air and 5%CO2 respectfully at 28 days. Also Ve/VCO2 was 44% higher in 7% CO2 in ETO treated rats compare to SHAMs at 28 days. This could indicate that ETO can cause hyperventilation by influencing general metabolism. We observed no such effect in hypoxia groups.

Conclusions
Our study suggests that ETO does not induce changes in minute ventilation and chemoreflex responses in healthy female rats but has an effect on body metabolism and O2 consumption.

This research has been facilitated by WCHRI through the generosity of the supporters of the Lois Hole Hospital for Women.

Participant #: 193
Presenter: Ivan Domingo
Supervisor: Bhavsar, Amit
Title: Platinum pays: why heavy metal may cause childhood cisplatin-induced hearing loss
Authors: Ivan K. Domingo, Asna Latif, Amit P. Bhavsar

Theme: Children's health and well-being

TITLE: Platinum pays: why heavy metal may cause childhood cisplatin-induced hearing loss
AUTHORS: Ivan K. Domingo, Asna Latif, Amit P. Bhavsar

INTRODUCTION

Cisplatin, a platinum-based chemotherapeutic, is one of the most effective agents available for use in children. It can increase 5-year survival rates for several different types of solid-state cancers. Unfortunately, cisplatin is also known to cause several adverse drug reactions known as cisplatin-induced toxicities (CITs). These include, but are not limited to, cisplatin-induced peripheral neurotoxicity (CIPN), cisplatin-induced nephrotoxicity (CIN), and cisplatin-induced ototoxicity (CIO). Metanalyses suggest that up to 84% of children treated with cisplatin develop CIN and 30-60% of cisplatin-treated children experience CIO and cisplatin-induced hearing loss, predisposing them to a number of physical and psychological comorbidities later down the line - drastically affecting their mental health and development and socioeconomic prospects in the process. The development of these CITs appears to depend on the activity and expression of Toll-like Receptor 4 (TLR4) though the underlying mechanisms linking them have yet to be elucidated. TLR4 canonically binds bacterial lipopolysaccharides (LPS) and mediates inflammation in response, but it has also been found to mediate hypersensitivity reactions to Group 9 and 10 metal ions, like nickel. Given cisplatin has a platinum core and platinum is a Group 10 metal, we at the Bhavsar Lab endeavored to find out how exactly cisplatin may be interacting with TLR4.

METHODS

To determine if cisplatin was capable of activating TLR4 and triggering an immune response, we treated human embryonic kidney (HEK293) cell cultures equipped with human TLR4 (hTLR4) and its co-receptor, MD2, with either no agonist, LPS, nickel, platinum (II), platinum (IV), or cisplatin, for 48HRs. We measured pro-inflammatory cytokine secretion as an indicator of inflammatory responses overall. Soluble forms of hTLR4 (s-hTLR4) were used in similar experiments to determine whether hTLR4 could compete for agonist bindings and protect against the induction of pro-inflammatory responses. HEK293 cells, without hTLR4/MD2, were also used; we introduced mutated forms of hTLR4 deprived of known metal-binding amino acid residues, prior to being treated as above. Last but not least, we used microscale thermophoresis to determine if TLR4 could bind cisplatin directly and completely independent of other factors. Soluble hTLR4 proteins were mixed with different concentrations of the aforementioned agonists and binding events were monitored based on fluctuations in heat-induced changes to localized fluorescence.

RESULTS

TLR4 triggered pro-inflammatory cytokine secretion in response to platinum ions and cisplatin reliant on established metal-binding residues. Preliminary thermophoresis data and s-hTLR4 experiments both support that TLR4 can bind cisplatin directly.

CONCLUSION

Pediatric cisplatin-induced hearing loss, and other CITs, may be due to a TLR4-mediated allergic reaction to heavy metal(s).

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 116
Presenter: Andrea Eaton
Supervisor: Ball, Geoff DC
Title: Priority topics for child and family health research according to parents and healthcare providers.
Authors: Eaton A, Dyson M, Gokiert R, Rajani H, O'Neill M, Maguire J, Birken C, Ladha T, Zhang M, Ball GDC

Theme: Children's health and well-being

Introduction. A key part of patient-oriented research includes prioritizing research questions identified by stakeholders. Research focusing on stakeholder-identified priorities improves healthcare engagement, health research engagement, and patient health outcomes. Our objective was to identify and prioritize unanswered research questions that stakeholders (parents/caregivers and HCPs) have regarding child and family health.

Methods. Partnering with stakeholders, we have engaged parents/caregivers and pediatric HCPs at the Northeast Community Health Centre (NECHC; Edmonton, AB). Together, we will determine which research questions are the most relevant and meaningful for child and family health research. Our study activities began in July 2019, concluding with a final workshop in October 2021. Using the James Lind Alliance (JLA) priority setting methodology, we are identifying the 'top ten' unanswered research questions in child and family health. First, we established a steering committee that included parents (n=5) & HCPs (n=6) to guide and inform all study processes. Second, parents (n=100) and HCPs (n=25) from the NECHC completed surveys to share their unanswered questions regarding child and family health. Third, questions were collated and subsequently prioritized by parents (n=100) and HCPs (n=25) using a second survey. Finally, questions that were prioritized by >50% of survey respondents moved forward to a mediated workshop for our steering committee and stakeholders to discuss and finalize the 'top ten' list.

Results. Data from our initial survey included 1,265 unique submissions from 125 stakeholders. Submissions were reviewed for redundancies and organized to create a list of 389 unique questions related to child and family health. Comparing these questions with high-quality, evidence-based sources (e.g., Canadian Paediatric Society), 108 unique questions remained unanswered, which were then rank-ordered by stakeholders. In this ranking process, twenty-six questions were selected by >50% of respondents. These questions moved forward to the mediated workshop for stakeholders to review and finalize the 'top ten' list of unanswered research questions. Mental health and screen time emerged as the most prominent themes of the highest ranked questions. Priority questions also covered diverse topics, including behavioural development, COVID-19, emotional regulation, social development, and behaviour management.

Conclusion & Future Directions. Parents and HCPs at the NECHC reported a variety of unanswered questions. The 'top ten' list of unanswered research questions for child and family health will be finalized in October 2021. Our final list of questions will be shared widely with stakeholders and researchers to inform and support future research activities, locally at the NECHC, provincially and nationally.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 93
Presenter: Seham Elmrayed
Supervisor: Kumar, Manoj
Title: Are small-for-gestational age preterm infants at increased risk of high blood pressure? A systematic review and meta-analysis.
Authors: Seham Elmrayed, Manoj Kumar, Suzanne C. Tough, Fatima Sabet, Michael Kramer, Maria-Beatriz Ospina, Diane Lorenzetti, Niels Rochow, Ian Griffin, Thibault Senterre, Belal Alshaikh, Sheila McDonald W, Tanis R Fenton.

Theme: Pregnancy and developmental trajectories

Introduction:
Neonatal healthcare providers are concerned whether they must make a trade-off between supporting growth of smaller infants in the NICUs and their long-term cardiovascular outcomes. In the Barker hypothesis, individuals born small-for-gestational age (SGA) are considered at increased risk for higher blood pressure (HBP) at older ages. A common approach used in developmental epidemiology evaluating associations between birth weight and later HBP is to adjust for body size at later age and then identify risk factors. We examined the evidence on the effects of adjusting for potential baseline confounders and of over-adjusting for later body size in the analysis of SGA preterm infants' risk for higher systolic BP (SBP).

Methods:
This systematic review was conducted in accordance with a pre-specified PROSPERO protocol (CRD42020162353) using the PRISMA guidelines. We searched MEDLINE, CINAHL and EMBASE databases (up to February 2021) and reference lists of included articles. Risk of bias was assessed using the ROBINS-I tool. Studies were screened and assessed in duplicate by two independent reviewers.

Studies were categorized as crude analyses (no adjustment), adjusted (adjustment/restriction for potential baseline confounders including age and/or sex) and overadjusted (adjusted for later body size). Random effects models in RevMan were used to estimate weighted mean differences (WMD) of BP by birth weight group.

Results:
We identified 37 studies reporting birth weight and risk for later SBP in preterm populations, of which nine (24%) overadjusted for later size. 14 studies provided data for the meta-analyses, some providing data for several types of adjusted analyses. Most studies were of moderate risk of bias. Preterm infants born SGA did not have higher systolic blood pressure (SBP) than those preterm infants born who were not SGA: crude (WMD: 1.76 mmHg [95% CI: -7.53, 11.05], I2= 86%, 3 studies, n=177); adjusted (WMD: -0.72 mmHg [95% CI: -2.26, 0.81], I2=37%, 10 studies, n=1929); and overadjusted analysis for later body size (WMD: -0.75 mmHg [95% CI: -1.73, 0.23], I2=0%, 5 studies, n=1600). There were no significant differences in effect size estimates among these subgroups (p = 0.87, I2=0%).

Conclusions:
Contrary to the Barker hypothesis, our systematic review does not support the concept that SGA increases the risk for HBP in infants born preterm. A sizeable fraction of studies overadjusted for later body size. Although we did not observe an effect of overadjustment, studies that overadjust run a high risk of bias.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 55
Presenter: Yuliya Fakhr
Supervisor: Hemmings, Denise G
Title: Sphingosine Kinase 1 Activation Mediates Tumor Necrosis Factor-α Induced Preeclamptic-like Phenotype of the Placental Syncytium
Authors: Fakhr Y, Koshti S, Webster K, Hemmings DG

Theme: Pregnancy and developmental trajectories

Introduction: Preeclampsia (PE), an inflammatory pregnancy disorder, is linked to inadequate placental syncytial function, high syncytial shedding and release of pro-inflammatory cytokines which further exacerbate the PE condition. The syncytium is the site of maternofetal transfer and hormone production. In PE, elevated pro-inflammatory tumor necrosis factor-α (TNF-α) hinders syncytial formation. In other cell types, TNF-α exerts its effects by modulating sphingosine 1-phosphate (S1P) levels through activation of sphingosine kinase 1 (SK1), its main synthesizing enzyme. Elevated S1P hinders syncytialization. But, if this occurs downstream of TNF-α-signaling and via SK1 activation is unclear.
Hypothesis: Elevated TNF-α disrupts syncytial function, increases syncytial shedding and its release of pro-inflammatory cytokines by activating SK1 in placental explants.
Methods: Term placental explants were treated for 48 hrs beginning on day 4, the start of syncytial regeneration, with TNF-α (0,10 ng/mL) and/or SK1 activity inhibitor PF-543 (1 μM). Syncytial formation was measured with human placental lactogen and chorionic gonadotropin (CG) assays (n=6). Cell death and shedding were measured by release of lactate dehydrogenase (LDH) and placental alkaline phosphatase (PLAP) positive particles (n=5). Pro-inflammatory cytokines were measured with multiplex cytokine kits (42 cytokines, n=5). Analyses were by one-way or two-way ANOVAs.
Results: TNF-α decreased CG release (p=0.001) but inhibiting SK1 did not reverse this effect. TNF-α increased LDH release (p=0.002). Inhibiting the kinase with PF-543 in presence of TNF-α decreased LDH to untreated control levels (p=0.07) with a treatment interaction (p=0.006). Similarly, TNF-α increased shedding of PLAP-positive particles (p=0.03) and inhibiting SK1 blocked this effect with a treatment interaction (p=0.02). This suggests that SK1 activity, which elevates S1P, mediates TNF-α-induced cell death and syncytial shedding. TNF-α increased the release of 22 cytokines from placental explants, 20 of which were independent of SK1 activation. Inhibiting SK1 blocked the TNF-α-increased interferon-□ induced protein 10 and interferon-□ release (p=0.03, p=0.001) with a treatment interaction (p=0.03, p=0.06). Additionally, inhibiting SK1 on its own decreased TNF-α release from syncytium (p=0.002).
Conclusion: TNF-α hinders syncytial function, induces placental death and syncytial shedding, and increases pro-inflammatory cytokine release. TNF-α effects on syncytial hormone production are independent of SK1 activation. But, TNF-α effects on placental cell death and syncytial shedding are mediated by the kinase activation or its production of S1P. TNF-α induces placental release of pro-inflammatory cytokines, however, only interferon-□ induced protein 10 and interferon-g and are dependent on SK1 activation. Thus, SK1 only partially mediates the TNF-α-induced preeclamptic placental phenotype.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 128
Presenter: Brianna Fehr
Supervisor: Parent, Eric C
Title: Patient-reported Outcome Measures Used in the Conservative Care of Scoliosis: A scoping review
Authors: Kendra Gagne, Brianna Fehr, Matthew Vaclavik, Cody Bourgoin, Eric Parent*, Courtney Hebert, Megan Bouwmeester, Sarah Cheslock, Rebecca Collins, Stefan Potgieter, Mark Coles, Sanja Schreiber, Sabrina Donzelli, Camille Warner

Theme: Children's health and well-being,Lifelong women's health

Introduction: It is unclear which patient-reported outcome measures (PROMs) can capture the effect of conservative care of scoliosis. Our focus is on conservative care because most available tools aim to assess the effects of surgery. The Cobb angle is often the primary outcome used to monitor scoliosis but guidelines suggest monitoring outcomes important to patients. Prior to investigating PROM measurement properties, an inventory is needed. The purpose of this review was to inventory the PROMs used to assess conservative treatments for each scoliosis diagnoses targeted, which outcome domains were evaluated, and in which languages.
Methods: We searched Medline (OVID) with a strategy as per the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) guidelines and informed by proposals in the International prospective register of systematic reviews (PROSPERO). We included studies of patients diagnosed with adolescent idiopathic scoliosis (AIS), adult idiopathic scoliosis (adult IS), adult degenerative scoliosis (ADS), or adult spinal deformity (ASD), and that reported on PROMs. We excluded studies of patients aged <10 years old in >20% of the sample, which did not present quantitative data, or only reported on peri- or post-operative results. Sixteen reviewers screened titles and abstracts before reviewing full texts. We extracted the PROMs used, the outcome domain assessed, the population(s), and language(s) in which the PROM was used.
Results: Our search found 3738 studies. After removing 14 duplicates, we screened 3724 titles and abstracts, then, 900 relevant articles were screened in the full-text stage. Data extraction was done for 488 included studies.
A total of 145 PROMs were identified across 22 languages and 5 populations. The definitions of adult IS and ADS were often unclear, with many articles combining these diagnoses with others (eg. kyphosis) under the term ASD.
The most frequently used PROMs for AIS were the Scoliosis Research Society-22 (SRS-22, 22.5%), SRS-22 revised (SRS-22r, 6.9%), and the Short Form-36 (SF-36, 6.1%). For ADS, the Oswestry Disability Index (ODI, 37.2%), Visual Analogue Scale (VAS, 19.0%), and SF-36 (8.8%) were most often used. The PROMs most used for Adult IS were the ODI (31.5%), SRS-22 (16.7%), and the SF-12 (7.4%). The ODI (33.0%), SF-36 (14.8%), SRS-22 (13.5%), VAS (6.4%), and the SRS-22r (11.4%), were the most used PROMs for ASD.
The outcome domains assessed by the PROMs were health-related quality of life (22.8%), disability (20.7%), pain (17.2%), psychological (16.6%), perceived appearance (6.9%), physical activity, comorbidity, and sleep (2.1%), perceived change, satisfaction, fear avoidance, predicting adherence to brace-wear, and multiple domains (1.4%), fatigue, health status, dyspnea, and intelligence (0.7%).
The most common languages other than English were Chinese (6.6%), Japanese (5.3%), German (4.4%), Spanish (4.2%), Polish (3.8%), Turkish (3.7%), French (3.3%), Italian (2.9%), and Swedish (2.2%).
Conclusion: This inventory will assist in conducting a systematic review to determine the PROMs that demonstrate the best measurement properties in the nonoperative treatment of scoliosis. This review will help create a database of core outcomes.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 161
Presenter: Sabrina Fox
Supervisor: Waskiewicz, Andrew
Title: BMP3 is a novel regulator of ocular and craniofacial development
Authors: Sabrina C. Fox, Sonya A. Widen, Lisa B. Prichard, Pranhidi Baddam, Daniel Graf, Ordan J. Lehmann and Andrew J. Waskiewicz

Theme: Pregnancy and developmental trajectories

Introduction: The ocular fissure is a transient opening present in the ventral eye. Failure of ocular fissure closure results in coloboma, a congenital disorder characterized by gaps in ocular tissues. Coloboma affects approximately affects 2-19/100, 000 individuals and is a major cause of pediatric blindness. Coloboma is also frequently diagnosed alongside other congenital abnormalities, the most common being craniofacial defects. Previous work has identified the Transforming Growth Factor-Beta (TGF-β) and Bone Morphogenetic Protein (BMP) signalling pathways as major regulators of fissure closure, and sequencing of human patients with microphthalmia/coloboma revealed potentially deleterious variants in BMP3 (a known TGF-β ligand). Therefore, we hypothesize that BMP3 is an important regulator of ocular fissure closure.

Methods: CRISPR/Cas9 mutagenesis was used to create a frameshift mutation in zebrafish bmp3, and the presence of open optic fissure in these mutants was assessed using laminin antibody immunohistochemistry. In-situ hybridization was used to determine the spatial expression of bmp3. Phosphorylated Smad3 immunofluorescence was used to assess TGF-β signalling in the ventral eye. The pharmacological treatment Specific Inhibitor of Smad3 (SIS3) was used to inhibit TGF-β signalling, and treated embryos were scored for the presence of open fissures at 72 hpf and compared to control embryos. Neural crest cells were visualized in zebrafish using the sox10:GFP transgenic strain, which fluorescently label neural crest cells in embryonic zebrafish. Craniofacial development in adult and larval fish was assessed using micro-computed tomography (micro-CT) and Alcian blue staining, respectively.

Results: We have shown that bmp3 mutant zebrafish embryos have aberrant ocular fissure closure. We have also shown that bmp3 is expressed in the zebrafish head mesenchyme during early ocular development. Additionally, we have found that TGF-β signalling is active adjacent to the ocular fissure, and bmp3 mutant embryos are sensitized to a suboptimal dose of TGF-β inhibitor, suggesting that bmp3 signals through Smad3 phosphorylation. Interestingly, there is a population of neural crest cells adjacent to the ocular fissure that are responsive to TGF-□ signaling, and the number of neural crest cells in the ocular fissure is reduced in bmp3 mutants. Adult bmp3 mutants also have abnormal craniofacial anatomy. Analysis of larval cartilage suggests that these abnormalities likely arise via aberrant craniofacial development during embryogenesis, however the mechanism by which bmp3 facilitates this process is unknown.

Conclusion: These results demonstrate that Bmp3 is a novel regulator of optic fissure closure. Analysis of Smad3 phosphorylation and synergy with SIS3 support a novel mechanism whereby Bmp3 regulates migratory neural crest in the vicinity of the ocular fissure. In addition to ocular defects, we have also identified craniofacial defects in bmp3 mutant zebrafish, a feature commonly seen in other models of coloboma, further supporting a shared etiology between these two congenital abnormalities. This work will ultimately assist in the accurate diagnosis and counselling of pediatric patients with congenital ocular and craniofacial abnormalities.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 110
Presenter: Kendra Gagné
Supervisor: Parent, Eric C
Title: Immediate Effect of Daily Living Postures on Kyphosis and Lordosis Measurements from 3D Ultrasound Images in Adolescent Idiopathic Scoliosis
Authors: Gagne, Kendra; Fehr, Brianna; Parent Eric C.; Warner, Camille; Hebert, Courtney; TraInberg, Kennedy; Rosenberger, Jade A.; Eberhardt, Jacqueline; Shearer, Kathleen; Lou, Edmond

Theme: Children's health and well-being

Introduction: Adolescents with Idiopathic Scoliosis (AIS) spend most of their day performing activities of daily living (ADLs). Many with AIS present with hypokyphosis, which is associated with decreased sagittal balance. A relationship exists between impaired sagittal balance and quality of life. Spinal alignment can be quantified using non-invasive 3D Ultrasound (3DUS) imaging to provide posture recommendations that encourage balanced spinal alignment while limiting hypo- or hyper-kyphosis and lordosis. Our aim was to compare the immediate effect of 14 ADL positions on kyphosis and lordosis measurements in AIS.

Methods: Consecutive volunteers were recruited at the Scoliosis Clinic in Edmonton with Cobb angles of 10-45°, aged 10-18, and with right thoracic, left lumbar double curves. Participants were scanned in 14 postures via 3DUS: standing (STD), model, sitting [natural (NatSit), cross-legged (SitCross), lotus, leaning forward and sideways on a desk (SitLean)], and wearing a backpack (Bag) and shoulder bag. Right (R) and left (L) positions were used when applicable. An evaluator used custom software digitizing the centre of the laminae to measure kyphosis and lordosis angles. Repeated measures ANOVAs with least significant difference post-hoc tests compared positions.

Results: The 31 females were 14.3±2.2 years old, 160.4±10.0cm tall and weighed 54.1±12.5kg. Their standing thoracic, lumbar, kyphosis and lordosis curve angles were 28.3±10.3°, 27.1±9.4°, 21.7±11.8°, and 26.1±14.3° respectively.

Compared to standing: ModelR, ModelL, and BagR positions significantly increased lordosis. All sitting positions significantly decreased kyphosis and lordosis angles. All other positions had no significant effect on kyphosis or lordosis. BagR produced the highest kyphosis angle overall, and SitLeanL produced the lowest kyphosis (22.0±11.9°, 12.8±9.6° respectively). ModelL produced the highest lordosis angle, and LotusR produced the lowest lordosis (35.3±15.5°, -6.9±20.2°, respectively).

Comparing sitting positions: There were no differences in kyphosis angles among sitting positions. LotusR and LotusL significantly decreased lordosis in comparison to NatSit. LotusR also significantly decreased lordosis compared to SitCrossR and SitCrossL. In contrast, SitLeanL significantly increased lordosis compared to LotusR and SitLean. All other sitting position comparisons were not significant. Overall, NatSit produced the highest kyphosis angle, and SitLeanL produced the lowest kyphosis (16.1±11.4°, 12.8±9.6° respectively). NatSit produced the highest lordosis angle and LotusR produced the lowest (4.5±20.5°, -6.9±20.2° respectively).

Comparing bag positions: There were no significant differences among bag positions for kyphosis or lordosis angles. Overall, BagR produced the highest kyphosis angle, BagL produced the lowest (22.0±11.9°, 20.2±14.6° respectively). BagR also produced the highest lordosis angle, Bag produced the lowest lordosis (33.2±15.5°, 29.8±19.9° respectively).

Conclusion: The present study offers more support for recommending the ModelL, the NatSit, and the backpack bag positions, which did not worsen the hypokyphosis characteristics of AIS. Our previous findings had showed that these positions improved curve angle and vertebral twist.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 162
Presenter: Juan Garcia Rivas
Supervisor: Clugston, Robin
Title: The effect of retinoic acid signaling inhibition by teratogen administration in the developing diaphragm
Authors: Garcia Rivas, J.F. Rocke, A.W. Clugston, R.D.

Theme: Children's health and well-being,Pregnancy and developmental trajectories

Introduction: Congenital Diaphragmatic Hernia is a life-threatening condition with a high level of mortality that affects ~1 in 3,000 newborns. Depending on the complexity of the malformations, the diaphragmatic hernia can be accompanied by other abnormalities like lung hypoplasia, facial clefts, etc. In 2003, Greer et al. proposed the retinoid hypothesis, which states that the underlying cause of this defect was related to the retinoid signaling cascade. We hope to strengthen the retinoid hypothesis by demonstrating that different vitamin A concentrations in the diet of the dams will have an effect on the incidence of diaphragmatic defects in the offspring.

Methods: All studies were conducted in timed-pregnant BALB/c mice. Upon successful plug testing, female mice were given a vitamin A deficient diet (0 IU/g) or a diet with excess vitamin A (25 IU/g). At gestational day 8.5, mice were weighed to confirm pregnancy, and a combination of teratogens known to inhibit the retinoic acid signaling cascade was given to the dams by gavage in olive oil (Nitrofen [500 mg/kg body weight] and Bisdiamine [125 mg/kg body weight]). At gestational day 15.5, the mice were euthanized, and the fetuses were dissected. The diaphragm and other organs were analyzed qualitatively using stereomicroscopy.

Results: Preliminary data shows that fetuses from dams that were given a vitamin A deficient diet showed an increase in occurrence in diaphragmatic hernias, lung hypoplasia, facial clefts, among other abnormalities. In contrast, the fetuses from dams that were given diets with excess vitamin A had a lower incidence in the developmental defects described above as well as congenital diaphragmatic hernia.

Conclusion: Our findings further complement the retinoid hypothesis and the importance of proper vitamin A intake during pregnancy. Newborns from mothers with lower intake of vitamin A than the recommended might have a higher chance of having developmental defects, including Congenital Diaphragmatic Hernia. This understanding of the way that diaphragmatic defects form in newborns might provide more information into ways to prevent these abnormalities. As the rate of mortality is quite high, it is paramount that further insight is obtained to better understand the proper development of the diaphragm and the importance of vitamin A during fetal development.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 201
Presenter: Mansi Garg
Supervisor: Godbout, Roseline
Title: ATM activates DDX1 to protect the cells from oxidative stress
Authors: Mansi Garg and Roseline Godbout

Theme: Children's health and well-being

Introduction: Ataxia telangiectasia (A-T) is a group of inherited multisystem disorders that often become apparent during early childhood, usually before 5 years of age. The disease is characterized by oculocutaneous telangiectasia, uncoordinated body movements, cancer predisposition, immunodeficiency, and increased sensitivity to ionizing radiation. The disease is caused by mutation in the ATM gene (A-T mutated). ATM protects our cells from various stresses by assisting in DNA damage repair, releasing cytotoxic stress, gene regulation, and cell growth.
Earlier reports have shown that DEAD Box 1 (DDX1) is part of the MRN-ATM complex that plays a role in DNA double-strand break (DSB) repair. DDX1 is phosphorylated and recruited by ATM. DDX1 is an RNA helicase that is essential for early embryonic development and stress regulation. We are investigating the role of DDX1 and ATM in the cellular response to stress in A-T patients.
Methods: We used fibroblasts from healthy (GM38) and A-T patients (AT2BE and AT5BI). To determine the role of DDX1 and ATM in stress response, the control, DDX1 and/or ATM depleted cells were treated with 0.5 mM arsenite for 45 min. The cells were stained with DCF-DA or MitoSOX Red and analyzed by flow cytometry to determine the elevated levels of cellular and mitochondrial reactive oxygen species (ROS), respectively. For DDX1-RNA binding, the cells were UV-crosslinked and whole cell lysates were used to pull down RNA bound to DDX1 using anti-DDX1 antibody. The RNA was extracted, reverse transcribed and enrichment of target RNAs was evaluated by RT-qPCR.
Results: A-T cells had higher ROS levels than healthy fibroblasts. To determine the role of ATM in elevated ROS levels, we analyzed ATM-depleted cells for oxidative response and found that the depletion of ATM was linked to higher ROS levels. Moreover, depletion of DDX1 also resulted in high ROS levels leading to poor protection against oxidative stress. These results indicate a role for both ATM and DDX1 in protecting the cells from oxidative stress.
DDX1's role in stress recovery may be linked to its RNA binding property. We observed enrichment of 12 previously identified target RNAs in DDX1-immunoprecipitated fractions under stress conditions. Interestingly, when A-T fibroblasts were exposed to arsenite-induced stress, there was a decrease in the RNAs bound to DDX1, suggesting that loss of ATM affects the RNA binding properties of DDX1.
Conclusions: These results provide mechanistic insight into the role of ATM and DDX1 in the stress recovery pathway in A-T patients, and suggest that DDX1 plays an important role in stress regulation which may be affected by its interaction with ATM. We propose that the effect that ATM has on DDX1's role in stress resolution is a contributing factor to neurodegeneration in A-T patients.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 170
Presenter: Lexis Garneau
Supervisor: Harvey, Gillian
Title: Co-design for complex health communications: The importance of including intersectional analysis
Authors: Lexis R. Galarneau, Kelsey Speed, Elaine Hyshka, Susan Sommerfeldt, Lianne M. Lefsrud, Aidan Rowe, Gillian Harvey

Theme: Lifelong women's health

Introduction: Naloxone is an opioid antagonist that can reverse an opioid poisoning, making it vital in responding to opioid emergencies. In Alberta, a naloxone kit contains portable vials of naloxone with needles or intranasal naloxone sprays. Naloxone kits are not always used correctly and in some cases, though available, they are not used at all. Research on emergency responses typically focuses on men. To address this research gap, we aim to describe how information design can be used to help women better understand opioid poisonings and response.
Methods: Using a co-design methodology, we are conducting semi-structured qualitative interviews over the phone with women in Edmonton (Alberta) who have witnessed a poisoning or have been in the presence of people who use drugs where a poisoning could occur. Questions pertain to participant knowledge of and experience with naloxone kits, barriers and improvements to poisoning responses, and gender specific differences in emergency responses. We audio recorded the approximately one-hour interviews, which are later transcribed verbatim with identifiable information removed. Using NVivo Qualitative Software, we are conducting thematic analysis; we are also quantifying numeric data where appropriate (e.g., number of participants who have seen a kit, who have used a kit). Once 20 interviews are completed, final coding will be performed to obtain thematic coverage.
Results: Since June 2021, we have conducted 16 interviews. Current participants have previously seen a naloxone kit and most report carrying one; however, the majority have not used naloxone. Participants have identified several priorities for naloxone training, namely, hands-on training by someone experienced in poisoning response. Naloxone kits have been deemed straightforward to use; however, suggested improvements include more detailed instructions, a colourful, less bulky kit, visible support numbers (e.g., mental health support after responding to a poisoning). Current concerns regarding naloxone kit use include worrying about administration (e.g., placing the needle in the wrong spot) and worrying if they would be in danger. Emerging gender specific themes include beliefs that women may be more willing to help in emergencies due to an instinct to care, as well as notions that men may more willing to help due to being calmer in emergency situations.
Conclusion: Our preliminary analysis suggests our results will be useful in understanding where and how women prefer to access opioid related information, challenges to timely poisoning responses, and how to support women to feel more comfortable responding to emergencies.

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Participant #: 45
Presenter: Trina Gartke
Supervisor: Wine, Eytan
Title: Short chain fatty acids modulate pathobiont invasion in an inflammatory bowel disease model
Authors: Trina Gartke, Dr. Michael Bording-Jorgensen, Dr. Heather Armstrong, Dr. Eytan Wine

Theme: Children's health and well-being

Introduction: An altered gut microbiome has been implicated in inflammatory bowel diseases (IBD), but mechanisms remain unknown. A potential consequence of the altered gut microbiome is that proper fermentation of fibers in the diet may be impaired, leading to a changed microenvironment, including changes in the breakdown products of fibers into short chain fatty acids (SCFAs). Most therapies suppress the immune system, which is especially problematic in children. Nutritional therapy is a unique therapy for children with IBD but is difficult to complete; therefore, further understanding of how diet interacts with the gut microbiome is critical. This study seeks to determine how SCFAs may influence bacterial invasion and contribute to IBD development and progression, which could lead to future avenues for dietary or therapeutic recommendations to treat IBD, especially in the pediatric population.
Methods: The research conducted was lab-based and hypothesis-driven. Select patient- and lab-derived gut bacteria were used to infect epithelial or macrophage cells in vitro, with cells exposed to SCFAs beforehand (to assess the impact of SCFAs on bacterial invasion). A gentamicin protection assay (kills only extracellular bacteria) was used to quantify the invasive bacteria. Different SCFA conditions (guided by published data) were compared to control using one-way ANOVA with multiple group comparisons.
Results: The SCFAs formate and propionate significantly decreased the rate of intracellular bacterial survival for both adherent-invasive Escherichia coli ($P < 0.0001$ and $P < 0.0005$ for formate and propionate, respectively) and commensal E. coli ($P < 0.0001$ for formate and propionate). There appeared to be no effect of SCFA exposure on epithelial intracellular bacterial invasion, regardless of SCFA type for either E. coli strain. Bacteroides fragilis cultured from an IBD patient only showed increased epithelial intracellular invasion for butyrate compared to control ($P < 0.05$). B. fragilis cultured from a non-IBD patient demonstrated increased epithelial intracellular invasion with all the SCFAs studied compared to control ($P < 0.05$). B. fragilis from an IBD patient showed increased invasiveness compared to a strain of the same bacterium from a non-IBD patient.
Conclusion: Measuring the invasion capacity of E. coli demonstrated a significant reduction in intracellular survival in macrophages after incubation with the SCFAs formate and propionate. Whether the modest decrease seen with formate and propionate is clinically or biologically relevant is uncertain, and requires further probing. SCFAs appear to increase the invasiveness of B. fragilis in a non-IBD environment compared to an IBD environment. However, invasiveness seems to be increased in an IBD setting compared to a non-IBD setting for B. fragilis, regardless of SCFAs. These observations suggest that SCFAs may have a role in influencing bacterial invasion of host cells, depending on the bacterial and host cell type, and that an inflamed gut environment also influences the invasiveness of bacteria. It is crucial to continue investigating the effects of SCFAs on the gut microbiome in an IBD setting to help guide appropriate dietary or therapeutic recommendations, to facilitate remission.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 180
Presenter: Jennifer Gelfand
Supervisor: Chandra, Sue
Title: Addressing gaps in perinatal resources for Newcomers and Refugees in Edmonton, Alberta
Authors: Jennifer Gelfand, Sarah Scratch, Uilst Bat-Erdene, Maria Ospina, Sue Chandra.

Theme: Pregnancy and developmental trajectories

Introduction: Immigrant and refugee women in Canada are known to have higher rates of adverse pregnancy outcomes compared to Canadian born women. These include: increased rates of low infant birth weight, surgical intervention at delivery and postpartum depression. This is partially due to barriers in accessing accurate healthcare resources. Multiple studies have demonstrated that language is a barrier to accessing perinatal healthcare for women who do not speak a country's native language. Childbirth related fear is also reported to be higher in foreign born women, with evidence that this group requires culturally sensitive and targeted support from healthcare providers.

Proposed research: The purpose of this qualitative project is to explore the experiences of immigrant and refugee women in accessing perinatal resources in Edmonton. This will inform the development of a perinatal website intended for Newcomers and Refugees to Alberta.

Methodology: Multicultural Healthcare Brokers (MCHB) is an organization that provides support to Newcomers in Edmonton. Surveys were administered to 33 brokers who work directly with immigrant communities. The inclusion criteria was women who work as MCHB with women of childbearing age in their communities. Surveys included open and closed ended questions, with the main question asking about resources, or lack thereof, for their pregnant clients. Main themes and sub themes were manually extracted by researchers, analyzed using NVivo software, and compared to increase validity of results.

Results: 33 MCHB filled out these surveys, representing 25 languages. 23 (69.7%) brokers reported they were somewhat, moderately or extremely concerned about their clients' knowledge about perinatal health. Language barrier was the major barrier to resources, with pregnancy being the main topic clients wished to talk about. Multilingual resources (13) and take home- resources, including text and video (9), were most reported as information MCHB wanted access to for their clients.

Implications: The implications of these findings are twofold. Firstly, it informs our website development. Due to language barriers being a major theme, translators were recruited to translate website information into Arabic, Spanish, Russian , Farsi, Punjabi and Somali . WCHB stated that videos were a preferred delivery method of information. Videos about perinatal health are being created and published onto the perinatal website.
Secondly, the results from the survey demonstrated that there are many barriers to perinatal healthcare for immigrant and refugee women in Edmonton that are not fully understood, nor have been addressed. In order to further inform practise and deepen our understanding of these barriers, focus groups with Ethiopian and Somali communities in Edmonton have been organized. This will further inform the creation of a culturally sensitive resource. Further, by examining single ethnic communities, it will allow researchers to understand what barriers are universal to immigrants, and what barriers are culture specific.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 69
Presenter: Saima Ghafoor
Supervisor: Kannu, Peter
Title: Genetic analysis of skeletal disorders in a Pakistani population through whole exome sequencing
Authors: Saima Ghafoor, Karina da Costa Silveira, Maleeha Azam, Peter Kannu

Theme: Children's health and well-being

Introduction
Genetic skeletal disorders are an inherited and heterogenous group of rare bone conditions with a prevalence rate of 1/5000 live births. In Pakistan, approximately 55% of genetic skeletal disorders are characterized by cases polydactyly, syndactyly, synpolydactyly, split hand and foot malformation. Over 19 different genetic skeletal disorders resulting from mutations in 43 genes have so far been reported in the Pakistani population.
Whole exome sequencing (WES) is technique used to test the protein coding regions (exons) of a gene to identify disease causing variants. The technique is very useful when an underlying genetic disorder is suspected, but the genetic cause cannot be narrowed down to a finite list of candidate genes. The aim of this study is to identify pathogenic variants that define the diagnosis and etiology of various types of skeletal disorders in the Pakistani population.
Methods
35 families with various skeletal disorders were recruited from different regions of Pakistan. The following data was collected: demographic data (age, sex, and ethnicity), clinical phenotype, age at diagnosis, radiological data, pedigree, and previous genetic tests. Blood samples affected and healthy individuals of the families were collected and DNA extracted by the phenol/chloroform extraction method and stored at -20ºC. Whole Exome Sequencing (WES) was performed (3 trios, 2 quad and 1 proband) at Macrogen Inc. - Korea (Library Truseq DNA library and TruSeq DNA Exome, Platform Novaseq). Sanger Sequencing was performed to confirm candidate gene variants and facilitate segregation analysis.
Results
So far, WES was performed in 6 selected families and a pathogenic homozygous mutation found in 1 consanguineous family (16.7%) with 3 siblings affected by a spondylar-epi-metaphyseal dysplasia. We identified a known pathogenic missense variant (c.697G>A, p.Asp233Asn) in the GALNS gene which causes MPS type IV. Sanger sequencing revealed the 2 other affected siblings were homozygous for this variant, while an unaffected sibling and the parents were carriers. We have not been able to determine a genetic cause in 3 families and remaining families are under analysis.
Conclusion
We have identified the genetic cause of unexplained short stature in a consanguineous Pakistani family. Unaffected siblings have a 2/3s chance of being a carrier and genetic testing can assist in precisely determining carrier status. MPS IV is an autosomal recessive condition and a couple who are carriers have a 25% chance of a pregnancy affected by MPS IV. Enzyme replacement treatment is now available for this condition, but the cost is prohibitive and treatment is not available to all affected individuals in the world.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 163
Presenter: Shrimanti Ghosh
Supervisor: Boulanger, Pierre
Title: Predicting Brachytherapy Tandem-Related Uterine Deformation in Locally Advanced Cervical Cancer using Deep Learning with Free Form Deformation
Authors: Shrimanti Ghosh, Kumaradevan Punithakumar, Geetha Menon, Fleur Huang, Pierre Boulanger

Theme: Lifelong women's health

Introduction:
To cure locally advanced cervical cancer (LACC), brachytherapy (BT) remains the gold standard for boosting to sufficiently high doses of radiotherapy. Selection of the most suitable BT applicator components (length, diameter, and angle) to insert for each patient relies on good clinical judgment, informed by educated predictions of complex interplay between pelvic anatomy and applicator geometry. With potentially large distortions caused by the presence of BT applicators, such speculations lack accuracy and can result in sub-optimal dosimetry. Our purpose is to develop a deep learning (DL)-powered predictive model for tandem-related uterine distortion to guide technical decisions in LACC BT procedures. No previous study has quantified the deformation between pre-and post-applicator insertion images acquired for cervical cancer BT.
Methods:
Eighty T2-weighted MR image pairs from LACC patients, taken before BT (pre-BT) and following tandem and ring insertion (at-BT), were used. The uterine surface, uterine cavity, vaginal canal, and external os were manually delineated on both image sets. At first, corresponding pre-BT and at-BT image pairs were rigidly aligned using bony anatomy with an intensity-based semi-automatic rigid registration method. A DL network was trained to automatically segment the uterus using convolutional neural networks with autoencoders on pre-BT images. A transfer learning approach using a pre-trained U-net then predicted the at-BT uterus shape and position from pre-BT MRI. Following this, a shape-based nonrigid registration/free form deformation method was used to handle complex and large deformations due to applicator insertion.
Results:
All methods were trained, validated, and tested using 70% (5600 images), 15% (1200 images), and 15% (1200 images), respectively. Images were rotated clockwise and anti-clockwise to generate additional training examples to train the DL models. For evaluation, we used Dice Coefficient (DC), and Hausdorff Distance (HD) between ground truth and the segmentation obtained using the DL methods. Higher DC and lower HD values correspond to better segmentation. In comparison to the ground truth, automatic uterus segmentation using DL from pre-BT images yielded an average DC and HD of 0.94 and 4.0 mm, respectively. Further, predicting the at-BT uterus shape and position using the pre-trained U-net resulted in a 0.88 DC and 5.8 mm HD. The presence of the uterine tandem was found to introduce a median point-to-point displacement of 25.0 [10.0 - 62.5] mm and 40.0 [12.0 -68.0] mm of the uterine surface and uterine cavity, respectively, from the pre-BT position.
Conclusion:
Predicting deformation from natural anatomy before BT to anatomy in presence of an applicator is challenging as the uterus and surrounding organs deform in a unique way relative to each other and for every patient. Our novel DL method can successfully predict tandem-deformed uterine shape and position from MR images taken prior to BT implant procedure. This holds the promise of better, faster, and more streamlined clinical/technical decision-making before BT applicator insertion and dose plan optimization, potentially enabling more consistent application of BT personalization for LACC and improved dosimetric outcomes.

This research has been facilitated by WCHRI through the generosity of the supporters of the Lois Hole Hospital for Women.

Participant #: 135
Presenter: Madison Godfrey
Supervisor: Dytoc, Marlene
Title: Identifying quality improvement opportunities in a vulvar dermatology clinic
Authors: Laura C Soong MD, Trang T Vu MD PhD, Pamela Mathura MBA, Madison Godfrey BSc, Marlene T Dytoc MD PhD FRCPC

Theme: Lifelong women's health

Introduction: Vulvar concerns are a common reason for women to visit a health care provider and for specialist care referral. Based on review of the literature, further research on how to optimize efficiency, patient centered care, and delivery of physician education in vulvar dermatology is needed. We aim to review our local vulvar dermatology clinic patient data to identify quality improvement opportunities to further meet the needs of our patients and referring physicians.
Methods: A retrospective chart review of 187 new consultations in the vulvar dermatology clinic from May 2019 to May 2020 was completed. Demographic, referral, and clinic visit information was gathered and analyzed.
Results: The gaps identified were that patients used self-remedies while awaiting appointment and could be treated by the referring physicians, considering wait time and travel distance to first appointment. Documentation of sexual function and quality of life was sparse. Further, referring physicians' clinical descriptions were often vague, which may impact referral triage.
Conclusions: We identified several quality improvement opportunities focusing on patient and physician education, use of telemedicine, and a focus on quality of life documentation. Next steps will involve further development, implementation, and evaluation of the identified interventions.

This research has been facilitated by WCHRI through the generosity of the supporters of the Lois Hole Hospital for Women.

Participant #: 166
Presenter: Kara Goodkey
Supervisor: Voronova, Anastassia
Title: Loss of an epigenetic regulator Ankrd11 in in neural stem cells results in abnormal brain development
Authors: Kara Goodkey, Yana Kibalnyk, Tim Footz, Anastassia Voronova

Theme: Children's health and well-being

INTRODUCTION: KBG syndrome is a rare neurodevelopmental genetic disorder that has been diagnosed in ~500 children worldwide. Patients with this disorder have mutations in the Ankrd11 (Ankyrin repeat domain 11) gene, which is a chromatin remodelling gene and thus plays a large role in global gene expression, as chromatin impacts the accessibility of genomic DNA. This causes a broad range of phenotypes in patients including aberrant brain development, global developmental delay, autism, and intellectual disability. Using a Yoda mouse model with a missense mutation in one copy of Ankrd11, our lab has shown that Ankrd11 regulates embryonic neural stem cell (NSC) proliferation and neurogenesis (formation of neurons). However, an appropriately functioning brain requires proper development of not only neurons, but also glial cells, such as astrocytes and oligodendrocytes. Oligodendrocytes are of particular importance as they form myelin (major white matter component) in the brain and are required for efficient neural communication and development. Oligodendrocytes and/or myelin are often aberrant in children with neurodevelopmental disorders. Moreover, oligodendrocytes can be targeted pharmacologically to restore proper cognition and behaviour in mouse models with neurodevelopmental disorders. Yet, the role of Ankrd11 in oligodendrogenesis (formation of oligodendrocytes) is not known.
METHODS: To answer this question, we developed a novel mouse model where Ankrd11 can be inducibly knocked out in NSCs (precursor to the oligodendrocyte lineage) via a Cre/Lox system (NestinCreERT2;Ankrd11fl/fl or Ankrd11nscKO). This mouse is superior to the Yoda mouse as it models a vast majority of loss-of-function mutations that occur in KBG syndrome patients. We induced Ankrd11 knockout at embryonic day (E) 14, a time point prior to the start of oligodendrogenesis, and analyzed brain development during embryogenesis and after birth.
RESULTS: First, we confirmed that NSCs isolated from Ankrd11nscKO E15 cortex display reduced proliferation, in agreement with results from the Yoda mice. Analysis of E18 Ankrd11nscKO cortex demonstrates an increase in the proliferation of oligodendrocyte precursor cells (OPCs), obligate progenitors of oligodendrocytes. Notably, these cellular changes occurred specifically in the rostral areas of the murine brain. Despite the induced increase in OPC proliferation, there was no increase in the total number of OPCs. Thus, we predict that the loss of Ankrd11 may increase OPC differentiation. Our initial in vitro experiments show NSCs isolated from Ankrd11nscKO show a significant increase in mature oligodendrocyte differentiation. We are currently verifying this effect in vivo. Furthermore, we found that the loss of Ankrd11 embryonically causes major structural changes to the brain in juvenile mice at postnatal (P) day 15.
CONCLUSIONS: Our results suggest that Ankrd11 plays a role in oligodendrocyte lineage cell formation. These results would help explain the mechanism of common symptoms and phenotypes in KBG patients and may provide novel therapies or cellular targets for pharmacological intervention for KBG syndrome and other similar neurodevelopmental disorders.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 178
Presenter: Sandra Gouda
Supervisor: Foulds, Jessica L
Title: Care and outcomes of children hospitalized with periorbital and orbital cellulitis.
Authors: Sandra Botros Gouda, MD
Jessica L. Foulds, MD

Theme: Children's health and well-being

INTRODUCTION
Periorbital and orbital cellulitis are bacterial infections which are clinically distinct but often treated together. Periorbital cellulitis is an infection of the tissues anterior to the orbital septum, caused by local spread; Orbital cellulitis is an infection of the tissues posterior to the orbital septum, usually as a complication of sinusitis. The Chandler scale classifies the severity of orbital cellulitis from I to V. Children represent a large burden of patients with orbital cellulitis, and up to 51% are admitted to hospital.

Prior studies on periorbital and orbital cellulitis have been single-centered, usually in academic tertiary care hospitals or large multi-site US studies. No prior study has evaluated the care and outcomes of Canadian children hospitalized with orbital cellulitis using data from multiple sites across multiple provinces.

We aim to describe the care and outcomes of Canadian children hospitalized with periorbital and orbital cellulitis. Specifically, we aim to: 1) describe diagnostic testing, treatment interventions and clinical outcomes of Canadian children hospitalized with periorbital and orbital cellulitis; 2) describe trends over time; 3) describe hospital-level variation; and 4) explore risk factors associated with surgical intervention and longer length of stay.

We present the preliminary data on the Edmonton cohort of patients as part of this multicentre study.

METHODS
Hospital health records were collected for all children 2 months to 18 years admitted to the Stollery Children's Hospital with Periorbital or Orbital cellulitis over a a 10-year time period (date of admission from 1st January 2009 to 31st December 2018, inclusive).
Local Edmonton data was extracted as one part of a multi-centre study which currently includes 10 sites across Canada.
Descriptive statistics were performed using SAS Ver 9.4.
Continuous variables were summarized using means, medians and interquartile ranges (IQRs) and categorical variables with frequencies and percentages.

RESULTS
167 patients were identified at our site, and 164 of those had complete charts available. 123 met inclusion criteria and were enrolled, and 41 were not enrolled.
81 patients (66%) were male, and 42 (34%) were female. 35% were diagnosed with periorbital cellulitis, while 65% were diagnosed with orbital cellulitis. Mean age on admission was 89 months (SD 57). There were 104 (84.6%) who received a CT scan during their admission. Of those who received CT scans, 24% were classified as Chandler I, 37.5% as Chandler II, 34.6% as Chandler III, and 3.8% as Chandler IV. Surgical intervention was needed for 30 patients (24.4%).

CONCLUSION
There is a lack of studies evaluating the care and outcomes of children in Canada hospitalized with periorbital and orbital cellulitis. We describe initial data including demographics and descriptive statistics on a local cohort of patients as part of a larger multi-centre retrospective study. Our local data show a high percentage of patients (84.6%) received CT scans despite low Chandler scores. We plan to perform further anaylsis for predictors of outcomes and variability across multiple study sites, and identify potential areas for focused clinical care optimization.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 90
Presenter: Katie Gourlay
Supervisor: Ali, Samina
Title: Quantifying the intensity of adverse events in children receiving ibuprofen and oxycodone following acute fracture

Authors: Katie Gourlay BSc, Rhonda J. Rosychuk PhD, Silvia Ortiz MSc, David W. Johnson MD, Aran Yukseloglu MD, Bruce Carleton MD, Sylvie Le May RN, PhD, Amy L. Drendel DO, MS, Samina Ali MD.

Theme: Children's health and well-being

Introduction: Treatment of pain is an essential component in optimizing an injured child's quality of life and experience. Ibuprofen and oxycodone are widely used for treating childhood fracture pain. While oxycodone is generally associated with increased frequency of adverse events (AEs) compared to ibuprofen, little is known on the comparative intensity of AEs associated with these medications.
Methods: This retrospective cohort study was conducted at the Stollery Children's Hospital emergency department. Patients aged 4 to 16 years diagnosed with a fracture in the emergency department who were prescribed either ibuprofen or oxycodone for pain management were recruited from 2010 to 2014. Demographic and clinical characteristics were collected from patients by trained research assistants using a structured chart review. Families were called for the first three days after discharge and asked to report the frequency and intensity of AEs, as well as report whether their child's ability to eat, sleep, play or attend school was impaired. Families were also asked to report their child's rated pain before and after analgesia using the Faces Pain Scale - Revised.
Results: A total of 240 children were included in this study (ibuprofen n=176, oxycodone n=59). Children using oxycodone were more likely to report any AE ($p<0.001$), nausea ($p<0.001$), vomiting ($p<0.001$), drowsiness ($p<0.001$), constipation ($p=0.003$), and dizziness ($p<0.001$), compared to those using ibuprofen. Using an 11-point rating scale, children receiving oxycodone reported more severe abdominal pain (oxycodone: mean 5.4 SD 3.1; ibuprofen mean 2.5 SD 1.4) on Day 1 ($p=0.02$) and worse constipation (oxycodone: mean 4.9 SD 2.1; ibuprofen mean 3.2 SD 2.2) over all three days ($p=0.04$). Children with upper limb fractures were more likely to experience impairment in playing (oxycodone 93.8%, ibuprofen 65.7%, $p<0.001$) and attending school (oxycodone 80.9%, ibuprofen 57.6%, $p=0.004$) when prescribed oxycodone, while children with lower limb fractures experienced similar impairment in function, regardless of medication prescribed.
Conclusion: Oxycodone is associated with more frequent AEs overall and higher intensity gastrointestinal AEs compared to ibuprofen. Lower limb fractures are distressing regardless of medication, while functionality with upper limb fractures appears worse in children prescribed oxycodone. Researchers should consider incorporating AE intensity into future studies to improve comparisons of analgesic medications. Clinicians should be aware of the differences in intensity and frequency of AE's when caring for children in pain.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 50
Presenter: Amber Hager
Supervisor: Mager, Diana
Title: Characterization of myopenia and skeletal muscle fiber types in children with end-stage liver disease at time of liver transplantation
Authors: Hager A, Dunichand-Hoedl A, Mazurak V, Dajani K, Dziwenkocox, C Gavreau C, Anderson B, Shapiro, J, Bigam D, Kneteman, NM, Noga M, Montano-Loza, Yap J, Gilmour SM, Mager DR

Theme: Children's health and well-being

Introduction: Myopenia, or low skeletal muscle mass (SMM) occurs in 30-40% of children awaiting liver transplantation (LTx) and is associated with poor outcomes post-LTx. Beyond SMM, muscle fiber size and type may also be affected. In humans, skeletal muscle fibers are characterized by myosin heavy isoforms (MyHC) and consist of both slow twitch (Type I) or fast twitch (Type IIa [oxidative], IIx/d [glycolytic]) fibers. Fiber subtypes are differentially sensitive to atrophy from a variety of physiologic and pathologically induced states. For example, Type I fibers are more sensitive to inactivity whereas Type II fibers are more vulnerable to chronic disease and aging. No information is currently available regarding skeletal muscle histology (muscle fiber type/size) associations with myopenia in children with end-stage liver disease (ESLD) undergoing liver transplantation. The study objective was to describe the differences in histological features of skeletal muscle in ESLD children with and without myopenia at time of liver transplantation (LTx).

Methods: Children were recruited from the Stollery Children's Hospital Pediatric LTx Clinics. SMM (cm2) was quantified at multiple muscle sites (psoas, paraspinal, abdominus, oblique) from slices obtained at the L3-vertebrae from abdominal imaging (MR/CT) using using Slice-o-matic® software. Skeletal muscle mass index (SMMi; cm2)/height (m)2) values were compared to age-sex matched healthy controls. Myopenia was defined as SMMi z-scores <-2. Rectus abdominus (<1 cm3) biopsies were collected at the LTx incision site. Muscle fiber tissues were demarcated using laminin and dystrophin immunofluorescence stains for quantification of muscle fiber area, total muscle fiber count and muscle fiber types. Fiber types were classified based on isoforms of myosin heavy chain. Comparison between ± myopenia was done using Mann-Whitney tests for non-parametric data and t-test for parametric data.

Results: 16 children (0.8 - 15.1 years; 9M/7F) with cholestatic liver diseases have been included. N=13 have been transplanted, N=2 subjects are currently awaiting transplant, and N=1 died on the wait list. Most children had liver disease associated with biliary atresia (n=6; 38%), followed by Alagille's syndrome (n=3; 19%) and other (n=7; 44%). Myopenia was present in 33.3% of children (n=5/15 MRI/CT scans analyzed). Percentage of MyHC fibers type I, IIA IID were 56.8 ± 11.1%, 47.3 ± 16.6% and 8.2 ± 3.2%, respectively. Children with myopenia tended to have a lower total number of Type I muscle fibers (136 ± 75 vs 287 ± 36; p=0.08) but no significant differences in the proportions of MyHC type 1A, type IIA and Type IID fibers in children ± myopenia was observed.

Conclusions: This preliminary data suggests that although children with myopenia tended to have lower total number of type I muscle fibers, no significant differences were seen in the seen in the proportion of muscle fiber subtypes in children with and without myopenia.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 159
Presenter: Morteza Hajihosseini
Supervisor: Dinu, Irina
Title: Survivorship bias in outcomes of children after cardiac surgery for congenital heart disease
Authors: Morteza Hajihosseini, Sara Amiri, Ari Joffe, Joseph Atallah, Gonzalo Guerra, Gwen Bond, Charlene Robertson, Irina Dinu, and the Western Canadian Complex Pediatric Therapies Follow-up Group

Theme: Children's health and well-being

Introduction:
Recent advances in technology and surgical practices have allowed complex surgical interventions on increasingly younger infants and children with potentially lethal heart defects. Over the past three decades, the mortality of patients receiving these complex interventions has decreased significantly, resulting in increased survival for infants with more complications. The unobserved degree of sickness in survivors can confound their overall, long-term health patterns and neurodevelopmental and neurocognitive outcomes.
This study aimed to assess the effect of adjusting for unobserved confounders using propensity score adjustment on post-surgical outcomes, and compare to the crude trends.
Methods:
The retrospective follow-up study was conducted on 272 infants less than and equal to 6 weeks of age who underwent cardiopulmonary bypass surgery at the Stollery Children's Hospital in Edmonton, Alberta, between 1997 and 2016. The outcomes of interest were full-scale IQ (FSIQ) and functional outcome measured by the Adaptive Behavior Assessment System (ABAS-II). We adjusted the effect of socioeconomic status, chromosomal abnormality, Glenn surgery, Fontan surgery, and 4.5 years summary of CPR, ECMO, dialysis, convulsions, and sepsis on FSIQ and ABAS-II by calculating a propensity score based on clinical variables affecting the ICU length of stay.
Results:
The results showed that 10 days is the optimal clinical cut point for ICU length of stay with 83.10% accuracy. Of 272 infants, 56 (20.59%) stayed in ICU for less than 10 days. The propensity score was calculated using multiple logistic regression on ICU length of stay based on characteristics of patients and clinical variables.
Socioeconomic status and 4.5 years summary of cardiopulmonary resuscitation (CPR), extracorporeal membrane oxygenation (ECMO), convulsions, and sepsis fell under the univariate regression p-value threshold of 0.2 for FSIQ. Adjusted multiple linear regression on FSIQ showed 7.92 (0.2, 15.6) decrease in FSIQ score for infants with convulsions. In addition, infants with sepsis had a significant lower FSIQ score 8.51 (2.9, 14.1).
Univariate regression model for ABAS-II showed that socioeconomic status, Fontan surgery, and 4.5 years summary of CPR, ECMO, convulsions, and sepsis fell under the univariate regression p-value threshold of 0.2. Adjusted models showed a significant decrease in ABAS-II score for infants with ECMO 12.7 (0.1, 14.3) and sepsis 8.0 (1.1, 14.9) respectively.
Conclusion:
Our method can be applied beyond the pediatric cardiac surgery outcomes research to a wide range of clinical studies where survival is improving, and there is a critical need for evaluating trends in a variety of outcomes.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 67
Presenter: Leah Hammond
Supervisor: Rasmussen, Carmen
Title: Developmental trajectories of executive function and functional abilities in children with perinatal stroke
Authors: Leah Hammond, John Andersen, Jacqueline Pei, Jerome Y. Yager, Adam Kirton, Brian L. Brooks, Lisa Smithson, & Carmen Rasmussen

Theme: Children's health and well-being

Introduction: Perinatal stroke is a vascular brain injury which occurs between the 20th gestational week and the 28th postnatal day. A range of functional impairments, including difficulties with executive function (EF), have been noted in school-aged children with perinatal stroke. However, it is unclear whether impairments continue to accumulate throughout childhood and adolescence. Therefore, our primary aim was to describe the longitudinal trajectories of daily EF and functional abilities in children and adolescents with perinatal stroke.

Methods: This study has a prospective longitudinal design. Time 1 (T1) data was collected from 2017-2019 and Time 2 (T2) data was collected in 2021. Participants included 8 primary caregivers of eligible children with radiologically confirmed perinatal stroke, identified from the Alberta Perinatal Stroke Project. All children were aged 6-16 years at T1 and had a diagnosis of neonatal arterial ischemic stroke or arterial presumed perinatal ischemic stroke. At each timepoint, caregivers completed standardized, survey-based measures of their child's daily EF (Behavior Rating Inventory of Executive Function 2; BRIEF2) and functional abilities (Pediatric Evaluation of Disability Inventory - Computer Adaptive Test; PEDI-CAT). T scores were described descriptively, and reliable change indexes (RCIs) were generated to describe individual developmental trajectories. BRIEF2 T scores could not be calculated for one participant, so a sample size of 7 was used for all BRIEF2 analyses.

Results: Most mean scores on BRIEF2 composites fell within the average range at both timepoints (T1: 57.14 - 61.14; T2: 57.14 - 62.43). Mean scores decreased between timepoints on all BRIEF2 composites, except for the Emotional Regulation Index (T1: 57.14; T2: 62.43). Based on RCI values at the 90% confidence level, 5 children (71.4%) experienced a reliable change on one of the four BRIEF2 composites. Of those who showed any reliable changes, 3 (60.0%) displayed reliable improvements to their EF abilities on one of the four composites. Most changes were not reliable, reflecting typical developmental trajectories.

Most mean PEDI-CAT domain scores fell within the low average range (T1: 33.50-45.13; T2: 23.00-39.75). Mean scores decreased between timepoints on all PEDI-CAT domains, indicating worse functional abilities, relative to normative peers. RCI values revealed most children with perinatal stroke displayed reliable decreases to PEDI-CAT domain scores over time (Daily Activities: 6/8, 75.0%; Mobility: 7/8, 87.5%; Social/Cognitive: 7/8, 87.5%; Responsibility: 4/8, 50.0%), at the 90% confidence level. All participants experienced a reliable decrease to T scores in at least two domains of the PEDI-CAT.

Conclusions: Among this small sample of children with perinatal stroke, alterations to developmental trajectories for daily EF abilities do not appear to be present. However, children with perinatal stroke displayed alterations to developmental trajectories for functional abilities. These findings suggest Daily Activities, Mobility, and Social/Cognitive function may become areas of increasing difficulty throughout childhood and adolescence for individuals with perinatal stroke. Further research with larger samples is needed.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 82
Presenter: Jessica Harasym
Supervisor: Gross, Douglas
Title: (Mis)Understandings about communication post-concussion: A proposal for a qualitative collective case study investigating perspectives of youth and their families
Authors: Jessica Harasym, Shanon Phelan, Douglas Gross

Theme: Children's health and well-being

Introduction:
Young people aged 10-24 years old have the highest concussion rates in Alberta. With perspectives and needs distinct from both children and adults, youth are underrepresented in concussion research. Youth is a pivotal life stage. Young people often feel pressure to do well at school and fit in with friends. A concussion can suddenly change a youth's ability to meet these demands. While many young people recover soon after a concussion, some youth have longer-lasting symptoms, including communication difficulties. Memory and reading concerns may make it difficult to complete schoolwork or remain connected with friends through texts or emails. Trouble finding the right word and slowed thinking can make it hard to keep up with a conversation. Stuttering can make giving a class presentation a struggle.

Research Question:
What are the effects of post-concussion communication difficulties on daily life for youth, including impacts on a) daily routines; b) participation in school/work and community activities; c) relationships with family members; d) relationships with peers; e) (re)negotiation of identities; f) a sense of belonging/loneliness?

Methods:
A qualitative collective case study design will be used to study post-concussion communication difficulties, in-depth and in context. Cases will be centred around youth experiencing communication difficulties post-concussion. Ecocultural theory will be the guiding theoretical framework, allowing for the consideration of environmental and sociocultural factors while investigating how post-concussion communication difficulties affect youth's routines, relationships, identities, health and well-being.

We will recruit 6-12 cases consisting of 1)15-24-year-olds with self-identified post-concussion communication difficulties, 2) a family member or friend invited by each participant (12-24 participants total), and 3) participant-generated data (e.g., photographs, video-diary entries, or artwork) that represents their concussion experiences.

Data will be gathered through multiple in-depth interviews. We will work with the participants to co-construct a visual representation of how their injury and recovery have shaped their daily lives using photographs and other artifacts. In-depth thematic analyses will be completed for each case and across cases to explore participants' collective experiences.

Results:
This project will be the first of its kind to study the experience of post-concussion communication difficulties from the perspective of youth and their families. The results have the potential to guide the design of education programs, assessments and intervention programs aimed at improving youth communication health.

Conclusion:
Concussions can place youth at risk for academic difficulties and negatively impact their emotional and mental health, including lower rates of friendship and increased loneliness. Despite these risks, current research and concussion services rarely consider communication difficulties and their effects on sociocultural aspects of daily life. With a better understanding of youth's unique experiences, parents, teachers, and service providers can tailor services to facilitate communication in the context of daily routines and meaningful activities.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 119
Presenter: Rose He
Supervisor: Eckersley, Luke
Title: Risk of Major Congenital Heart Disease in Pre-gestational Maternal Diabetes is Modified by Hemoglobin A1c
Authors: Rose He, Lisa K Hornberger, Susan Crawford, Cleighton Boehme, Luke Eckersley

Theme: Pregnancy and developmental trajectories

Introduction: The association between pre-gestational maternal diabetes (MD) and an elevated risk of congenital heart disease (CHD), a defect in the heart structure, is well-recognized. However, the contribution of poor glycemic control based on hemoglobin A1C (A1c) has been less clear. As all mothers with MD and gestational diabetes diagnosed in the first trimester (presumed MD) are recommended to undergo fetal echocardiography screening, MD is one of the most common referral reasons for fetal echo. A prior study found that major CHD (mCHD), defined as requiring operation in the first year of life, rarely was diagnosed in MD mothers referred for fetal echo. As fetal echo is a labor-intensive clinical service with few trained practitioners in our province and worldwide, there is a need to streamline resource use by screening the mothers most at-risk of having a child with CHD.
Aims: To determine (1) the incidence of mCHD among those with MD and also stratified by types of MD (gestational diabetes versus pre-existing diabetes, including Type 1 and 2) and (2) the effect of covariates on risk of mCHD.

Methods: We identified cases of mCHD among all pregnancies in Alberta from 2008-2018 using linkage of surgical, echocardiography and fetal cardiac databases. These cases were linked to the Alberta Perinatal Health Program registry with identification of MD, gestational diabetes and other potential covariates among all pregnancies. Maximum blood A1c level prior to 16 weeks gestation was extracted from laboratory data. Data are described as incidence per 1000 births or medians and interquartile ranges (IQR). Risk ratios were calculated and log-binomial regression multivariable modelling for risk factors prediction of mCHD was performed (Stata/IC 14.2).

Results: There were 1412 cases of mCHD in 594,773 Alberta births in the study period (2.4/1000). MD was present in 12.5/1000 births, and gestational diabetes in 65/1000 births. MD was associated with increased risk of mCHD (48 cases of mCHD of 7497 births with MD, 6.4/1000). The risk ratio for mCHD associated with MD was 2.8 (95% CI 2.1, 3.7), p<0.001. mCHD was present in 85 of 36,772 births with gestational diabetes (2.3/1000 births, risk ratio 1.0 (95% CI 0.8, 1.3), p=0.94).
Maximum A1c at <16 weeks gestation was higher in cases of MD with mCHD than MD without mCHD (mCHD 8.4% (IQR 6.9, 10.2); no mCHD 6.9% (IQR 5.9, 8.2), p=0.001). In cases of gestational diabetes, A1c<16 weeks was similar between those associated with mCHD (5.5%, IQR 5.3, 5.8), and without mCHD (5.5% IQR 5.3, 5.8).
The stratified risks for mCHD associated with A1c ≤6.1%, 6.1% - 8.5% and ≥8.5% were 3.6/1000, 7.7/1000, 20.9/1000 births respectively. The risk ratio for mCHD associated with pre-existing diabetes and an A1c ≥8.5% was therefore 8.9 (95% CI 5.2, 15.3), and 9.9 (95% CI 5.6, 16.7) when adjusted for multiple gestations, child's gender, maternal pre-pregnancy weight and age.

Conclusion: Pre-gestation MD is associated with a risk ratio for mCHD of 2.8, which increased to 9.9 in those with HbA1c greater than 8.5%. This data may allow refinement of referral indications for high-risk pregnancy screening.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

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Participant #: 152
Presenter: Negar Heidari
Supervisor: Hornberger, Lisa K
Title: Natural History of Atrial Septal Defects Diagnosed in Term Neonates
Authors: Negar Heidari, Dr. Lisa K. Hornberger

Theme: Children's health and well-being

Introduction: A commonly found congenital heart disease in newborns through echocardiography is atrial septal defect (ASD) where the wall between upper chambers of the heart (atria) has a hole. The most common type of ASD is called secundum ASD based on location and etiology. ASDs can cause multiple health issues if untreated, and, as such, knowledge about their natural history is important for timely monitoring and intervention. Furthermore, with increasing use of echo in the neonatal intensive care unit, an understanding of the natural history will facilitate more appropriate triaging for pediatric cardiology follow-ups. One study of infants suggested that secundum ASDs <3mm spontaneously close whereas those ≥3mm may not. With this knowledge, all newborns with ASDs ≥3mm receive cardiology follow-up, which may lead to unnecessary resource use if they are likely to close or not require intervention. We hypothesized that the majority of secundum ASDs ≥3mm identified at <1 month age undergo spontaneous closure or significant size reduction (≤3mm, not warranting monitoring) in the first 2 years of life.
Methods: To assess our hypothesis, we performed a retrospective cohort study of all term newborns (≥35 gestational age) who underwent echocardiography, were diagnosed with an ASD ≥3mm within the Royal Alexandra Hospital from 2010-2018 and had at least one repeat echo. In total, we assessed 124 patients.
Results: Among all assessed patients, 58 had an ASD 3-5mm in size, 57 had an ASD 5.1-8.0mm in size, and 9 had an ASD >8mm in size on the neonatal echo. The percentage of ASDs that closed spontaneously or reduced to a size of ≤3mm within a mean period of 15 months were 93%, 89%, and 67% in each group, respectively. Out of 13 patients with persisting ASDs ≥3mm in size, 3 required ASD closure intervention, 2 of whom had an initial ASD measure >8mm. In other words, less than 2.5% of all patients with ASDs ≥3mm required ASD closure.
Conclusion: Our findings confirm that the majority of neonates with ASDs experience spontaneous closure/significant size reduction and indicate that we can stop monitoring asymptomatic newborns with ASDs <8mm in size. Considering the mean follow-up period of 15 months in this study, we also recommend extending the follow-up period to 2 years for patients being monitored so that the true closure capacity of ASDs can be observed.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

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Participant #: 148
Presenter: Lauren Higa
Supervisor: Hemmings, Denise G
Title: Expression of syndecan-1, a receptor for Plasmodium falciparum infected red blood cells, may be determined by the sex of the placental syncytiotrophoblast
Authors: Lauren Higa, Rebecca Reif, Catherine J. Mitran, Stephanie K. Yanow, and Denise Hemmings

Theme: Pregnancy and developmental trajectories

Introduction: Placental malaria is established when erythrocytes infected with Plasmodium falciparum sequester in the placenta, leading to adverse health outcomes for both the mother and fetus. This adherence is mediated by the expression of VAR2CSA on the surface of the infected red blood cell, which binds to chondroitin sulfate A (CSA) glycosylated syndecan-1 (SDC-1), expressed on the placental syncytiotrophoblast. Past studies suggest that fetal sex may be a risk factor for placental malaria, with placentas from female fetuses being at higher risk of malaria infection; however, the mechanism behind this is currently unknown. We hypothesized that female placentas express higher levels of SDC-1 on the syncytiotrophoblast, leading to increased infected red blood cell adherence to the placental barrier and worse placental malaria outcomes.

Methods: To assess whether there is a sex difference in placental SDC-1 expression, we obtained placentas from women with full-term, uncomplicated pregnancies delivered by caesarean section. Fetal sex was blinded until analysis of samples was completed. We performed immunofluorescence assays to quantify SDC-1 expression localized to the syncytiotrophoblast and evaluated SDC-1 mRNA levels from whole placental lysates by RT-PCR. We are currently optimizing a western blot protocol to further investigate a potential sex difference in SDC-1 expression in placentas from male and female newborns and will be conducting experiments to examine sex differences in P. falciparum infected red blood cell adherence to villous explant tissues.

Results: Initial immunostaining results showed significantly higher SDC-1 expression in female placental syncytiotrophoblast ($p=0.0059$, $n=23$), suggesting a sex-dependent difference in SDC-1 expression. We are now confirming these sex differences by co-staining for SDC-1 with the specific syncytiotrophoblast marker, placental alkaline phosphatase to allow for more precise SDC-1 quantification. By RT-PCR there were no significant differences in SDC-1 mRNA levels between male and female placentas ($p=0.3021$, $n=37$). However, the SDC-1 mRNA for RT-PCR was isolated from total placental tissue, whereas immunostaining was specific for SDC-1 expression in syncytiotrophoblast. This difference in specificity for the syncytiotrophoblast may account for the differing results obtained by these two methods. Alternatively, translation but not transcription of SDC-1 may be sex-specific.

Conclusion: There may be sex-dependent differences in SDC-1 expression in the syncytiotrophoblast. This expression difference could impact the adherence of P. falciparum infected red blood cells to the placenta.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 96
Presenter: Nataliia Hula
Supervisor: Davidge, Sandra
Title: Prenatal hypoxia alters endothelin-1-mediated coronary artery function in adult rat offspring in a sex-specific manner
Authors: Nataliia Hula, Ricky Liu, Mazhar Pasha, Anita Quon, Raven Kirschenman, Floor Spaans, Christy-Lynn Cooke, Sandra T. Davidge

Theme: Pregnancy and developmental trajectories

Introduction: Fetal hypoxia is linked to cardiovascular (CV) dysfunction in the offspring in later life. Our laboratory previously reported impaired cardiac function in adult offspring exposed to prenatal hypoxia, however the mechanisms remain unknown. The coronary circulation is crucial for proper cardiac oxygenation and plays an essential role in maintaining cardiac performance. Endothelin-1 (ET-1) is a a key vasoactive factor in the coronary circulation that signals through the endothelin-A (ET(A)R) and endothelin-B receptors (ET(B)R) and is vital for normal physiological processes. However, enhanced ET-1 signaling in the vasculature has been associated with the development and progression of various CV diseases. Thus, we hypothesize that coronary artery function is impaired in adult prenatally hypoxic offspring via enhanced ET-1-dependent vasoconstriction.

Methods: Pregnant Sprague-Dawley rats were exposed to normoxia (21% O2) or hypoxia (11% O2; p-Hypoxia) on gestational days 15-21 (term=22 days). Male and female offspring were aged to 4 months, the left anterior descending artery was isolated and its function was evaluated using wire myography (n=7-11/group). ET-1-mediated vasoconstriction was assessed in the presence/absence of antagonists of the ET(A)R (BQ-123) or ET(B)R (BQ-788). Data were summarized as area under the curve (AUC). Coronary artery ET-1, ET(A)R and ET(B)R levels were assessed with immunofluorescence (n=5/group). Data were compared by two-way ANOVA (Sidak`s post hoc test); $p<0.05$ was significant.

Results: Prenatal hypoxia did not affect coronary artery responsiveness to ET-1. ET(A)R inhibition reduced ET-1 responsiveness in all groups, independent of prenatal exposure or sex. In normoxia males, BQ788 tended to decrease ET-1 responsiveness, while increasing ET-1-mediated responses in the prenatal hypoxia group (AUC: Normoxia/control: 6.96±0.45 vs. Normoxia/BQ788: 5.28±0.46, and p-Hypoxia/control: 6.52±0.9 vs. p-Hypoxia/BQ788: 7.53±0.55, interaction: p=0.03). In females, BQ788 did not affect ET-1 responses in the normoxia group, while BQ788 decreased ET-1-mediated vasoconstriction in the prenatal hypoxia-exposed females (AUC: Normoxia/control: 7.05±0.45 vs. Normoxia/BQ788: 7.45±0.68, and p-Hypoxia/control: 8.04±0.6 vs. p-Hypoxia/BQ788: 5.75±0.67; interaction: p=0.03). ET(B)R levels were elevated in prenatally hypoxia-exposed males only (Normoxia: 100%±10.27 vs p-Hypoxia: 144%±14.68, p=0.02), while ET-1 and ET(A)R levels were not altered by prenatal hypoxia in either sex.

Conclusions: While coronary artery responsiveness to ET-1 was similar between groups, we observed sex-specific alterations in the contribution of ET(B)Rs to ET-1-mediated coronary artery responsiveness in prenatally hypoxic offspring. Elevated ET(B)R levels may indicate an early offspring adaptation to the hypoxic environment in utero and contribute to the prenatal hypoxia-induced changes in coronary artery function. Considering the widespread consequences of CV diseases in the world in men and women, understanding the mechanistic and sex-specific pathways that are involved in early programming of CV diseases may provide the potential to pursue further development of therapeutic interventions.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 199
Presenter: Tara Janes
Supervisor: Pagliardini, Silvia
Title: Remembering how to breathe: Can a progestin-based drug rescue breathing in a rodent model of central chemoreflex impairment?
Authors: Tara A. Janes, Silvia Cardani, Olena Didenko and Silvia Pagliardini

Theme: Children's health and well-being,Pregnancy and developmental trajectories

Introduction: From the moment of birth, breathing sustains life in an automatic and unassuming way that we rarely notice its occurrence on conscious level. Sadly, there are children for which dysregulation of autonomic neural control results in a condition where they "forget to breathe." This is exemplified by congenital central hypoventilation syndrome (CCHS), in which the mutation of a single gene critical for neural function (Phox2b) generates severe abnormalities arising in infancy including shallow breaths and recurrent apneas. Key to this pathology is dysregulation of central CO2-sensing neurons, which stimulate breathing during apnea. Without this function, apneas can quickly become fatal. No cure exists for CCHS; treatment in children involves tracheostomy and mechanical ventilation leaving patients susceptible to infection. Remarkably, a serendipitous discovery found that a progestin contraceptive containing etonogestrel restored CO2-sensitivity in two female CCHS patients, but follow-up studies were ambiguous. Here, we hypothesized that etonogestrel would restore respiratory responses to CO2 in a rat model of central chemoreflex impairment and reveal brainstem regions that may compensate for the loss of primary CO2-sensing neurons.
Methods: A rat model of central chemoreflex impairment was created by ablating key CO2-sensing neurons in the brainstem of adult females using a neuron-specific toxin (saporin). Minute ventilation, breath frequency, tidal volume and O2/CO2 metabolism were measured by whole body plethysmography before, and 2 weeks after toxin injection in room air and during inhalation of CO2 (5%, 7%). Rats were then implanted with etonogestrel (s.c.) for 4 weeks; controls received sham surgery. Respiratory measurements were made once per week; tissues were collected at the end of the protocol for histological analyses.
Results: Toxin injection did not affect breathing in room air but minute ventilation was blunted by 15% and 34% during inhalation of 5% and 7% CO2, respectively. This effect was due to lower breathing frequency. Remarkably, 4-weeks of etonogestrel treatment restored minute ventilation during CO2 inhalation to baseline values. This was due to frequency response recovery; tidal volume was not affected by toxin injection or etonogestrel. Histology confirmed a reduction in CO2-sensing neurons (PHOX2B+) at the injection site. Nuclear progesterone receptors, through which etonogestrel exerts its effects, were not present on surviving CO2-sensing neurons in the lesion area suggesting that compensatory responses occur elsewhere in the nervous system.
Conclusions: These data support our hypothesis that etonogestrel can "rescue" CO2-sensing in a rat model of central chemoreflex impairment and are consistent with previous clinical observations. Importantly, these results suggest that the brain can compensate for the loss of primary CO2-sensing neurons. Future studies to identify these brain regions and the mechanisms of recovery hold promise for targeted pharmacological interventions that are currently lacking for children with CCHS. Finally, elucidating the mechanisms by which progesterone affects neural function is fundamentally important as this hormone is predicted to have diverse roles in health and disease.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 182
Presenter: Carlos Jarquin
Supervisor: Hartling, Lisa
Title: Co-designing an mHealth app with parents for managing acute childhood illnesses
Authors: Carlos Jarquin, James Benoit, Shannon Scott, Lisa Hartling

Theme: Children's health and well-being

Introduction
The COVID-19 pandemic demonstrated the importance of equitable and accessible healthcare for Canadian families. Mobile health-based solutions have been used to deliver healthcare services while maintaining social distancing measures. There are gaps in evidence-based mobile health solutions for parents managing acute childhood illnesses. We are co-designing an evidence-informed smartphone application with parents to address these gaps. This app will house a suite of evidence-based knowledge translation (KT) tools co-created with parents. These tools provide parents with easily accessible and relevant resources for their children's health. They allow parents to take a more empowered approach to their children's health by increasing parental confidence in health care decisions.

Methods
This project involves developing a novel app with an iterative human-centered approach, taking experiential responses and information from parents to meet their identified needs. We began by creating app designs based on an environmental scan of apps available to parents. Then, we presented app designs to our parent advisory group and refined the app design from their feedback, before returning to our advisory group for further discussion and design refinement.

Parents from diverse backgrounds provided feedback throughout the human-centered design process of the app. Our final app design reflects and respects this heterogeneity. In developing the KT tools, we consider how user attributes such as gender shape how the tools are used. We depict different gender identities and family structures in the KT tools. In providing these tools, our proposed solution represents diversity in family roles, providing parents with accessible, comprehensible, and parent-vetted information.

Results
After two rounds of input from parents, our app provides easy access to a suite of KT tools and incorporates requested features including a list of references for each KT tool, a symptom checker, and an interactive map of nearby medical clinics. The list of references under each tool shows its evidentiary basis. The symptom checker uses plain language medical terminology to accommodate a broad range of parent health literacy. The map of local clinics gives parents the ability to find and sort Canadian clinics based on wait time, proximity, and degree of care.

Conclusion
Parents strongly support the creation of a co-designed mHealth app for managing acute childhood illnesses. Our iterative co-design process and emphasis on interdisciplinarity within a human-centered design framework has been successful for prioritizing and refining the app's layout and features. Our app will provide a mechanism to broadly disseminate evidence-based KT tools to support parents in managing their child's illness, with potential to transcend geographic and socioeconomic barriers.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 176
Presenter: Samar Kauser
Supervisor: Meherali, Salima
Title: Understanding Sexual and Reproductive Health Needs of Immigrant Adolescents in Canada: A Scoping Review
Authors: Samar Kauser, Samantha Louie-Poon, Mehnaz Rehmani, Megan Kennedy, Shannon Scott, Bukola Salami, Helen Vallianatos, Salima Meherali

Theme: Children's health and well-being

Background: Canada is a major destination country for immigrants globally. Despite the importance of immigrants in Canadian society, there is a scarcity of research on the sexual and reproductive health and rights (SRHR) needs of immigrant adolescents in the country.

Methods: A scoping review was undertaken following the PRISMA-ScR statement to identify and assess the existing literature regarding SRHR needs of immigrant adolescents in Canada. Of the 1514 articles retrieved from our search strategy, 15 studies met our inclusion criteria.

Results: The results from our review identifies three unique themes related to immigrant adolescents' SRHR needs: knowledge needs, access to SRHR education and services, and approaches to SRHR education and services. Immigrant adolescents' knowledge needs includes needs on HIV/STI transmission and protection, unintended pregnancy, sexual activity, family planning, pubertal education, navigating the health care system, and confidentiality legislations. Our results revealed that immigrant adolescents' access SRHR education and services through both school-based and community-based settings. Lastly, approaches to SRHR education and services for immigrant adolescents should include cultural sensitivity, an intersectional approach, interactive learning, a strength-based approach, and reassuring confidentiality rights.

Conclusion: The multi-faceted SRHR needs of immigrant adolescents in Canada demonstrates that future research, program development, and policymaking requires careful consideration of these intersecting forces. Inclusive SRHR education and services can be achieved through the employment of a critical cultural approach and intersectional strategies.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 53
Presenter: Samar Kauser
Supervisor: Meherali, Salima
Title: The sexual and reproductive health needs of immigrant adolescents: A qualitative study
Authors: Samar Kauser, Samantha Louie-Poon, Salima Meherali

Theme: Children's health and well-being

Background: Despite the large number of immigrant adolescents in Canada, research on their knowledge of sexual and reproductive health and rights (SRHR) and information needs is nearly nonexistent. This qualitative study sought adolescent sexual and reproductive health needs from the perspective of immigrant adolescents.

Methods: Based on the findings from a scoping review previously conducted between September 2020 to January 2021, we used a semi-structured interview schedule to conduct individual virtual interviews with immigrant adolescents between 14 to 19 years. Between May to June 2021, 19 interviews were conducted with adolescent participants. Thematic data analysis was undertaken on NVivo software.

Preliminary Results: Of the 19 adolescent participants, 18 identified as female and 1 identified as male. Adolescents were between the ages of 14 and 19 years, with the majority of participants at the post-secondary level of education (n=16). The adolescent interviews revealed 9 major themes: 1) adolescent-parent dynamic, 2) barriers to accessing SRHR education and services, 3) pre-existing SRHR knowledge, 4) current lack of SRHR knowledge, 5) needs related to SRHR informational sources, 6) existing sources of SRHR knowledge, 7) SRHR thoughts changing over time, 8) topics related to a SRHR digital strategy, and 9) location of accessing SRHR services.

Expected Results: This results from this qualitative study will contribute to the knowledge base of SRH needs of immigrant adolescents in Alberta. Targeting immigrant adolescents and using engaging modalities could increase their involvement in healthcare decision making, expand efficiencies in SRH-care utilization, and improve SRH and overall health outcomes. The findings of the study will inform the design of a future multi-setting study to develop tailored innovative knowledge translation strategies, for immigrant adolescents to optimize adolescents SRH outcomes.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 85
Presenter: Yana Kibalnyk
Supervisor: Voronova, Anastassia
Title: The role of Ankrd11, a chromatin remodeler and KBG syndrome risk gene, in cardiovascular development
Authors: Yana Kibalnyk, Ronan Noble, Daniela Roth, Maria Alexiou, Stephane Bourque, Daniel Graf and Anastassia Voronova

Theme: Children's health and well-being,Pregnancy and developmental trajectories

Introduction: KBG syndrome is a rare developmental disorder, with about 500 cases known worldwide. It is characterized by multiple organ abnormalities, including brain, craniofacial, and cardiac malformations. It is caused by deficiency in the gene ANKRD11 (Ankyrin Repeat Domain 11), an epigenetic regulator that interacts with histone acetylases and deacetylases (HATs and HDACs) to control global gene expression. Our lab showed that Ankrd11 regulates brain and craniofacial development, yet its role in heart development is unknown. This is an important question to address as many KBG patients display heart anomalies that often require open heart surgeries. Both craniofacial and heart development are notably shaped by the neural crest, an embryonic tissue vital to organogenesis. KBG patients show both craniofacial and cardiac phenotypes consistent with neural crest dysregulation, making the neural crest an ideal target to study cardiac defects in a KBG model.

Methods: To identify the role of Ankrd11 in heart development, I am using a mouse model with conditional knockout of Ankrd11 in the neural crest (Ankrd11lox/lox;Wnt1Cre2 or Ankrd11ncko), and analyzing them for developmental defects. I am also using neural crest lineage tracing coupled with neural crest cultures and RNA sequencing to analyze the mechanism behind Ankrd11ncko cardiac neural crest dysregulation.

Results: My results demonstrate that Ankrd11ncko embryos display a congenital heart defect termed persistent truncus arteriosus, where the aorta and pulmonary trunk fail to separate into distinct vessels, as well as a common origin of the brachiocephalic and left common carotid arteries. This suggests a failure of the neural crest to remodel the common outflow tract of the heart into the pulmonary trunk and aorta. Echocardiography reveals that affected embryos also show cardiomegaly (increased size) and decreased ventricular contractility. As Ankrd11ncko embryos die at birth, this points to fatally defective heart function. Preliminary findings using the neural crest lineage tracing suggest that the defect may be caused by abnormal cardiac neural crest differentiation at the outflow tract. We are currently verifying this with RNA-sequencing of the wild-type and Ankrd11ncko outflow tract tissue.

Conclusion: My work demonstrates a novel role for Ankrd11 in regulating the neural crest-mediated remodeling of the heart outflow tract that has profound consequences on heart function. Together with abnormal craniofacial development in the Ankrd11ncko mice, my results suggests a key role for the neural crest tissue abnormalities in the KBG syndrome pathogenesis. Moreover, my results will contribute to our understanding of epigenetic regulation of neural crest function in heart development. I hope the results from this project will inspire novel therapies for patients with KBG syndrome and congenital heart malformations at large.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 190
Presenter: Danielle Klassen
Supervisor: Storey, Kate E
Title: Examining school-community partnerships to strengthen school-based health promotion
Authors: Danielle Klassen, Claudine Champion, Genevieve Montemurro, Jenn Flynn, Kim Raine, Kate Storey

Theme: Children's health and well-being

Introduction: Schools are an important setting to promote the health and well-being of children and youth during critical developmental years. The evidence-based comprehensive school health (CSH) approach is an internationally recognized framework that supports the creation of healthy school communities through the promotion of wholistic health through changes to the environment, teaching and learning, policies, and the establishment of partnerships. Research has demonstrated that partnerships are fundamental for effective implementation and are considered an essential condition for the successful implementation of CSH. Previous research by our team has also shown that projects taking a CSH approach, such as APPLE Schools, impact the broader community. However, there is limited research on what school-community partnerships look like in school-based health promotion practice. The purpose of this study was to understand if and how schools and communities that are part of APPLE Schools work together to foster support for school-based health promotion from the perspectives of both school staff and community stakeholders.

Methods: Qualitative description was the guiding method for this study. Four school communities in Canada were purposively selected based on their experiential knowledge of APPLE Schools and partnerships within a school-community context. Telephone and Zoom interviews were conducted with school staff (n=11) and community stakeholders (n=7). Interview questions explored how schools and communities formed partnerships, what made the partnerships effective, what barriers were present, and the perceived impact on practices both in the school and in the broader community. All interviews were audio-recorded and transcribed verbatim. Data was analyzed using inductive content analysis.

Results: Findings showed key facilitators to initiate partnerships were school administrators (e.g., principals) and parents. School-community relationships strengthened health promotion within the school through donations, volunteering, resources, and expertise. Community stakeholders were passionate to be involved with improving the health of children and youth and often built upon school-based initiatives by promoting the same activities in the community.

Conclusions: This study demonstrated how school and community partnerships can support and improve health promotion within and beyond school walls. Mutual goals of healthy child development were seen in both partner groups. This provides valuable knowledge to school communities to strengthen health promotion efforts within and outside of schools at a community-level.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 146
Presenter: Lisa Knisley
Supervisor: Scott, Shannon
Title: Examining the experiences of Indigenous families seeking health information for their sick or injured child: a scoping review protocol
Authors: Knisley, L.; Sun, C.; Driedger, S.M., Hartling, L., Sanguins, J., Scott, S. D.

Theme: Children's health and well-being

Introduction: The Truth and Reconciliation Commission drew attention to the inequalities and systemic harms experienced by Indigenous peoples in Canada and called on the Canadian government and healthcare professionals to close the gap related to Indigenous communities' access to appropriate health care services. Métis people have expressed a need for reliable health information, and that health systems have left much of their information needs unmet. Métis parents have recognized culture and a positive sense of Métis identity as important elements of raising children, and as key components that are missing from healthcare services. The Manitoba Metis Federation (self-governing organization representing Red River Métis) identified a need for Red River Métis families to have meaningful resources when seeking emergency care for their children. A scoping review will inform the adaptation of an existing child health resource (e.g., infographic, video) by 1) mapping the literature on Indigenous families' experiences seeking health information to care for a sick or injured child; and 2) identifying the barriers and facilitators to accessing this information.

Methods: Joanna Briggs Institute methodology was used to develop the research question, What is the extent and nature of the literature available on the experiences of Indigenous families seeking health information for their sick or injured child? and review design: Population- Indigenous families (e.g. parents, relatives, guardians) of children aged 0-21 years; 2) Concept - peer-reviewed/grey literature on the experiences of Indigenous families seeking child health information; 3) Context - child health information seeking at home, hospital or other healthcare setting. The inclusion criteria were not limited to Métis families to explore what is known in an Indigenous context. The search strategy, developed with a research librarian in Indigenous health, included: 1) searching SCOPUS, PsycINFO, MEDLINE, CINAHL, EMBASE databases; 2) searching Google Advanced for grey literature; 3) snowball sampling (backward & forward reference searching); 4) scanning tables of contents of key journals not sufficiently indexed in databases.

Results: 4822 citations were identified through electronic databases and data extracted from 27 articles. Grey literature searching is underway. No article was found that focused solely on Métis families. Most articles were from Australia (n=11) followed by Canada (n=9), the U.S. (n=5), and New Zealand (n=2). Preliminary findings suggest Indigenous families experience racism, culturally unsafe care, geographical and financial barriers when seeking health information. Health information that considers language and cultural preferences, acknowledges the family's decision-making role and is available within a family's community may facilitate information seeking.

Conclusion: There is a gap in the literature on Métis families' experiences seeking child health information. A consultation exercise with a community advisory committee will review results and inform future research. Scoping review results and advisory committee reflections will be integrated with findings from other project stages to inform the adaptation of a child health resource for Red River Métis famil

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Participant #: 72
Presenter: Yan Shu Kong
Supervisor: Fu, Yangxin
Title: RNA cytosine methyltransferase NSUN2 promotes tumorigenic phenotypes in epithelial ovarian cancer
Authors: Yan Shu Kong, Zhihua Xu, Helen Steed, Lynne-Marie Postovit, and YangXin Fu

Theme: Lifelong women's health

Introduction. Epithelial ovarian cancer (EOC) is the most common type of ovarian malignancy and the leading cause of gynecologic cancer death. Current Standard treatments against advanced EOC lacks efficacy, and there is an urgent need to develop novel therapeutic strategies, such as targeted therapies. RNA modifications, also known as RNA epigenetics or epitranscriptomics, modulate the biology, function, and expression of RNAs, which constitute an additional level of regulation of gene expression. Emerging evidence suggests that RNA modifications are often dysregulated in cancer via the aberrant expression or mutation of the RNA-modifying enzymes, which alters the epitranscriptome, resulting in aberrant mRNA expression and/or translation that enhances tumorigenesis. NSUN2 is a member of the NSUN family of methyltransferases, and it introduces 5-methylcytosine (m5C) to various species of RNAs. Importantly, NSUN2 is implicated in several types of cancers, but its role in EOC remains unknown. The objective of this study is to determine the tumorigenic functions and the underlying mechanisms of NSUN2 in EOC.

Methods. The association of NSUN2 expression with survival of EOC patients was determined by analyzing The Cancer Genome Atlas (TCGA) dataset. NSUN2 expression was examined in a panel of EOC cell lines and patient-derived xenografts (PDXs) by western blotting and immunohistochemistry (IHC), respectively. NSUN2 was knocked down via shRNA in the EOC cell line OVCAR8 and primary EOC cells isolated from ascites of EOC patients. The effect of NSUN2 knockdown on the growth of OVCAR8 and primary EOC cells was determined by neutral red uptake and clonogenic assays, and the expression of proteins associated with proliferation and survival was examined by western blotting.

Results. Analysis of the TCGA dataset showed that high expression of NSUN2 is strongly associated with shorter overall survival of EOC patients. Knockdown of NSUN2 in OVCAR8 and primary EOC cells decreases cell growth and colony formation, which is concurrent with the increased expression of cell cycle inhibitor p27Kip1, and decreased expression of pro-survival protein Bcl-xL. Our results suggest that NSUN2 promotes survival and proliferation of EOC cells, likely through the introduction of m5C to mRNA transcripts associated with these processes.

Conclusion. Our in vitro results suggest that NSUN2 plays a pro-tumorigenic role in EOC. We will determine the role of NSUN2 in vivo using mouse xenograft models and identify the mRNA transcripts that are regulated by NSUN2 using RNA-sequencing and mass spectrometry. This study will determine whether NSUN2 can be a novel therapeutic target for EOC.

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Participant #: 211
Presenter: Asna Latif
Supervisor: Bhavsar, Amit
Title: Genetic variations in Toll-like Receptor 4 reveal its role in mediating cisplatin-induced hearing loss in childhood cancer patients
Authors: Asna Latif, Ghazal Babolmorad, Ivan Domingo, Niall Pollock, Cole Delyea, Aja Rieger, Ted Allison, Amit Bhavsar

Theme: Children's health and well-being

Background and aims

Cisplatin is a highly versatile, platinum-based chemotherapeutic used in the treatment of various cancers and solid tumours in children. Unfortunately, it is limited by its association with irreversible hearing loss, or ototoxicity, in treated children and impacting the quality of life of childhood cancer patients as well as compromising the cisplatin dosages that can be administered for cancer treatment. CIO tends to impact a wide range of pediatric patients, with 30-70% developing hearing loss after treatment. This range suggests that genetic variation has a role in developing susceptibility to CIO. Pharmacogenomic analyses have revealed that genetic variations in an immune receptor gene, Toll-like receptor 4 (TLR4), contribute to varying susceptibility to CIO. Interestingly, while the interactions of TLR4 with platinum are unknown, TLR4 has previously been shown to mediate contact hypersensitivity to other heavy metals with similar properties. This implicates that similar interactions between TLR4 and the platinum component of cisplatin are involved in mediating CIO, and contribute to varying susceptibilities to CIO in pediatric cancer patients.

In this study, we investigated the role of TLR4 in mediating CIO by interacting with cisplatin and its platinum-based structure and evaluated the efficacy of small molecules in protecting against toxicity to better understand the role of TLR4 in rendering hearing loss in pediatric cancer patients. Additionally, mutations in the TLR4 gene that have been shown to contribute to varying susceptibilities to CIO were implemented in-vitro to assess their effect on TLR4 activity.

Methods

To investigate the effect of TLR4 mutations on its activity, a mutation of interest was implemented into a TLR4 gene and cloned into a luciferase vector, then treated with cisplatin and assessed for activity levels. To investigate the interactions of TLR4 with platinum, isogenic cell lines expressing or lacking TLR4 were treated with cisplatin/platinum or known ligands of TLR4 and measured for inflammation or cell death. Cisplatin-induced inflammation was assessed following genetic inhibition of tlr4 in both a physiologically relevant mouse embryonic inner ear cell line from as well as in-vivo in zebrafish. Rescue effects of small molecule inhibitors of TLR4 were investigated in cells treated with cisplatin.

Results

The presence of TLR4 increased cell stress, inflammation, and death in response to cisplatin treatment both in vitro and in vivo and was involved in distinct interactions with platinum. Genetic inhibition and small molecule inhibitors of TLR4 protected against these effects and reveal it as a promising target for oto-protective therapies to prevent CIO in childhood cancer patients.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 168
Presenter: Stuart Lau
Supervisor: Ospina, Maria
Title: Prevalence of Neurodevelopmental Disorder among Indigenous Children: A Systematic Review
Authors: Stuart Lau, Natalie Czuczman, Liz Dennett, Matthew Hicks, Maria B. Ospina

Theme: Children's health and well-being,Pregnancy and developmental trajectories

Introduction
Neurodevelopment involves sensory-motor, cognitive, and social-emotional domains which can be influenced by biological and psychosocial factors. Poor neurodevelopment in early childhood can result in missing developmental milestones and neurodevelopmental disorders (NDs) that translate into negative consequences on long-term health and well-being. Indigenous children in countries with similar colonial histories (Australia, Canada, New Zealand, and the USA) face a disproportionate burden of infant mortality, chronic diseases, and injuries compared to non-Indigenous children. Previous studies have found that Indigenous children have higher disability rates compared to the general population. However, the prevalence of NDs among Indigenous children around the world remains undetermined and warrants a systematic evaluation of the current scientific literature.
Methods
A protocol for the systematic review was registered in the PROSPERO database (CRD42021238669). Comprehensive searches of 5 biomedical databases from 2005 to Feb 15, 2021 were conducted to identify cohort and cross-sectional studies that evaluated the prevalence of NDs in Indigenous and non-Indigenous children in Australia, Canada, New Zealand, and the USA. Two independent reviewers conducted study selection, data extraction/analysis, and risk of bias assessment. Risk of bias was assessed using the Newcastle-Ottawa scale for cohort and ecological studies (adapted), and the Quality Assessment Tool for Prevalence Studies by Hoy et al. for cross-sectional studies. Prevalence odds ratios (pOR) with 95% confidence intervals (CI) were calculated in random-effects meta-analyses for each ND outcome.
Results
From the 863 studies identified, 24 studies met the inclusion criteria. Twelve studies were conducted in Australia, one in Canada, four in New Zealand, and seven in the USA. There were four studies that evaluated attention-deficit/hyperactivity disorder (ADHD) prevalence, 12 for autism spectrum disorder (ASD), nine for intellectual disability (ID), and five for motor disorders (MD). Most cohort studies (10/16) were at high risk of bias. All cross-sectional studies (n=7) had low risk of bias. The prevalence of ADHD, ASD, ID, and MD for Indigenous children ranged from 2.7-3.9%, 0.07-3.0%, 1.3-3.9%, and 0.18-0.47%, respectively. In contrast, prevalence in non-Indigenous children ranged from 1.7-5.6%, 0.31-3.3%, 1.0-2.3%, and 0.22-0.37%. In cross-sectional studies, Indigenous children had increased odds of ADHD (2 studies; pOR=1.70; 95% CI: 1.18-2.44) and decreased odds of ASD (3 studies; pOR=0.80; 95% CI: 0.71-0.89) compared to non-Indigenous children. In cohort studies, higher odds of MD (2 studies; pOR=1.57; 95%CI: 1.35-1.84) and lower odds of ASD (4 studies; pOR=0.46; 95% CI: 0.28-0.76) were found in Indigenous Children compared to non-Indigenous children. An insufficient number of studies precluded meta-analyses for other NDs.
Conclusion
Preliminary analyses indicate that Indigenous children have a similar burden of NDs compared to non-Indigenous children. For ADHD and MD, prevalence rates are greater in Indigenous children and lower for ASD compared to their non-Indigenous counterparts. Future steps include identifying sources of heterogeneity among included studies.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 86
Presenter: Christy Lee
Supervisor: Alexander, R Todd
Title: Mutation of a little-known gene causing rickets because of low blood phosphate levels
Authors: Christy Lee, Todd Alexander

Theme: Children's health and well-being

Introduction
Hypophosphatemic rickets is a childhood disease characterized by increased urinary phosphate wasting, resulting in poorly mineralized bones. This disorder is typically caused by a mutation in the PHEX gene. However, a 9-year-old female with poorly mineralized bones and urinary phosphate wasting lacked a PHEX gene mutation and in all other known genes that cause this disease. Furthermore, like patients who have PHEX gene mutations, she displayed increased fibroblast growth factor 23 (FGF23). High levels of this osteoblast and osteocyte-produced hormone lead to renal phosphate wasting and poorly mineralized bones. Due to the patient's age, phenotype, and lack of known cause for her disease, we performed whole-exome sequencing on her and her parents. A trio analysis identified 9 de novo mutations, including one in a gene expressed in osteoblasts - SVEP1(c.6617A>C, p.Glu2206Ala). This results in a small hydrophobic residue replacing a large hydrophilic one and has not been reported in any database, making it a good disease-causing candidate. We hypothesize that SVEP1 regulates FGF23 production; we predict that over-expressed SVEP1 will increase FGF23 release from osteoblasts and that this will also reduce the ability to mineralize bone.

Methods
To test our hypothesis, we used murine osteoblast MC3T3 cells as a model system. We made stable cell lines overexpressing SVPE1 by using a vector containing SVEP1 with a myc tag and a geneticin resistance cassette. We tested for SVEP1 overexpression using immunofluorescence, immunoblot, and real time PCR techniques.

Results
The results of our experiments showed that the transfected cells have increased SVEP1 and FGF23 expression. We are currently characterizing these models by measuring the amount of FGF23 secreted into media by ELISA and measuring the ability for the cell line to calcify matrix with a colourimetric assay.

Conclusion
This research is ongoing but we hope to demonstrate that increased SVEP1 increases FGF23 excretion and thus urinary phosphate wasting and rickets. This work will provide answers regarding the aetiology of the patient's disorder and also provide a valuable tool to test possible therapies.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 196
Presenter: Sicheng (Delia) Lee
Supervisor: Hyakutake, Momoe
Title: Evaluation of patient satisfaction and perspectives of virtual care in urogynecology at the Lois Hole Hospital for Women during the COVID-19 pandemic
Authors: Sicheng (Delia) Lee, Annick Poirier, Christina Yang, Maryna Yaskina, Momoe Hyakutake

Theme: Lifelong women's health

Introduction
Pelvic floor disorders (PFD) comprise a group of conditions affecting female reproductive and urinary health, which can negatively impact physical and psychosocial wellbeing. Because services provided through the urogynecology clinic at the Lois Hole Hospital for Women were considered non-essential during the COVID-19 pandemic, hundreds of women with PFD had their appointments cancelled or postponed. This resulted in the need to conduct appointments with physicians, physiotherapists, and nurses remotely, through various virtual platforms. Given the sudden transition to these new modalities, this study sought to determine the extent to which patients with PFD were satisfied with virtual care and the impact of the pandemic on their pelvic floor conditions. We hypothesized that patients would experience decreased satisfaction with virtual care as compared to in-person care.

Methods
The target population for this study was women aged 18 years or older with PFD who had appointments at the clinic from September 2020 to the present day. An online survey was created using REDCap, consisting of questions related to patients' appointment experiences (in-person visit, phone, Zoom, or Telehealth) with corresponding Likert scales and free-text comment boxes to assess the degree to which patients were satisfied with the quality of care and comfort level with using virtual modalities. The survey also captured demographic characteristics and patients' self-reported pelvic floor symptoms, which were assessed using the Pelvic Floor Distress Inventory, a validated questionnaire, to evaluate how pandemic restrictions affected pelvic floor health. Patients arriving for their appointments in the clinic were provided with links to the survey or were sent the survey link along with regular mailed communications from the clinic.

Results
While data collection is still ongoing, preliminary survey responses (n=7) show that women (age range = 25-80 years) preferred in-person to virtual appointments. All participants answered "disagree" or "strongly disagree" when asked whether a phone call or a virtual visit would have been more appropriate to meet their needs compared to an in-person appointment. Patients who had their original appointment rebooked due to pandemic restrictions (29%) reported being "satisfied" or "very satisfied" with the timing and clarity of communications received from the clinic regarding their appointment changes, respectively. Those older than 55 years of age (43%) felt uncomfortable using virtual platforms to communicate with healthcare providers despite having access to a personal electronic device with videoconferencing capabilities or lacked access to such a device. Delays in waiting to be seen for an appointment at the clinic and the perception of decreased continuity of care during the pandemic were also experienced by survey participants (43% and 14%, respectively).

Conclusion
Our data thus far suggest that virtual platforms may have a limited role in providing care that meets the specific health needs of those with PFD; however, further insights into patient experiences with virtual care are needed to better inform the improvement of healthcare delivery and access in the urogynecology clinic in the future.

This research has been facilitated by WCHRI through the generosity of the supporters of the Lois Hole Hospital for Women.

Participant #: 189
Presenter: Kelycia Leimert
Supervisor: Olson, David
Title: IL-1B is a central driver of inflammation in human fetal membranes and peripheral leukocytes
Authors: Kelycia B. Leimert, Magdalena M. Princ, Tania Rodezno, Lisa Finestone, Xin Fang, Sylvain Chemtob, David M. Olson

Theme: Pregnancy and developmental trajectories

Introduction: The transition of the uterus from a state of pregnancy to labour is an inflammatory process. Before the appearance of labour symptoms, many circulating peripheral maternal leukocytes migrate into the uterus due to a chemoattractant signal released from the fetal membranes. Here the gestational tissues and the leukocytes release more inflammatory cytokines and chemokines that attract more leukocytes, amplifying the inflammatory response. The cytokine, Interleukin(IL)-1B, plays a vital role in this transition. Rytvela is an allosteric IL-1 receptor antagonist that effectively delays preterm delivery and reverses the effect of fetal inflammation in many experimental animal models. In this study, we replicate this biological event using primary leukocytes and human fetal membrane explant models developed in our lab. We hypothesize that IL-1B will upregulate cytokine and chemokine release and that rytvela will reverse those effects.

Methods: 6mm fetal membrane (hFM) explants were excised and prepared from placentas collected from term non-labouring women undergoing elective caesarean sections at the Royal Alexandra Hospital in Edmonton, AB. Leukocytes were isolated and prepared from peripheral blood samples collected from term non-labouring women. Explants and leukocyte suspensions were then treated for 6h with 0, 0.1, 1, or 10 ng/mL IL-1B, with or without 10^-6 M rytvela. We measured mRNA expression levels of receptors and enzymes in hFM explants (n=7) and chemokine receptors in leukocytes (n=4-5) using RT-qPCR. We used multiplex assays to measure the concentration of up to 40 different cytokines and chemokines in the culture medium of explants (n=4) or leukocytes (n=3). Stat analysis: one-way or two-way ANOVA on log-transformed data with Tukey post-hoc testing when appropriate, significance at $p<0.05$.

Results: Treating hFM explants with IL-1B significantly upregulated the outputs of 28 cytokines ($p<0.05$). Rytvela co-administration significantly downregulated 13 of those 28 cytokines, often to control levels. ($p<0.05$). The IL-1B-induced change in hFM mRNA expression of MMP2, MMP9, COX-2, IL-1R1, or IL-6R was not statistically significant; therefore, rytvela also had no effect. Leukocytes treated with IL-1B alone increased their release of 23 cytokines ($p<0.05$). IL-1B also increased mRNA expression levels of chemokine receptors CXCR1 (4.3-fold), CXCR2 (3.1-fold), CXCR5 (1.95-fold), and CX3CR1 (3.1-fold), and rytvela decreased these expression levels ($p>0.05$).

Conclusions: IL-1B drives inflammatory amplification in human leukocytes and fetal membranes; rytvela effectively blocks much of this amplification. Since inflammatory amplification is the underlying driver for myometrial contractility, preterm birth therapeutics should not only target contraction but also inflammation.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 149
Presenter: Ricky Liu
Supervisor: Davidge, Sandra
Title: Placenta-derived extracellular vesicles from normal pregnancies induce endothelial dysfunction in human umbilical vein endothelial cells.
Authors: Ricky Liu, Roberto Villalobos-Labra, Anita Quon, Floor Spaans, Christy-Lynn Cooke and Sandra T. Davidge

Theme: Pregnancy and developmental trajectories

INTRODUCTION: Preeclampsia (PE) is a pregnancy complication characterized by new-onset hypertension after 20 weeks of gestation and evidence of end-organ dysfunction (e.g. proteinuria). The pathogenesis of PE is still unknown, but it is thought that systemic vascular/endothelial dysfunction is central to the development of this syndrome. A poorly developed placenta is proposed to be key in the impairment of vascular function in PE by directly releasing deleterious factors into the maternal circulation, such as syncytiotrophoblast-derived extracellular vesicles (STBEVs). STBEVs were shown to impair vascular function; however, the specific mechanisms are not known. We propose that STBEVs affect endothelial function via the lectin-like oxidized LDL receptor (LOX-1), an endothelial scavenger receptor which is upregulated in vessels of PE women. LOX-1 activation results in ERK and NF-kB activation, increased oxidative/nitrative stress, endothelial cell activation and apoptosis, all signs of endothelial dysfunction in PE, however, whether STBEVs induce these signs of endothelial dysfunction remains unknown. We hypothesize that STBEVs induce endothelial dysfunction by increasing ERK and NF-kB activation, increasing markers of oxidative/nitrative stress, and inducing endothelial cell activation and apoptosis.
METHODS: Human umbilical vein endothelial cells (HUVECs; n=4-9) were isolated from umbilical cords from normal pregnancies and treated with or without STBEVs isolated from normal placentas (100 µg/mL). ERK activation/phosphorylation (20 min. incubation, Western blotting) and NF-kB activation (1-6h incubation translocation to nucleus, immunocytofluorescence) were evaluated. Nitrative stress (nitrotyrosine levels, immunofluorescence), oxidative stress (ROS levels, DHE staining), and levels of NADPH oxidase 4 (NOX4, main ROS synthesizing enzyme in endothelial cells, Western blotting), intercellular adhesion molecule 1 (ICAM-1, marker of endothelial activation, Western blotting), and caspases 3 and 9 (markers of apoptosis, Western blotting) were assessed after 24h of incubation. Data were analyzed by students' t-test, or one-way ANOVA with Dunnett's post hoc test (NF-kB); $p<0.05$ was considered significant.
RESULTS: Exposure of HUVECs to STBEVs increased ERK (1.69±0.28 fold, $p=0.03$) and NF-kB nuclear translocation (3h: 1.71±0.22 fold, $p=0.02$; 6h: 2.11±0.22 fold, $p=0.001$) compared to untreated cells. STBEVs also increased NOX4 (1.44±0.13, $p=0.003$), ROS (1.28±0.07 fold, $p<0.0001$) and nitrotyrosine (1.44±0.04 fold, $p<0.0001$) levels in HUVECs. Compared to untreated cells, STBEVs did not induce any changes in ICAM-I, caspase 3 and 9 expression.
CONCLUSION: Our preliminary data suggest that STBEVs induce endothelial dysfunction by activating ERK, NF-kB, increasing NOX4 expression, and inducing oxidative and nitrative stress, all downstream pathways associated with LOX-1 activation. While these findings suggest that LOX-1 may be involved in the effects of STBEVs on endothelial function, further studies are required to confirm this role for LOX-1. Overall, these outcomes contribute to understanding the mechanisms underlying vascular dysfunction in PE women and allow for the development of new strategies to prevent and treat women affected by this syndrome.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 99
Presenter: Samantha Louie-Poon
Supervisor: Scott, Shannon
Title: Racism and the mental health of East Asian diasporas in North America: A scoping review
Authors: Samantha Louie-Poon, Sobia Idress, Tabatha Plesuk, Carla Hilario, & Shannon Scott

Theme: Children's health and well-being

Background: The COVID-19 pandemic heightened anti-Asian racism towards East Asian diasporas in North America. Experiences of racism encountered by East Asian communities have been documented to negatively impact their mental health.

Methods: A scoping review was undertaken following Arksey and O'Malley's (2005) methodology to (a) map the foci of literature on racism and the mental health of East Asian diasporas in North America and (b) identify gaps in the current literature.

Results: A total of 1309 articles were identified in May 2021. Based on the inclusion criteria, 35 records were included. Two distinct mental health foci were found: mental health outcomes and mental healthcare access and utilization. Majority (n=22) of the articles focused on racism at the interpersonal level. Six articles provided anti-racism solutions at the personal level such as overcoming biases. Five articles targeted anti-racism solutions from both the personal and institutional levels, while 1 article addressed barriers at the institutional level such as dismantling sanctioned power hierarchies.

Conclusion: The expanding knowledge base on COVID-19-related racial discrimination is reminiscent of previous literature examining the history of anti-Asian racism in North America. Greater attention is still needed to navigate impactful anti-racism solutions for the mental health of East Asian populations in North America.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 54
Presenter: Samantha Louie-Poon
Supervisor: Meherali, Salima
Title: Understanding sexual and reproductive health needs of immigrant adolescents in Canada: A scoping review
Authors: Samantha Louie-Poon, Mehnaz Rehmani, Megan Kennedy, Shannon Scott, Bukola Salami, Helen Vallianatos, Salima Meherali

Theme: Children's health and well-being

Background: Canada is a major destination country for immigrants globally. Despite the importance of immigrants in Canadian society, there is a scarcity of research on the sexual and reproductive health and rights (SRHR) needs of immigrant adolescents in the country.

Methods: A scoping review was undertaken following the PRISMA-ScR statement to identify and assess the existing literature regarding SRHR needs of immigrant adolescents in Canada. Of the 1514 articles retrieved from our search strategy, 15 studies met our inclusion criteria.

Results: The results from our review identifies three unique themes related to immigrant adolescents' SRHR needs: knowledge needs, access to SRHR education and services, and approaches to SRHR education and services. Immigrant adolescents' knowledge needs includes needs on HIV/STI transmission and protection, unintended pregnancy, sexual activity, family planning, pubertal education, navigating the health care system, and confidentiality legislations. Our results revealed that immigrant adolescents' access SRHR education and services through both school-based and community-based settings. Lastly, approaches to SRHR education and services for immigrant adolescents should include cultural sensitivity, an intersectional approach, interactive learning, a strength-based approach, and reassuring confidentiality rights.

Conclusion: The multi-faceted SRHR needs of immigrant adolescents in Canada demonstrates that future research, program development, and policymaking requires careful consideration of these intersecting forces. Inclusive SRHR education and services can be achieved through the employment of a critical cultural approach and intersectional strategies.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 88
Presenter: Ling (Lily) Lu
Supervisor: Ali, Samina
Title: Using a novel preference-informed complementary trial design to improve pain management of children's musculoskeletal injuries
Authors: Lily Lu, Manasi Rajagopal, Gareth Hopkin, Christopher McCabe, Lawrence Richer, Naveen Poonai, Maryna Yaskina, Anna Heath, Terry Paul Klassen, Samina Ali

Theme: Children's health and well-being

Introduction: Acute musculoskeletal (MSK) injuries are often associated with moderate-to-severe pain in children. An abundance of research confirms that pain management remains inadequate due partly to a lack of rigorous evidence to guide management. Recruiting families into trials that involve opioids can be challenging due to caregivers' beliefs and fears of opioid dependency. This multicentre trial of combination opioid and non-opioid or non-opioid alone for pediatric MSK pain involves a novel preference-informed complementary trial (PICT) design to interpret our results within the context of caregiver preference.

Methods: We developed a novel preference-informed complementary trial (PICT) design, whereby two trials are conducted simultaneously to determine the effectiveness of oral ibuprofen+oral hydromorphone comparing to oral ibuprofen+oral acetaminophen and oral ibuprofen alone. Caregivers of children 6-17 years presenting to the emergency department (ED) with acute limb injury with a self-reported pain score ≥5 are given the choice of which trial they wish to participate in: an opioid-inclusive, 3-armed trial, or a non-opioid, 2-armed trial before randomization. Both trials are designed as randomized, double-blind, placebo-controlled, superiority-trials. The goal is to enroll a minimum of 536 children across six Canadian pediatric EDs.

Preliminary Results: Recruitment began in April 2019 and is projected to continue until Summer 2022. We have recruited 522 participants (n=296 upper extremity, n=225 lower extremity injuries) as of July 2021; 346 were enrolled in the non-opioid trial and 176 in the opioid trial. The non-opioid trial has recruited n=164 females (47.4%) with a mean age of 11.0 years (SD 2.9); n=83 females (47.2%) were recruited for the opioid trial with a mean age of 11.6 years (SD 2.9). The PICT methodology allows families with strong preferences to participate, thereby improving the external validity by recruiting more representative populations.

Conclusion: Using a novel PICT design, we are conducting two randomized controlled trials simultaneously to determine the effectiveness of different oral analgesics in children with MSK injuries. This new design will allow researchers to understand patients' preferences, improve the external validity of trials of interventions subject to strong preferences, and engage and empower participants.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 115
Presenter: Jimmy Lu
Supervisor: Lemieux, Joanne
Title: Determining the role of rhomboid protease GlpG in pathogenic bacteria colonization: a potential solution to recurrent bacterial infections
Authors: Jimmy Lu, Elena Arutyunova, Heather Armstrong, Steven Verhelst, Eytan Wine, M. Joanne Lemieux

Theme: Lifelong women's health

Extra -intestinal pathogenic E. coli (ExPEC) colonization occurs naturally in the gut microbiome, however, when these strains spread to non-native niches, it leads to pathologies such as skin and urinary tract infections (UTI). If untreated, UTIs can spread further, resulting in a more serious condition: pyelonephritis, an infection in one or both of the kidneys. In the case of pregnant women, UTIs can result in vertical transmission to neonates leading to sepsis and morbidity, which is a significant problem in developing nations. Currently, UTIs are one of the most prevalent bacterial infections in women, with a predicted 1 in 2 women experiencing a UTI in their lifetime. This is largely due to their shorter urethra, giving bacteria a shorter distance to travel to the bladder. Treatments available today for UTIs are limited to antibiotics. This can lead to recurrent urinary tract infections as bacteria become resistant to the administered antibiotics. In order to investigate new, novel therapeutics to combat the problem of antibiotic resistance, a deeper understanding of the mechanism behind UTIs and bacterial infections is necessary. Recent studies have shown that glpG, the rhomboid protease gene, is essential for ExPEC colonization in the mouse gut suggesting GlpG could be a potential target to inhibit bacterial colonization as a means to combat bacterial infections.
Our preliminary data shows that when the glpG gene is inactivated in a laboratory E. coli strain using CRISPR/Cas9 mutagenesis, the bacteria display reduced pili formation on the other surface relative to the wild-type strain when visualized by transmission electron microscopy. Pili are long, filamentous appendages that assist bacteria in adhering to surfaces, such as host epithelial cells, subsequently leading to bacterial invasion. Our in vitro model measuring bacterial invasion in a human bladder cell line showed that when the glpG gene is inactivated in laboratory strain E. coli, there is significantly lower levels of invasion compared to the wild-type strain. These findings suggest that the GlpG protease plays a key role in bacterial virulence and may be a strong target for therapeutics against bacterial infections. To test if GlpG can be inhibited in live bacteria, we developed an assay to first measure GlpG activity in living E. coli cells. Using inhibitors specific to GlpG developed by our collaborators, we have shown that enzymatic activity is inhibited up to 50% in live E. coli. These inhibitors will be optimized using molecular GlpG-inhibitor modeling/crystallography to achieve greater inhibition of GlpG. Together, this is aimed to facilitate rational drug design as alternatives to conventional antibiotics for the purpose of treating UTIs and recurrent UTIs.

This research has been facilitated by WCHRI through the generosity of the supporters of the Lois Hole Hospital for Women.

Participant #: 89
Presenter: Richard Mah
Supervisor: Bourque, Stephane
Title: Perinatal Iron Deficiency Alters Patterns of Cellular Senescence and Apoptosis in the Developing Kidney in a Sex-Dependent Manner
Authors: Richard Mah, Andrew Woodman, Claudia Holody, Ronan Noble, Stephane Bourque

Theme: Children's health and well-being,Pregnancy and developmental trajectories

Introduction: Iron Deficiency (ID) is the most common nutritional deficiency worldwide with pregnant women most at risk. Perinatal ID has been associated with reduced nephron endowment and renal dysfunction later in life. It is unclear which mechanisms dictate changes observed in nephron formation; therefore, we sought to assess how perinatal ID alters patterns of cellular senescence and apoptosis, with are both important mechanisms in the developing kidney. We also assessed markers of oxidative stress and antioxidant defense due to their critical roles in modulating senescence and apoptosis. We hypothesized that ID alters patterns of senescence and apoptosis during development in tandem to increased oxidative stress and reduced antioxidant defenses, which may underlie future renal dysfunction.

Methods: Six-week-old Sprague Dawley dams were fed an iron-restricted (3-10 mg/kg) or iron-replete (37 mg/kg) diet two weeks prior to and throughout gestation. Offspring kidneys were collected within 24h of birth, cryopreserved, and subsequently cryo-sectioned. Apoptosis was assessed by TUNEL assay and caspase 3 and 9 activity assays. Cellular senescence was assessed via senescence-associated β-galactosidase (SA-βGal) activity. RT-qPCR was used to assess the expression of various antioxidant enzymes [catalase, superoxide dismutase (SOD)1 and 2, glutathione peroxidase, and glutathione reductase]. DNA oxidation was assessed by an 8-OHdG kit and glutathione levels were measured using available kits.

Results: ID resulted in neonatal anemia and decreased birth weight ($P<0.05$). Renal TUNEL staining and caspase 3 activity were increased in male ($P=0.01$; $P=0.009$) but not female ($P=0.85$; $P=0.96$) perinatal ID offspring. Caspase 9 activity was not affected in either sex. Perinatal ID reduced SA-βGal activity in the kidneys of both sexes ($P<0.01$). Perinatal ID increased expression of Sod1, Sod2, and glutathione reductase in male but not female offspring ($P<0.01$), but catalase and glutathione peroxidase expression was not altered. ID resulted in reduced total glutathione levels in male ID offspring ($P<0.01$) but 8-OHdG was not altered by ID.

Conclusion: Perinatal ID reduces renal developmental senescence in both sexes after birth. Male, but not female offspring exhibit altered antioxidant activity and increased apoptosis due to ID, potentially as a response to increased oxidative stress. These data suggest ID impacts pathways of senescence, apoptosis, and oxidative stress during development which may underlie future renal dysfunction in male offspring.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 210
Presenter: Radha Maradiya
Supervisor: Yokota, Toshifumi
Title: CRISPR-Cas9 genome editing restores dystrophin expression in skeletal and cardiac muscles in the canine X-linked Duchenne muscular dystrophy (DMD) dog model
Authors: Radha Maradiya, Rika Maruyama (ORCID ID: 0000-0002-5656-6930), Toshifumi Yokota (ORCID ID: 0000-0001-7316-3546)

Theme: Children's health and well-being

Introduction:
Duchenne muscular dystrophy (DMD) is a lethal genetic disorder resulting in progressive muscle degeneration. Since the DMD gene is X-linked, it affects males almost exclusively, with a prevalence of 1:3500 males. Its onset is in early childhood, usually between the ages of 2-3, and often patients are in a wheelchair by the age of 12. Mutations in the DMD gene occur more frequently at various mutation hotspots and result in the lack of dystrophin protein. This protein is found in skeletal and cardiac muscles and it strengthens muscle fibers, protecting them from injury. Currently, most DMD patients have no treatment option except for symptomatic treatments. However, a promising therapeutic approach for genetic diseases, including DMD, is Clustered regularly interspaced palindromic repeat (CRISPR)/Cas9-mediated genome editing. Many studies are developing genome editing therapies for the C-terminal mutation hotspot in the DMD gene, however, no study has applied this therapy to the N-terminal mutation hotspot in vivo. Our project examines the safety and effectiveness of the CRISPR/Cas9-mediated genome editing for the N-terminal mutation hotspot in vivo, which is a location that lacks effective treatment. By removing exons 6-9 by non-homologous end-joining, it is predicted to restore in-frame dystrophin mRNA, resulting in the production of a truncated, but functional dystrophin protein. We hypothesized that this treatment will increase dystrophin expression accompanied by amelioration of dystrophic phenotype in the DMD dog model.

Methods:
Our interventional study used both qualitative and quantitative methods to analyze the effectiveness of the CRISPR-Cas9 treatment. Skeletal and cardiac muscle samples were treated with adeno associated-viral vector 9 (AAV9)-mediated systemic delivery of CRISPR/Cas9 in Japan. After injection, frozen skeletal and muscle samples from wildtype, non-treated, and treated dogs were prepared for analysis. We looked at the right ventricle, tibialis anterior muscle, gastrocnemius, extensor digitorum longus, and the diaphragm. The pathological effects of the treatment were assessed by immunohistochemistry (IHC) for qualitatively assessing the presence of dystrophin, and hematoxylin and eosin staining for quantitative histological analysis.

Results:
The IHC showed significantly more dystrophin-positive fibres in the skeletal and cardiac muscles post-treatment, as compared to the non-treated. Histological analysis showed that the treated samples displayed a drastic decrease in the percentage of centrally nucleated fibres in the skeletal muscle, which is indicative of less fibre damage and regeneration. In addition, the variation of muscle fibre size, a feature of dystrophic skeletal muscle, was decreased after the treatment.

Conclusion:
This research indicates that our treatment is a promising therapeutic option for DMD patients carrying a mutation in the N-terminal mutation hotspot, which constitutes approximately 9% of DMD patients.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 142
Presenter: Susanna McDermott
Supervisor: Norris, Colleen M
Title: The impact of biological sex on the clinical characteristics and outcomes of adult patients diagnosed with SARS-COV-2 related myocarditis: a systematic review.
Authors: Susanna McDermott, Colleen M. Norris

Theme: Lifelong women's health

Hospitals and intensive care units are overwhelmed with COVID-19, as healthcare providers aim to care for their patients with evidence-based best practices. Many studies have been conducted exploring the clinical presentations and outcomes of SARS-CoV-2 patients to better understand the pathophysiology and effective interventions for COVID-19, and the extent to which the virus impacts major organs such as the kidneys, liver, and heart. Emerging data suggests that COVID-19 infection may result in myocarditis, which is an inflammation of heart muscle. This inflammation can be acute or chronic and affects individuals across the lifespan. However, there is a lack of discussion on the differences between biological sexes in the clinical presentation and outcomes of COVID-19 associated myocarditis. With consideration to the recognized disparities in female heart health, there is a demand for an in-depth review of this phenomenon. This systematic review will include an overview relevant literature on COVID-19 myocarditis and differences in clinical outcomes by sex, and synthesis of the results to learn more about the implications of sex on the outcomes of COVID-19 associated heart inflammation. This review will inform clinical practice related to women's heart health, specifically in the treatment of COVID-19 and its cardiovascular complications.

This research has been facilitated by WCHRI through the generosity of the supporters of the Lois Hole Hospital for Women.

Participant #: 214
Presenter: Qaasim Mian
Supervisor: Hawkes, Michael
Title: Implementing solar oxygen systems in Uganda: a qualitative study
Authors: Qaasim Mian, Sophie Namasopo, Robert Opoka, Michael Hawkes

Theme: Children's health and well-being

Introduction: Access to sustainable therapeutic oxygen for hypoxemia management in low-resource settings remains a significant global health issue. Our team has previously implemented solar-powered oxygen delivery (SPO2) systems for the management of pediatric pneumonia, the leading cause of childhood mortality worldwide, and demonstrated the feasibility, reliability and effectiveness of these systems. With demand for further access to oxygen for the treatment of childhood pneumonia, our team expanded solar oxygen delivery to twenty sites in Uganda from 2019-2021. Here we describe the implementation of solar-powered oxygen systems in Uganda and the experience of local users, including their knowledge, attitudes, and practices.

Methods: Qualitative study with four focus group discussions (FGDs) of five site champions each. Site champions were healthcare providers responsible for the oversight and data collection around solar oxygen delivery at their local health centre or referral hospital. Focus group discussion questions were probing and elastic, allowing participants to shape the discussion. Thematic analysis of the English translated transcripts was performed to synthesize qualitative data.

Results: Between 2019 and 2021, we implemented twenty solar-powered oxygen delivery systems at Health Centre IVs and referral hospitals across Uganda. FGDs (N=20) were conducted in September 2021 to understand the experiences of local users of the system. Site champions described limited and interrupted access to oxygen prior to implementation of the systems, improved patient outcomes with access to solar oxygen, and ongoing barriers in terms of education of patients and nurses around the use and effectiveness of oxygen. Additionally, new uses for solar oxygen beyond the scope of pediatric pneumonia management, including providing therapy for newborns or children with malaria, was highlighted by multiple participants.

Conclusions: SPO2 is an effective and sustainable means of oxygen delivery in low-resource settings with local conflict. FGDs with local site champions highlight the effectiveness of these systems in the management of pneumonia and other hypoxemic conditions, as well as ongoing issues around patient and staff education that should continue to be addressed.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 172
Presenter: Farag Mosa
Supervisor: Barakat, Khaled H. S.
Title: Studying the binding modes of various AhR ligands using a computational approach.
Authors: Farag Mosa, Ayman O.S. El-Kadi, Khaled Baraket

Theme: Lifelong women's health

Introduction: The aryl hydrocarbon receptor (AhR) is a ligand-activated transcriptional factor and regulates the expression of various genes. It plays a promoting role in the initiation, promotion, progression, invasion, and metastasis of cancer cells. The full-length AhR encompasses various domains, including bHLH, PAS A, PASB & transactivation domain. The PAS B domain plays a crucial role in regulating the activity of AhR by interacting with either AhR agonists/antagonists through its ligand binding domain (LBD). Here we focus on using computational modelling to study the structure of the PAS B region and understand how AhR ligands interact with residues in LBD. Methods: The crystal structure of the PAS B domain from mouse and human is not available; hence, we used different homology modelling algorithms to build their 3-dimensional (3-D) structures. The models were then refined using molecular dynamics (MD) simulations, followed by data mining and clustering analysis to extract their most dominant conformations. Compounds were then tested for their binding to the LBD using molecular docking simulations and energy affinity. Results: Structures for (HIF-1α) and (HIF-2α) were used as templates to build different models for the PAS B domain. HIF-1/2α showed ~31% sequence similarities to PAS B. 17 different PAS B models were built using different homology modelling algorithms and were evaluated using the Ramachandran plot. The most dominant conformations from human and mouse models represent 83% and 65%, respectively, used to dock various AhR ligands. Conclusions: Molecular docking and binding affinity predict how AhR LBD interacts with AhR modulators in their binding pocket and identifies the essential residues interacting with the different AhR ligands.

This research has been facilitated by WCHRI through the generosity of the supporters of the Lois Hole Hospital for Women.

Participant #: 83
Presenter: Rukhmani Narayanamurthy
Supervisor: Unsworth, Larry
Title: Localized drug delivery using pH and temperature-responsive nanoparticles to treat brain injury in newborns
Authors: Rukhmani Narayanamurthy, Jung-Lynn Jonathan Yang, Edward Armstrong, Jerome Y Yager, Larry D Unsworth

Theme: Children's health and well-being

INTRODUCTION
The interruption of oxygen and blood supply to the newborn brain around the time of birth is a risk factor for hypoxic-ischemic damage, leading to death or lifelong neurological impairments. Currently, therapeutic hypothermia is the only treatment to curb the extent of brain damage, though the effectiveness is limited. Anti-inflammatory drugs, such as dexamethasone, may inhibit the biochemical pathways of brain injury, but the challenge is to deliver drugs to the brain to avoid the side effects of systemic administration. We developed a novel drug delivery system using polypeptides that reversibly self-assemble into drug-loaded nanoparticles (<300 nm). As the nanoparticles release drugs in a manner dependent on temperature and pH, we take advantage of external head cooling and the distinctively acidic site of brain injury as cues for targeting the brain damage.

METHODS AND RESULTS
We use a neonatal rat model of hypoxic-ischemic brain damage for testing our drug delivery system. To effectuate selective brain hypothermia, we designed a "focal brain cooling chamber" for each rat pup, where each chamber consists of a syringe in which cooled water at 18°C was circulated through a coil of tubing fitted onto the rat's head. Furthermore, we identified the conditions under which nanoparticle formation with drug encapsulation occurs under physiological pH 7.4 and temperature, 37°C. We further identified the conditions under which nanoparticle formation with drug encapsulation occurs under physiological pH 7.4 and temperature, 37°C. The encapsulation efficiency was determined to be 1.3%. Littermates at postnatal day 7, both male and female, will be subjected to hypoxic-ischemic brain damage and then injected with dexamethasone-loaded nanoparticles and placed in cooling chambers to assess the combinatorial therapeutic effect of hypothermia with pharmacology. The nanoparticles are expected to release the drug at the injury site in response to change in temperature due to hypothermia and an acidotic pH environment. In addition to quantification of the released dexamethasone in the brain tissue using high-performance liquid chromatography, its pharmacological effect will be assessed by immunohistochemical staining of coronal brain sections for markers of apoptosis and microglial activation.

CONCLUSION
We anticipate that the drug delivery system will limit the extent of brain damage in the rat model and will open the possibility for clinical translation to improve survival and quality of life in infants with brain injury.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 215
Presenter: Kim Cuong Nguyen
Supervisor: Le, Lawrence H
Title: Measuring the Alveolar Bone Level in Adolescents: A Comparison of Ultrasound and CBCT
Authors: Kim-Cuong T Nguyen, Lawrence H. Le, Neelambar R. Kaipatur, Fabiana T. Almeida, Edmond H.M Lou, and Paul W. Major

Theme: Children's health and well-being

Introduction: Severe malocclusion can cause psycho-social problems in children and can lead to oral function issues such as difficulty in jaw movement, chewing, speech, and high susceptibility to periodontal diseases. Cone-beam computed tomography (CBCT) has been routinely used in orthodontic diagnosis and treatment planning. CBCT imaging typically delivers much higher radiation than conventional dental radiographs, which is harmful to children and adolescents, who are the most common orthodontic patients. Ultrasound is a non-invasive imaging method that uses reflections of mechanical waves and the target's acoustic properties to create an image without the use of harmful ionizing radiation. The aim of this study is to investigate the reliability and agreement of ultrasound and CBCT in measuring the alveolar bone level in adolescent orthodontic patients.

Materials and methods: 120 incisors from thirty orthodontic patients aged 12-17 years were scanned by an i-CAT 17- 19 dental CBCT system (Imaging Sciences International, Hatfield, PA, USA) with a 0.3mm voxel size and an ultrasound SonixTablet (Analogic, Vancouver, BC, Canada) with a 20 MHz phased array transducer. The distance from cemental-enamel junction to alveolar bone crest was measured by 4 independent raters for inter-rater reliability. The most experienced rater performed the measurement twice to evaluate intra-rater reliability and agreement between ultrasound and CBCT.

Result: Ultrasound had higher intra-rater (ICC = 0.85) and inter-rater reliabilities (ICC = 0.78) in measuring the alveolar bone level than CBCT (ICC = 0.69 and 0.76 for intra and inter-rater respectively). The average ultrasound measurement of the alveolar bone level of maxilla incisors was 1.31 ± 0.2 mm, in agreement with CBCT (1.27 ± 0.21 mm) while there was a significant difference between ultrasound (1.24 ± 0.22 mm) for mandibular incisors with the measurement of CBCT (1.43 ± 0.27 mm).

Conclusion: Ultrasound imaging has potential as an innovative, ionizing radiation-free, relatively inexpensive, portable, reliable clinical diagnostic tool to image dental tissues and assess the alveolar bone level in adolescent patients.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 129
Presenter: Jasmine Nguyen
Supervisor: Riddell, Meghan
Title: The role of atypical protein kinase c in regulation of endocytosis and exocytosis in the placental syncytium
Authors: Jasmine Nguyen, Khushali Patel, Sareh Panahi, Meghan Riddell

Theme: Pregnancy and developmental trajectories,Lifelong women's health

Introduction
The placenta is a fetally-derived organ that is the exchange site for nutrients and waste between mother and fetus. Placental dysfunction results in major pregnancy complications like intrauterine growth restriction (IUGR) or preeclampsia (PE). One of the key features of these complications is malfunction of the syncytiotrophoblast (ST), the single massive cell that covers the placenta's entire surface. The ST is unique because it lacks lateral cell borders and therefore has a discontinuous actin cytoskeleton, with separate apical and basal actin networks. The actin cytoskeleton provides structure to cell and is also important for endocytosis and exocytosis, the processes that allow for internalization and secretion of biomolecules in cells. Alterations in the actin cytoskeleton and endo/exocytosis have been observed in IUGR and PE, but the mechanisms that govern these fundamental functions remain largely unknown in ST. Atypical protein kinase Cs (aPKCs) are a group of proteins that regulate actin structure and endocytosis in other epithelial cells. We have discovered that aPKCs play a critical role in maintaining the actin cytoskeleton of the ST. However, the functional consequences of ST aPKC-dependent actin regulation remain to be addressed. Hence, here we examined the effect of aPKC inhibition on ST endocytosis and exocytosis.
Methods
10-12 wk. human placental explants were cultured +/- 5μM aPKC pseudosubstrate inhibitor for 2hrs and then incubated with rhodamine-transferrin. After extensive washing, explants were fixed, stained with anti-early endosome antigen-1 (EEA1) and Phalloidin (F-actin), and imaged by confocal microscopy. Colocalization of transferrin/EEA1 was quantified with Volocity software. To examine exocytosis, medium was collected from 10-12 wk. human placental explants after 12hrs +/- 5μM aPKC pseudosubstrate inhibitor. Human chorionic gonadotropin-β (hCG-β) was measured from the medium via ELISA assay and normalized to total protein.
Results
We observed a significant (P=0.0073, n=4) 2-fold increase in the colocalization of transferrin and EEA1 following treatment with aPKC pseudosubstrate inhibitor, indicating an increase in endocytosis. Early endosomes were also distinctly larger following treatment, which could indicate either endosome fusion or aggregation. Taken together, this demonstrates that aPKCs are important for regulating endocytic trafficking. Placental explants treated with aPKC pseudosubstrate inhibitor also show a 1.6-fold increase in relative extracellular hCG-β (P=0.0015, n=2), which suggests that aPKCs may also play a role in regulating exocytosis.
Conclusion
Our data show that aPKCs regulate endocytosis in the ST and may also modulate exocytic trafficking, most likely by regulating the maintenance of the apical actin cytoskeleton. Because only one endocytic cargo was used, future directions include examining other markers to assess if the observed relationship between aPKCs and endocytic regulation is cargo-specific. Understanding the mechanism by which endocytosis/exocytosis occurs normally in the placenta will allow us to better identify potential causes for placental dysfunction during pregnancy, leading to the development of treatments for pregnancy complications in the future.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 139
Presenter: Saad Nizamani
Supervisor: Graf, Daniel
Title: ELUCIDATING THE ROLE OF MMP14 IN THE TEMPOROMANDIBULAR JOINT
Authors: Saad Nizamani, Haiming Lin, Pallavi Parashar, Dawei Zhang, Xiaodan Xia, Maria Alexiou and Daniel Graf

Theme: Children's health and well-being

Introduction: Membrane-type matrix metalloproteinase 1 (MMP14) is a transmembrane zinc-endopeptidase that activates other MMPs and cleaves cell surface receptors; along with regulating the breakdown of the extracellular matrix (ECM). The temporomandibular joint (TMJ) connects the jaw (mandible) to the skull. An important pathology is idiopathic condylar resorption, a poorly understood condition of the TMJ most commonly observed in teenage girls. Here, we use an inducible MMP14 knockout model to assess the potential role of MMP14 in the maintenance of the TMJ.

Hypothesis: Loss of MMP14 alters cell-signalling and ECM leading to changes in TMJ condyle homeostasis.

Methods: Loss of MMP14 was achieved by injecting tamoxifen in adult mice for 7 days. Micro-CT was used to determine the changes in the TMJ condyle at 6 weeks. H&E staining was used for histological examination.
TRAP staining was used to identify osteoclast activity. Picrosirius red staining was used to study collagen fiber orientation. Immunofluorescence (IF) was used to identify Aggrecan. The stains and IF were done at 6 weeks post injection. Areas of interest were the interface of the condyle, along with the TMJ joint surface.

Result: In the Micro-CT analysis, the condyle of the mutant mouse showed significant changes to its bone and appeared coarser than the control. H&E staining showed changes to bone and cartilage surface, as well as deposition of fibrous tissue and increased cellularity at the muscle attachment sites of the condyle in the mutant . TRAP staining showed strong osteoclast activity at this interface and the subchondral region of the condyle. Picrosirius red staining showed disorganized fibres at the interface of the condyle. Aggrecan appeared increased in the MMP14 mutant.

Conclusion: Loss of MMP14 leads to a rapid and dramatic resorption of the condyle accompanied with deposition of fibrous tissue at the joint attachment sites, correlating well with the Micro-CT results. Tendon attachment to the bone transformed into fibrous tissue showing unexpected osteoclast activity suggestive of bone resorption between the disorganized fibres. Appearance of chondrocytes in the cartilage was changed and Aggrecan, an important cartilage ECM molecule, appeared increased.
Our study reveals that MMP14 is a key molecule maintaining TMJ homeostasis. Its loss is associated with dramatic condylar changes reminiscent of idiopathic condylar resorption. This mouse model provides a segway to investigate cellular processes involved with condylar resorption and should lead to better insight into this devastating condition.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 132
Presenter: Hannah Oatley
Supervisor: Hawkes, Michael
Title: The impact of birthweight on pneumonia severity in Uganda
Authors: Hannah K. Oatley, Robert O. Opoka, Sophie Namasopo, Manoj Kumar, Michael Hawkes

Theme: Children's health and well-being

Introduction: Low birthweight status is a recognized risk factor for severe and fatal paediatric pneumonia; however, its independent impact has not yet been elucidated. We hypothesized that low birthweight would be a risk for severe pneumonia, after accounting for current nutritional status, socioeconomic status, and other covariates.

Methods: We conducted a retrospective cohort study nested within a cluster RCT. Inclusion criterion were: age < 5 years, hospitalization, hypoxemia (SpO2 < 92%), and clinical diagnosis of pneumonia. Exclusion criterion were: preterm birth, missing data for birthweight or RISC score. Data were extracted from caregiver questionnaires and clinical records collected across 19 hospitals in rural Uganda between July 2019-December 2020. The primary outcome was pneumonia severity, represented by a composite clinical severity score, the Respiratory Index of Severity in Children (RISC). The independent (predictor) variable of interest was birthweight. Covariates included: severe acute malnutrition, designated by mid-upper arm circumference (MUAC) < 11.5cm; socioeconomic status, denoted by a multidimensional poverty index (MPI) score; and food availability designated by number of food items in granary. Multiple demographic and child health confounders were considered. A multilevel regression analysis accounted for the non-independence of the data. The RISC score was treated as continuous for linear and multilevel regressions, supplemented by non-parametric tests as a validity check.

Results: 881 children were included in the analysis. The median RISC score was 2 (IQR 1-4). Median birthweight was 3 kg (IQR 2.6-3.4 kg); 89 children (10%) had a low birthweight (<2.5 kg). For every 100 gram increment in birthweight, there was an associated .07 decrease in RISC score (p=.04), with non-parametric tests confirming statistical significance of the association. Age, sex, MUAC, and MPI were entered as a-priori confounders. Food availability was included based on univariate associations with birthweight and RISC. Multilevel regression showed that 20% of the variance in pneumonia severity was attributable to the site. Birthweight was not significantly associated with pneumonia severity once clustering and effects of confounders were controlled (change in -2*loglikelihood =.55, ns). Secondary analyses showed that MUAC was associated with pneumonia severity, after controlling for relevant confounders (change in -2*loglikelihood =23.25, p<.001). The final model with birthweight, MUAC and all confounders explained 7% of the total variance in pneumonia severity, with the strongest predictors being MPI and MUAC.

Conclusion: In this retrospective cohort study, low birthweight amongst term infants is not independently associated with pneumonia severity once appropriate analytic methods that deal with clustering and confounders are utilized.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 153
Presenter: Julia Parkman
Supervisor: Pin, Sophia
Title: Utility of pre-operative computed tomography imaging in management of primary endometrial carcinoma in patients presenting to the Cross Cancer Institute in Edmonton, Alberta
Authors: Dr. Julia Parkman, Dr. Helen Steed, Dr. Valerie Capstick, Dr. Sophia Pin

Theme: Lifelong women's health

Introduction: Endometrial cancer is the fourth most common cancer among women in Canada after breast, lung, and colorectal cancer. The standard of care for the management of early-stage endometrial cancer is surgical staging in the form of total hysterectomy, bilateral salpingo-oophorectomy, with possible pelvic and para-aortic lymph node dissection, most commonly performed by laparoscopy. However, neoadjuvant therapy or other surgical procedures may be recommended depending on cancer stage and tumor factors. The Gynecologic Oncology group at the Cross Cancer Institute (CCI) in Edmonton, Alberta requests computed tomography (CT) scans of the chest, abdomen, and pelvis for preoperative staging for all serous and clear cell endometrial cancers, as well as Grade 2 and 3 endometrioid adenocarcinomas of the endometrium. Given budgetary constraints, some patients are not able to obtain a staging CT scan prior to their proposed surgical date. This is concerning as it is thought that pre-operative imaging for selected patients provides additional information that may alter management recommendations. In the era of Choosing Wisely Canada, it is important to strategically choose investigations during patient workup. Unnecessary imaging contributes to a backlog in the system and limits timely access to imaging for emergent reasons. The objective of this study is to determine if preoperative CT imaging changes management for patients presenting with primary endometrial cancer in Edmonton, Alberta.

Methods: This is a single-site retrospective cohort study. Cases will be identified from an endometrial cancer database as well as from the Alberta Cancer Registry. Inclusion criteria include women with pre-operative pathology-confirmed endometrial carcinoma and a pre-operative CT scan, presenting to the CCI from January 2012 to December 2019, with a primary presentation of endometrial cancer. Change in management related to preoperative CT imaging will be measured as a dichotomous variable (Yes/No) and will be suggested by any management other than surgical staging in the form of total hysterectomy, bilateral salpingo-oophorectomy, with possible pelvic and/or para-aortic lymph node dissection, performed via a minimally invasive approach. Chart review will be used to confirm the change in management was driven by preoperative imaging, and not by other factors such as tumour histology on pre-operative sampling, patient co-morbidities or surgical history.

Expected Results: It is expected that a change in management related to preoperative CT imaging will be significant only in some subtypes of endometrial cancer.

Conclusion: The results of this study will guide clinicians managing patients with primary endometrial cancer, and encourage conservation of resources in Alberta's healthcare system, by identifying the patients most likely to benefit from preoperative CT imaging.

This research has been facilitated by WCHRI through the generosity of the supporters of the Lois Hole Hospital for Women.

Participant #: 131
Presenter: Mazhar Pasha
Supervisor: Davidge, Sandra
Title: Role of Endoplasmic Reticulum and Oxidative Stress in Advanced Maternal Age
Authors: Mazhar Pasha, Raven Kirschenman, Floor Spaans, Christy- Lynn Cooke, Sandra T. Davidge

Theme: Pregnancy and developmental trajectories

Introduction
Advanced maternal age (≥35 years) increases the risk of pregnancy complications, which may be due to poor cardiovascular adaptations to pregnancy in aged women. Aging is associated with vascular stiffness and endothelial cell dysfunction, potentially through increased oxidative stress. Recent research shows a strong interplay between oxidative stress and endoplasmic reticulum (ER) stress (cellular stress due to accumulation of misfolded proteins) leading to endothelial dysfunction. However, whether ER stress also impacts vascular adaptations to pregnancy at advanced maternal age is not known. We hypothesize that vascular adaptations to pregnancy are impaired at advanced maternal age, due to increased oxidative and ER stress.

Methods
Pregnant young (4 months) and aged (9.5 months of age; ~35 year in humans) rats were studied on gestational day 20 (term=22 days) and compared to age-matched non-pregnant rats (n=6-10/group). Mesenteric arteries were isolated to assess vascular function ex vivo using wire myography. Endothelium-dependent relaxation to methycholine (MCh) was assessed in the presence/absence of apocynin, an inhibitor of NADPH oxidases (NOX; enzymes that produce oxidative stress). Given the potential role of oxidative and ER stress in modulating endothelial function, NOX-4 protein levels, as well as ER stress markers (GRP78, P-eIF2α, CHOP, and XBP-1) were quantified in mesenteric arteries by Western blotting. All Western blot data were calculated as % of young non-pregnant controls. Data were analyzed by two-way ANOVA with Sidak's post test, $p<0.05$ was significant.

Results
MCh-induced vasodilation responses were not different between all groups. However, apocynin increased sensitivity to MCh only in aged non-pregnant rats (pEC50 [dose that induces 50% of max response]: control: 7.22±0.04 vs apocynin: 7.54±0.08; p=0.03). Mesenteric artery NOX-4 protein expression was higher only in aged non-pregnant vs young non-pregnant controls (NOX: 297.99±22.00%; p=0.003). Similarly, ER stress protein expression was higher in aged non-pregnant vs young non-pregnant controls (GRP78: 148.31±17.82%; p=0.03; P-eIF2α: 158.73±5.58%; p=0.03; CHOP: 155.18±16.66%; p=0.04; sXBP-1: 185.83±17.75%; p=0.01). Whereas no changes were observed in oxidative and ER stress proteins in aged pregnant vs aged non-pregnant rats.

Conclusion
Our results demonstrated increased modulation of vasodilation by NOX and elevated NOX-4 protein, only in aged non-pregnant rats, which reflects the detrimental role that oxidative stress has in aged vasculature. Further, an increased expression of ER stress proteins in aged non-pregnant suggests that ER stress may be a contributing source of oxidative stress, promoting vascular dysfunction in aging. Intriguingly, NOX inhibition had no impact on vascular function in aged pregnant vessels, nor were there any changes observed in oxidative and ER stress proteins levels. Thus, we speculate that in healthy aged vasculature, pregnancy may confer vascular protection. However, maternal aging is often associated with co-morbidities, thus future studies are warranted.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 113
Presenter: Vaishvi Patel
Supervisor: Ross, Sue
Title: Assessing menopause knowledge to help improve quality of life for menopausal women
Authors: Vaishvi Patel, Sue Ross, Beate C Sydora

Theme: Lifelong women's health

Introduction:
Menopause and the menopause transition period are characterized by profound hormonal changes which bring about mental and physical changes within the body. Due to menopause being a largely invisible and unmentioned and under-discussed topic in wider society, women often deal with menopause-related complications on their own. Social support and education have been shown to reduce negative menopausal experiences and improve quality of life. Through this study, we hope to assess the level of knowledge young adults have on menopause and to create interventions that target their knowledge gaps so that they could better support older women including their family members or other contacts. We postulated that there is a general lack of knowledge about menopause among young adults; increasing menopause knowledge may increase their understanding of women's experiences and difficulties during their menopause transition.

Methods:
We created an electronic questionnaire to assess the level of knowledge University students have on menopause and to define knowledge gaps. Survey questions were based on menopause literature and guidelines from the International Menopause Society (IMS) and the North American Menopause Society (NAMS) and were pilot tested on menopause clinicians (n=5), young people in target group age (n=14; 7 male and 7 female) and women experiencing menopause (n=4) to collect feedback for questionnaire improvement. The final questionnaire included questions on participant demographics, general menopause knowledge, and options to support menopause management. A knowledge self-assessment scale was provided at the beginning and the end of the survey. The questionnaire was distributed to University of Alberta students through student digest newsletters. Answers were collected anonymously in the secure web-based application REDCap, and students were given the opportunity to participate in a draft for a gift card. Descriptive statistics were applied to characterize participants and to compare menopause knowledge between different groups.

Results:
Out of 930 survey respondents, 746 (73 graduate and 673 undergraduate) completed the survey: the average age was 22.2 ± 5.1. Participants belonged to all faculties and included students from a variety of family settings and living conditions. Most participants were female (83.6%) and caucasian (53.3%). Both males and females reported increased knowledge confidence at the end of the survey; on average females reported higher levels of confidence than males. Interacting with a woman undergoing or past menopause was also associated with a higher level of menopause knowledge and confidence.

Conclusion:
Our results indicate gender, as well as a personal connection to menopausal women, affect the degree of menopause knowledge in young adults. We aim to further explore our data to identify specific knowledge gaps and to address the gaps with targeted educational programming. These resources will help young women to be better prepared for their own menopause, for partners to be able to understand their counterparts once they undergo menopause transition, and for both groups to show compassion and support for female relatives and friends undergoing this change.

This research has been facilitated by WCHRI through the generosity of the supporters of the Lois Hole Hospital for Women.

Participant #: 206
Presenter: Khushali Patel
Supervisor: Riddell, Meghan
Title: Atypical protein kinase C isoforms regulate placental syncytiotrophoblast actin cytoskeleton
Authors: Khushali Patel, Jasmine Nguyen, Sareh Panahi, Meghan Riddell

Theme: Pregnancy and developmental trajectories

Introduction
Intrauterine growth restriction (IUGR) is a common pregnancy complication that develops due to placental dysfunction. Malfunctioning of the syncytiotrophoblast (ST), the cell lining the placenta surface, is central to the development of IUGR. Under normal conditions, polarization drives the ST actin cytoskeleton to form membrane protrusions on its apical membrane, known as microvilli, which are supported by a filamentous actin (F-actin) core. Microvilli functionally increase the apical surface area for enhanced maternal-fetal exchange. Importantly, ST microvilli are lost via unknown mechanisms in IUGR. Active maintenance of cell polarity is crucial to maintain ST microvillar homeostasis, therefore disturbed ST polarity may lead to placental dysfunction and the development of IUGR.
Atypical protein kinase C (aPKC) isoforms are evolutionarily conserved apical polarity regulators. In other tissues, aPKCs regulate microvilli via actin and activation of ezrin- a key actin linker protein. Thus, we hypothesized that aPKC isoforms maintain the ST apical surface and polarity.

Methods
10-12 wk. human placental explants were cultured +/- 5μM myristoylated aPKC inhibitor for 6 hrs. and fixed for immunostaining and scanning electron microscopy. Immunofluorescent staining with anti-ezrin and anti-phospho ezrin (Thr567) antibodies; Phalloidin (F-actin) and Hoechst (nucleus) was performed and imaged with confocal microscopy.

Results
Confocal images (n=4) revealed 60% decrease in mean signal intensity of ST apical phalloidin (p=0.008) with aPKC inhibitor treatment. Additionally, confocal imaging (n=3) shows that in the absence of active aPKC, there is ~50% decrease in the phospho-ezrin: total ezrin ratio.

Conclusion
Our data suggests that aPKC isoforms regulate ST apical surface structure via regulation of actin remodelling and/or ezrin activation. The roles of individual aPKC isoforms will be addressed in the future using siRNA knockdown. Thus, by understanding the processes regulating ST microvilli homeostasis, we will be able to identify previously unrecognized mechanisms that may cause placental dysfunction. This could lead to the development of treatments for pregnancy complications and healthier pregnancies in the future.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 165
Presenter: Yuba Raj Paudel
Supervisor: Voaklander, Don
Title: Barriers and facilitators to implementation of newborn jaundice assessment clinical practice guideline in Alberta
Authors: Yuba Raj Paudel, Seija Kromm and Deborah McNeil

Theme: Children's health and well-being

Introduction
Alberta Health Service's (AHS) Clinical Practice Guideline (CPG) for screening and management of newborn jaundice was implemented in 2019. The CPG follows the Canadian Pediatric Society (CPS) guideline requiring universal screening of newborns for jaundice within specified timelines using accepted protocols. The aim of this study was to identify facilitators and barriers to implementing the guideline.

Methods
Using a cross-sectional qualitative research design, we conducted semi-structured interviews with Public Health (PH) from each AHS zone in early 2021. Interview data was analyzed thematically using both deductive and inductive approaches. The elements of the consolidated framework for implementation research (CFIR) provided structure for the interview guide and the deductive analysis. Current findings are based on 6 interviews with 6 public health managers from all AHS zones.

Results
Facilitators to implementation were: the ability to adapt guideline implementation based on each zone's local context and needs, CPG's alignment with existing practices (following the CPS guideline), ability of zones to use existing organizational structures, the province-wide applicability of the CPG to PH and acute care, knowledge of the guideline among PH leadership/service delivery teams, and a strong commitment of public health educators. However, PH nurses thought that the guideline was focused on acute care and had limited information on parental education and infant feeding. It also lacked details on PH nurses' roles. Barriers to implementation were: acute care and PH did not have a common understanding regarding the other's roles and responsibilities, limited or no commitment of some community physicians to follow the CPG, communication barriers such as acute care not always following the PH protocols , delays in sending the notice of birth to PH, lack of awareness of differences in PH practices and follow-up service availability between AHS zones. Finally, some thought that PH was not sufficiently involved in the guideline's development and the processes for guideline implementation did not take into account remote/rural challenges.

Conclusion
AHS' Jaundice CPG was perceived as an important tool to standardize screening and management of newborn jaundice. CPG development needs to include the roles of all applicable healthcare providers. As well, differences between AHS zones need to be accounted for to support implementation. This can also help improve patient/caregiver experience by increasing coordination of care and reducing delays in record keeping and patient follow-up. Strong engagement from and focus on educating PH nurses were important facilitators as PH nurses do patient follow-up and record keeping.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 92
Presenter: Thanh-Tu Pham
Supervisor: Lou, Edmond HM
Title: A Phantom Study to Validate Using Ultrasound to Image Hip Displacement in Children with Cerebral Palsy
Authors: Thanh-Tu Pham, Lawrence H. Le, Thanh-Giang La, John Andersen, Edmond H. Lou

Theme: Children's health and well-being

Introduction: Cerebral palsy (CP) is a group of permanent physical disabilities affecting movement and posture, resulting from disturbance to the developing brain. Individuals with CP often experience progressive musculoskeletal deformity which can contribute to lifelong functional limitations and chronic pain. Hip displacement is a common orthopedic deformity in children with CP, affecting one third of children in the population. Surveillance and early intervention of hip displacement has been demonstrated to prevent hip dislocation. Radiography is the current standard of care to assess hip displacement. Repeated exposure to ionizing radiation may increase cancer risks for pediatric patients. Non-ionizing ultrasound has shown promise as an alternative imaging modality to quantify hip displacement. However, validation of ultrasound imaging methods has not been investigated. The objective of this study was to assess the accuracy of ultrasound method in quantifying hip displacement.
Method: Reimer's migration percentage (MP), the ratio of femoral head-acetabulum distance (A) to the width of the femoral head (B), is used to quantify hip displacement. A 3D-printed hip phantom with known MP was used in this study. Markers were added to the phantom to highlight the landmarks used for the measurement. The phantom was immersed in a water tank to enable good coupling between the surface of the ultrasound transducer and the imaged hip joint. Anterior and lateral scans were acquired with latter's orientation rotated 90 degrees with respect to the former's. The distance A was directly measured on the coronal image of the hip whereas the width B was estimated by the diameter of a best-fitted circle to the partially visualized femoral head on the transverse image in a least square sense. An AP X-ray image of the hip phantom was taken for comparison. Two raters (R1 and R2), each with 2 years experience on X-ray measurements but no experience on ultrasound, performed the measurements. They measured 5 times of A and B on the radiograph and 5 times of A only on the ultrasonograph. The average and the standard deviation of the MP values from the 3D digital design, ultrasound, and X-ray were compared. The mean absolute differences (MAD) of the MP measurements between R1 and R2 on ultrasound and X-ray images were also reported.
Result: The MP obtained from the digital 3D design was 35.9% ± 0.2%. The MP values from the ultrasound and X-ray images were 35.1% ± 0.1% and 37.1% ± 0.2% by R1, and 35.2% ± 0.1% and 37.8% ± 0.2% by R2, respectively. The MADs of the MPs between the ultrasound and 3D design methods was 0.7% ± 0.1% and between the ultrasound and X-ray was 2.3% ± 0.4%. The MADs of the MP values between R1 and R2 on ultrasonograph and radiograph were the respective 0.1% and 0.7%.
Conclusion: The phantom study showed the ultrasound method provided more accurate assessment of hip displacement than the X-ray method when comparing with the 3D phantom design. The difference of MP measurement between the two raters on ultrasound was less than that on X-ray, but it was not statically significant (both are < 1%). Clinical study will be conducted to further validate the ultrasound method.

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Participant #: 188
Presenter: Magdalena Princ
Supervisor: Olson, David
Title: IL-6 upregulates inflammatory signaling in term pregnant maternal leukocytes, but not fetal membranes

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Theme: Pregnancy and developmental trajectories

Introduction: Interleukin (IL)-6 is a cytokine that influences birth timing in mice and is upregulated in gestational tissues as labour approaches at both term and preterm. In vivo studies have shown that IL-6 clearly has an important role in labour and delivery, but little is known about exactly how IL-6 acts in the mechanism of birth. Our objective was to elucidate the inflammatory actions of IL-6 in human cells and tissues, hypothesizing that IL-6 would stimulate the release of cytokines and chemokines and their receptors in fetal membrane tissues and maternal leukocytes.
Methods: Peripheral blood samples and placentas were collected from consenting women undergoing elective caesarean section (term non-labouring, TNL) or spontaneous term delivery (term labouring, TL) at the Royal Alexandra Hospital in Edmonton, AB. A 6mm tissue punch was used to excise fetal membrane (hFM) tissue explants. Explants were acclimated for 48 hours before treatment with 1, 10, or 100 ng/mL IL-6 for 6 hours. Cytokine/chemokine release was detected in the medium collected from the TNL fetal membrane treatments via multiplex assay (n=5). Leukocytes were isolated from whole blood samples and treated with 100ng/mL IL-6 for 6 hours. RNA was extracted from both hFM (n=2) and leukocytes (TNL n=3-4; TL n=3) and analyzed via RT-qPCR to detect changes in mRNA expression levels of cytokines or chemokine receptors. Statistical analysis: paired t-test or one-way ANOVA with Tukey post-hoc testing, significance achieved at $p<0.05$.
Results: Multiplex results from hFM tissues revealed no significant changes in cytokine/chemokine release upon stimulation with IL-6 at any dose. Moreover, preliminary RT-qPCR results from FM tissues further showed that IL-6 stimulation did not cause a concentration-dependent change in IL-6, CCL2, CXCL8, or CXCL10 mRNA levels. Conversely, IL-6 stimulated leukocyte mRNA receptor expression for CXCR1, CXCR2, CXCR5, and CX3CR1 for both TNL and sTL samples, but the change was not statistically significant ($p>0.05$).
Conclusion: Our preliminary work in term pregnant tissues demonstrates that IL-6 appears to play a greater inflammatory role at the level of the circulating maternal leukocytes than in hFM tissues. Much remains to be done to fully elucidate the role of IL-6 in both term and preterm delivery.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 60
Presenter: Neelam Punjani
Supervisor: Papathanassoglou, Elizabeth
Title: Experiences of Sexuality among Pakistani-descent Adolescent Girls: "Am I a bad daugther"
Authors: Neelam Punjani
Elizabeth Papathanassoglou
Kathy Hegadoren

Theme: Children's health and well-being,Lifelong women's health

Background

Adolescence is a critical period in the transition from childhood into adulthood, during the course of which young children aged 11-19 years' experience substantial physical, psychological, social, and emotional changes. Sexual health incorporates a wide range of interlinked mental, physical, and emotional factors. In Alberta, immigrant youth and children account for 31% of the total immigrant population. The experience of developing sexuality and any relationships with their well-being have not been studied among Pakistani-descent adolescents in Canada.

Purpose

The purpose of my research is to explore the experience of developing sexuality and their relationship to psychological well-being in middle- to late- adolescence girls of Pakistani-descent, living in Edmonton, Alberta.

Methodology

The Interpretive Description (ID) approach was used to study the complex phenomena in depth. A purposive sampling strategy was used to enroll adolescent girls (ages 14-19 years) and were interviewed using a semi- structured interview guide. Iterative and inductive analysis approach was used. NVIVO 11.0 was used to organize and manage the datasets generated in the study.

Results

Study results suggest that most of the adolescent girls have confusion about sexual identity and they concealed their identities due to fear and stigma from their portents and society. Many girls expressed that they face parental opposition towards early sexual health education. Also, the cultural differences between parents and children makes it difficult for young girls to explore their sexuality. Adolescent girls also lack sexual health decision making as it is mostly controlled by parents. The power relationships and dynamics between girls and their families because of typical patriarchal systems of gender made some of the girls in this study vulnerable to poor psychological outcomes such as anxiety and stress.

Conclusion

It is important to increase awareness of the psychological aspect of sexuality. My doctoral research incorporates patient engagement principles i.e., inclusiveness, support, mutual respect, and co-building through the creation, dissemination, and evaluation of a youth friendly sexual health interventions for adolescent girls to improve their psychological wellbeing. My research outlines the adoption of a solution-based approach to improve mental health of adolescent girls by co-creating interventions for them. An essential component of this research project was the involvement of adolescent girls through the many stages of development. As a result of my research young girls, will be empowered and more confident to be meaningful partners in sexual health decision making, which will make a meaningful contribution to patient-oriented research.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 208
Presenter: Jad-Julian Rachid
Supervisor: Bourque, Stephane
Title: Increases in mitochondrial respiration with ketone targeted therapy of perinatal iron-deficiency
Authors: Jad-Julian R. Rachid, Claudia D. Holody, Ronan M.N. Nobel, Heather Mast, Helene Lemieux and Stephane L. Bourque

Theme: Children's health and well-being,Pregnancy and developmental trajectories

Introduction:
Iron deficiency (ID) is the most common nutritional disorder in the world. The most susceptible subpopulations are pregnant women and young children. If left untreated, ID can adversely affect pregnancy outcomes, including increasing the risk of intrauterine growth restriction and preterm birth. With ID affecting developmental trajectories, children born to ID mothers are at a higher risk of developing cardiovascular disease in later life. We have identified mitochondrial dysfunction in the developing heart and kidney as potential mechanisms underlying the altered trajectories caused by perinatal ID, although the nature of this dysfunction is unclear. Neonatal hearts of ID offspring also exhibit reduced ability to produce certain metabolic substrates, such as ketones. In addition to being fuel substrates, ketones also exhibit antioxidant and anti-inflammatory effects. The aim of this study was to determine if maternal administration of ketone esters in the last week of gestation could elevate circulating ketone esters in ID neonates, and in turn, improve renal and cardiac mitochondrial respiration in the offspring.

Methods:
Female Sprague Dawley rats are fed either an iron-replete (37mg/kg) or an iron-restricted (3mg/kg) diet prior to and during pregnancy. Ketone esters (5mg/kg) were administered to the dam via daily subcutaneous injections. Mitochondrial function and hydrogen peroxide levels were assessed by high-resolution respirometry and fluorescence detection, respectively, using an OROBOROS O2K respirometer on fresh tissue homogenates (kidney and heart) at postnatal days (PD) 4 and 14.

Results:
At PD4, kidneys of male ID offspring treated with ketones had increased oxygen flux levels compared to control and vehicle-treated ID offspring across Leak state, N-, NS- and S-pathways. Kidneys of ID offspring treated with ketones at PD14 showed significant recovery of mitochondrial respiration back to control levels in both NS- and S-pathways. No clear effects of ketone ester treatment were observed in the heart at either PD4 or PD14, albeit a non-significant increase in cellular respiration in ketone-treated ID pups was seen at PD14. Vehicle-treated ID pups (PD4 and PD14) interestingly showed no changes in oxygen flux compared to control offspring. Similarly, hydrogen peroxide levels were low among all tissues, and no notable differences were apparent among treatment groups.

Conclusion:
Preliminary results suggest maternal treatment with ketone esters during gestation may improve mitochondrial function, although the effect may be independent of mitochondrial-derived hydrogen peroxide generation. Notwithstanding, further refinements and additional experiments are needed to understand the underlying processes by which perinatal ID affects offspring growth and development.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 33
Presenter: Jasmine Rai
Supervisor: Carson, Valerie
Title: Patterns of children's screen time, parent-child interactions, and cognitive development in early childhood: A pilot study
Authors: Jasmine Rai, Madison Predy MSc, Sandra Wiebe PhD, Christina Rinaldi PhD, Yao Zheng PhD, Valerie Carson PhD

Theme: Children's health and well-being

Introduction: The objectives of this pilot study were to examine patterns of screen time use in preschool-aged children, the correlations between patterns of screen time and cognitive development, and the differences in quality of parent-child interactions for two screen-based tasks and a storybook reading task.
Methods: Participants included 44 children aged 3 years and their parents from Edmonton, Alberta and surrounding areas. Screen time patterns (i.e., type, device, content, context) were measured using a 2-week online daily diary completed by parents. Demographic information was measured with a parental questionnaire. Cognitive development, including working memory, inhibitory control, self-control, and language were measured with four separate tests virtually through a recorded Zoom session. Parent-child interactions during video, electronic game, and storybook reading tasks were also measured virtually through a separate recorded Zoom session (n = 42). The Parent-Child Interaction System (PARCHISY) was used to code recorded observations to determine the quality of the interactions. Descriptive statistics, Spearman's Rho correlation, and a one-way repeated measures ANOVA with a post-hoc Bonferroni test were conducted.
Results: On average, children spent 103.5 minutes/day engaged in screen time, including 88.7 minutes/day watching a show/movie/video and 7.3 minutes/day playing an electronic game. Of the total minutes/day of screen time, 14.2 included educational content, 24.9 included using a mobile screen device and 48.1 included co-using with an adult. Total screen time (rs = -0.40; p = 0.01) and show/movie/video viewing (rs =-0.42; p=0.01) were significantly correlated with lower working memory. A medium effect size was also observed for the correlation between co-use and self-control (rs =-0.30; p=0.06). After adjusting for child age and parental education, correlations with working memory were attenuated (Total screen time and show/movie/video viewing: rs =-0.32; p=0.06). Additionally, educational screen time was significantly positively correlated with vocabulary (rs = 0.38; p = 0.02) while co-use was significantly negatively correlated with self-control (rs= -0.32; p = 0.05). A medium effect size was also observed for the correlation between educational screen use and inhibitory control (rs =0.33; p=0.07). No other significant associations or medium to large effect sizes were observed. Finally, the quality of parent child interaction scores was significantly different between all the three tasks, with the electronic game having the highest quality score and the video having the lowest quality score.
Conclusions: Preschool-aged children primarily used mobile and traditional screen devices to watch shows/movies/videos for entertainment purposes, and parent-child interaction quality was the lowest for this type of screen time. Additionally, this type of screen time was found to be negatively correlated with working memory. Conversely, high quality educational screen time, in particular electronic games that facilitate high quality parent-child interactions, was shown to have a potential benefit for cognitive development. Future studies in larger, more generalizable samples should confirm these findings.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 114
Presenter: Rebecca Reif
Supervisor: Hemmings, Denise G
Title: A Novel Physiological Model to Study P.falciparum Interactions in Placental Malaria
Authors: Rebecca Reif, Sumaiyah Shaha, Yuliya Fakhr, Catherine Mitran, Madeleine Wiebe, Stephanie Yanow and Denise Hemmings

Theme: Pregnancy and developmental trajectories

Introduction: Placental malaria poses a major health threat to women, resulting in fetal morbidity and low birth weight infants. It develops when infected red blood cells (iRBCs) adhere to chondroitin sulfate A (CSA) glycosylated syndecan-1 (SDC-1) on placental syncytiotrophoblasts via VAR2CSA, a parasite protein localized to the iRBC surface. Current vaccine efforts are directed at VAR2CSA to disrupt the interaction with CSA glycosylated SDC1 on the syncytiotrophoblast for protection against placental malaria. Current assays use CSA-coated plates; these are non-physiological and prone to high inter- and intra-assay variability. A more relevant tissue-based iRBC binding model will close the gap between in vitro assays, vaccine development and human clinical trials. We hypothesized that the development of a placenta tissue-based iRBC binding model will provide a physiologically relevant mechanism to test blocking efficiency of antibodies developed against VAR2CSA-based vaccines.

Methods: We developed a new model using villous tissue explants from human term placentas. We first confirmed that SDC-1 localized to the apical membrane of syncytiotrophoblasts layer in villous explants, making it a suitable tissue for this model (n=10). iRBCs were stained with ethidium bromide to detect parasite DNA and uninfected RBCs were stained with DiD. Infected or uninfected RBCs were added to explants and rocked. After washing, explants were fixed, whole mounted and RBC binding was quantified manually in 5 fields of view using fluorescent microscopy. Controls include chondroitinase cleavage of CSA from explants and soluble CSA competition (n=5). Blocking iRBC binding with rabbit anti-VAR2CSA IgG validated the assay (n=3).

Results: SDC-1 localized to the apical membrane of syncytiotrophoblasts. The iRBC binding between assays varied 19.7(%CV). The area of syncytiotrophoblasts will be quantified as a larger area may lead to more iRBC binding. Specific iRBC binding to CSA/SDC-1 on villous explants was reduced with chondroitinase treatment by 73.70±20.13%. Preincubation of iRBCs with soluble CSA or rabbit anti-VAR2CSA IgG reduced binding by 73.06±19.53% and 90.12±14.40%, respectively. Average background binding levels of uninfected RBCs was 36.00±5.771 compared to bound iRBCs 211.6±61.18 per 5 fields of view.

Conclusion: This study presents the development of a more physiological model to test the functional activity of antibodies from pre-clinical vaccine studies and human trials with candidate vaccines against placental malaria.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 197
Presenter: Laura Reifferscheid
Supervisor: MacDonald, Shannon
Title: COVID-19 vaccine acceptance during pregnancy in Canada
Authors: Laura Reifferscheid, Emmanuel Marfo, Ali Assi, Noni MacDonald, Samantha Meyer, Julie Bettinger, Joan L. Robinson, Manish Sadarangani, Sarah Wilson, S. Michelle Dreidger, Karen Benzies, Shannon E. MacDonald

Theme: Pregnancy and developmental trajectories

Introduction
Pregnant people infected with SARS-CoV-2 are at increased risk of severe COVID-19 illness leading to hospital and ICU admission compared to non-pregnant peers. In addition, COVID-19 illness increases potential for adverse pregnancy outcomes. Therefore, optimizing COVID-19 vaccine uptake in this population is a crucial public health measure. To increase COVID-19 vaccine uptake among pregnant people, it is important to understand the factors influencing COVID-19 vaccine acceptance. This study aimed to investigate COVID-19 vaccine acceptance among pregnant people in Canada, and explore associated factors.
Methods
We conducted a national cross-sectional survey among pregnant people from May 28 through June 07, 2021 (n=193). Respondents completed a questionnaire to determine COVID-19 vaccine acceptance, factors associated with vaccine acceptance, and rationale for accepting/not accepting the vaccine. The outcome variable of interest was vaccine acceptance, defined as either received or intend to receive a COVID-19 vaccine during pregnancy; we conducted a sensitivity analysis to confirm concordance between these two groups. To identify factors associated with vaccine acceptance, adjusted odds ratios (aOR) and 95% confidence intervals (95% CI) were calculated using logistic regression.
Results
Of 193 respondents, 57.5% (n=111) reported COVID-19 vaccine acceptance. Concern over vaccine safety was the most commonly cited reason for not accepting the vaccine (90.1% [n=73]). Most respondents who did not accept the vaccine (81.7% [n=67]) disagreed with receiving a vaccine that had not been tested in pregnant people. In the multivariate logistic regression model, agreement with the statement "I am completely confident that the COVID-19 vaccines that are available in Canada are safe" (compared to neutral/disagree; aOR 16.72, 95% CI: 7.22, 42.39), Indigenous self-identification (compared to White; aOR 11.59, 95% CI: 1.77, 117.18), and employment in an occupation prioritized for early COVID-19 vaccine access excluding healthcare (compared to unemployed; aOR 4.76, 95% CI: 1.32, 18.60) were associated with vaccine acceptance. In contrast, sociodemographic factors (age, income, and education), self-reported chronic illness, and perceived personal risk of COVID-19 disease were not associated with COVID-19 vaccine acceptance. Healthcare employment was not significantly associated with vaccine acceptance in the multivariate model.
Conclusions
Vaccine safety is a primary concern for pregnant people when deciding whether to receive the COVID-19 vaccine. Pregnant people were not included in initial clinical trials; thus, it is important that targeted efforts are made to communicate safety information that has emerged to this population. Safety information should be accompanied by clear messaging on the elevated risk of COVID-19 disease during pregnancy, as disease risk is either poorly understood or poorly valued in this population. Prioritization for early vaccine access was associated with vaccine uptake among some population subgroups, though more work is required to understand how prioritization impacts perceptions of disease and vaccine risk. Efforts should be made to understand COVID-19 vaccine acceptance among pregnant healthcare workers.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 204
Presenter: Jenna Richardson
Supervisor: Clugston, Robin
Title: The significance of maternal dietary intake and hepatic vitamin A stores in establishing vitamin A reserves in offspring
Authors: Richardson JM, Sanchez Enkerlin A, Clugston RD.

Theme: Pregnancy and developmental trajectories

Introduction:
Vitamin A (VA) deficiency is a serious global health issue in the developing world and can also occur in the developed world during stages of life where nutritional demands are higher, such as pregnancy, lactation, and early childhood. Given the importance of establishing sufficient reserves early in life, this study examines the contribution of maternal VA stores versus VA intake during gestation and lactation to examine if maternal dietary VA intake is the primary determinant of VA reserves in offspring, independent of maternal VA reserves.

Methods:
All studies were conducted in two groups of pregnant Balb/c mice, with differing dietary vitamin A intake during pregnancy and lactation. One group of dams received a VA sufficient diet (25 IU/g), and a second group received a VA deficient diet (0 IU/g) throughout pregnancy and lactation. Tissue samples were collected from offspring at birth (P1), during lactation (P7), at weaning (P21), and two weeks post-weaning (P35). Vitamin A content (retinol and retinyl ester) was readily integrated from chromatograms using high performance liquid chromatography analysis. Relative quantities of retinol and retinyl ester were determined using Prism software and compared using an unpaired Student's t-test. Physical parameters including the body weights and liver weights of all pups and dams were also recorded prior to tissue collection.

Results:
Our study suggests that there is a direct relationship between maternal diet manipulation and mean liver retinol and retinyl ester content in offspring. The livers from P7 pups displayed a statistically significant reduction (50%, $p=0.002$) of retinol between VA sufficient and VA deficient groups. Contrastingly, mean retinyl ester concentrations displayed a non-significant difference between sufficient and deficient VA manipulated diets. At P21 and P35, both mean retinol and retinyl ester quantities were reduced significantly when dams on VA sufficient diets were compared to those on deficient diets ($p=0.0125$ and $p=0.0460$, and $p=<0.0001$, respectively). Here, retinol and retinyl ester concentrations decreased 2.8 times and 1.8 times for P21 and 3.1 times and 6.4 times for P35 respectively. All other physical parameters (body weight, liver weight, age, litter size) displayed no significant differences between dams and pups of different diet groups.

Conclusion:
Our study has shown that maternal dietary VA intake is critical in establishing adequate VA reserves in offspring and suggests that maternal hepatic stores alone are insufficient. This study is significant because it generates new knowledge of VA transfer between mother and pup and has the potential to be translated into improved approaches to mitigate the effects of childhood VA deficiency.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 216
Presenter: Nicole Rodriguez
Supervisor: Kozyrskyj, Anita
Title: Sex-specific associations between infant food or atopic sensitization, and socio-emotional development
Authors: Nicole Rodriguez, Carmen Tessier, Piushkumar Mandhane, Jacqueline Pei, Elinor Simons, Theo J. Moraes, Stuart E. Turvey, Padmaja Subbarao, Anita Kozyrskyj

Theme: Children's health and well-being

Introduction:

Food sensitization is a first and strong indicator of immune deviation in the progression to other allergic conditions. Whereas sensitization to food or other allergens, and related inflammation, during critical windows of infant development may adversely affect progress towards neurodevelopmental milestones, this association has not been tested.

Methods:

The current study determined associations between atopic (any food or aeroallergen) or food sensitization (specific to egg, soybean, peanut, and milk) at age 1 year and neurodevelopment up to 2 years of age in the national CHILD Cohort Study, with a secondary aim examining whether these associations were sex-specific. Food and atopic sensitization were assessed by skin prick tests in one-year-old infants, with neurodevelopment, assessed using the cognitive, language, motor, and social-emotional subscales of the Bayley Scales of Infant Development (BSID-III) administered at 1 and 2 years of age.

Results:

In the current study, atopic sensitization was present among 16.4% of infants, while 13.4% had food sensitizations. Both atopic and food sensitization at 1 year of age was associated with statistically significantly lower social-emotional scores at that age, independent of the infant's ethnicity. These findings were sex-specific and only observed among boys, among whom social-emotional scores were lowered by 5 points if atopic sensitization was present (-5.22 [95%CI: -9.96, -0.47]) or if food sensitization was present (-4.85 [95%CI: -9.82, 0.11], p=0.06).

Conclusion:

In our study of healthy term infants, we found an inverse, cross-sectional association between atopic and food sensitization status, and social-emotional development scores in males but not females.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 205
Presenter: Daniela Roth
Supervisor: Graf, Daniel
Title: Bmp7 controls early intramembranous ossification through cross-talk with Wnt signaling
Authors: Daniela M. Roth, Pranidhi Baddam, Daniel Graf

Theme: Children's health and well-being,Pregnancy and developmental trajectories

Introduction: Cranial sutures, the fibrous joints found between skull bones, offer a unique biological system to study intramembranous bone formation by virtue of bone-forming cells being sequentially organized in physical layers. Initial interest in sutures arose from clinical malformations, however the field has since focused on identity of cells within sutures. While sutures of the skull and consequences of growth deficiency of the cranial vault are well studied, little is known about the spatiotemporal contribution of midfacial sutures to midfacial growth. We have recently characterized the Bone Morphogenetic Protein 7 (Bmp7) conditional knockout mouse (Bmp7ncko) as a model for midfacial hypoplasia with nasal airway obstruction, leading to disordered breathing. Based on the craniofacial malformations we observed in these mice, we hypothesize that midfacial sutures play an important role in growth of this region.

Methods: Using the Bmp7ncko model, I investigate if and how Bmp7 controls osteoblast differentiation in sutures, and correlate findings to the impact of its loss on formation of other intramembranous bones. Techniques like micro-CT analysis, immunostaining, histology, and in vitro primary osteoblast culture have revealed the underlying causes of this malformation.

Results: Bmp7ncko mice develop midfacial suture abnormalities from the age of 1 week onwards. Altered cellular architecture and bone remodeling lead to changes in the overall appearance of the postnatal internasal suture suggestive of premature ossification. I have observed changes to the organization of the layers within the sutures using stage-specific antibodies such as Runx2 corresponding to osteoblast maturation. Primary osteoblasts from Bmp7-deficient embryos show intrinsic changes to their gene expression profile compatible with enhanced osteogenesis, including loss of the Wnt inhibitor Dkk1. Interestingly, there is an opposite dysregulation of Wnt signaling in the internasal suture in situ at birth; we observe local upregulation of Wnt inhibitor Frzb and loss of non-phosphorylated beta-catenin.

Conclusion: Our data suggests an important role for Bmp7 in early bone development by controlling early osteogenic differentiation, presumably via cross-talk with Wnt signaling. Loss of Bmp7 affects bone formation at various levels, ranging from differences in osteogenic gene expression to osteoblast quantity. Thus, changes to suture behavior are a likely and so far insufficiently considered contributor to midfacial hypoplasia, adding to the complexity of our understanding of midfacial growth. This insight into the functionality of sutures in midfacial hypoplasia is crucial in a field like pediatrics, where minimally invasive options are mandated.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 194
Presenter: Luis Fernando Rubio Atonal
Supervisor: Ioannou, Maria
Title: Exploring the role of excitotoxicity in lipid droplet formation in neonatal injury
Authors: Luis Fernando Rubio Atonal, Wendy Cai, Maria S. Ioannou

Theme: Children's health and well-being

Infants (< 1 year old) are at elevated risk for brain injury due to accidental falls or assault. Traumatic brain injury accounts for around 25% of all injury-related infant deaths. Brain injury induces excitotoxicity, a process in which neurons die due to hyperactivity that causes oxidative damage to macromolecules including lipids. The death of neurons results in subsequent physiological and/or behavioral alterations depending on the area of the injury. Recent studies by our laboratory discovered lipid droplet accumulation in adult models of excitotoxicity. Lipid droplets are lipid storage organelles that form in response to and offer protection from oxidative stress caused by injury. Since the neonatal brain is more vulnerable to excitotoxicity, we hypothesized that lipid droplets may play a role in early brain injury. Using intact rat hippocampus as our model system, we tested for a correlation between droplet formation and neural activity by staining with BODIPY 493/503 and the early response gene c-Fos, respectively. We found lipid droplet accumulation in hippocampi extracted from postnatal day 0 (P0) animals, but this effect was not present by P10. Consistently, we found that P0 hippocampi had higher number of nuclei immunostained for c-Fos when compared to P10 rats in non-injured areas, indicating higher neuronal activity in neonates. Lipid droplets were abundant in microglia, with a limited number in astrocytes, neurons, and astrocyte precursors. Lipid droplets localized to the subiculum and/or entorhinal cortex, the region adjacent to the cut site suggesting they may be caused by injury-induced excitotoxicity. c-Fos expression was higher at the injury site compared to non-injured hippocampal regions in P0 rats, suggesting that excitotoxicity may contribute to lipid droplet formation. However, at the injury site, there was no difference in the number of c-Fos positive nuclei between P0 and P10 rats, prompting the question if there are other age-dependent mechanisms that regulate lipid droplet formation. We will continue to explore the role of excitotoxicity and other potential mechanisms in lipid droplet formation following neonatal brain injury. Ultimately, our study reveals a developmental regulation of lipid droplet formation in neonatal brain injury.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 126
Presenter: Tamara Sáez
Supervisor: Davidge, Sandra
Title: Does LOX-1 mediate the postpartum vascular dysfunction after a mouse pregnancy complicated by hypercholesterolemia?
Authors: Tamara Sáez, Raven Kirschenman, Anita Quon, Floor Spaans, Sandra T. Davidge

Theme: Lifelong women's health

Introduction: Women that have had preeclampsia are at risk of cardiovascular complications later in life, potentially via vascular dysfunction that persists postpartum. The lectin-like oxidized low-density-lipoprotein (oxLDL) receptor-1 (LOX-1) is highly expressed in maternal vasculature during preeclampsia. LOX-1 activation by oxLDL induces endothelial dysfunction, while also inducing activation of the angiotensin II type 1 receptor (AT1). We have previously shown that a high-cholesterol diet (HCD) in late pregnancy in mice (a mouse model of preeclampsia) induces vascular dysfunction via LOX-1. However, whether LOX-1, and its potential interaction with AT1, may be involved in the postpartum vascular dysfunction after a HCD in pregnancy, is unknown. We hypothesize that postpartum vascular dysfunction induced by a HCD in late pregnancy in mice is mediated by LOX-1, which involves AT1 activation.
Methods: To assess the specific role of LOX-1 in the postpartum vascular dysfunction, we used LOX-1 knock-out (KO) and wild type (WT) mice. Pregnant LOX-1KO and WT mice were fed a HCD between gestational day (GD) 13.5 and term (GD19), and WT and LOX-1KO pregnant control mice were fed a standard control diet (CD). After delivery, all females (4 groups in total; n=3-9/group) were fed a CD for 3 months postpartum (~5-7 years in human age). All mice were euthanized, and aortas were isolated to assess ex vivo vascular responses to the endothelium-dependent vasodilator, methacholine (MCh), by wire myography. MCh-induced vasodilation was evaluated in the presence or absence of L-NAME (nitric oxide synthase inhibitor; 100 µM) to assess nitric oxide (NO) contribution to vasodilation. In addition, some vessels were exposed to oxLDL (50 µg/mL) to induce LOX-1 activation, with or without the AT1 antagonist candesartan (CS; 1 nM) to evaluate a potential involvement of AT1, prior to MCh vascular responses. Data were analyzed by two-way ANOVA followed by Sidak's post hoc testing and presented as mean±SEM; $p<0.05$ was considered statistically significant.
Results: A HCD in late pregnancy resulted in reduced maximal MCh-induced vasodilation three months postpartum in WT females compared to WT-CD (WT-CD: 95.8±0.8 vs WT-HCD: 82.1±5.9%; p=0.057), while no effects of the HCD were found in the LOX-1KO mice postpartum. There were no differences in NO contribution to vasodilation between the WT and LOX-1KO groups postpartum. However, oxLDL exposure further impaired maximal vasodilation in aortas from WT-HCD postpartum compared to controls (control [no oxLDL]: 82.1±5.9 vs oxLDL: 63±3.6%; p=0.04); however, pre-incubation with CS before oxLDL exposure prevented the oxLDL-induced impairment in maximal vasodilation (oxLDL: 63±3.6 vs CS+oxLDL: 95.7±1.9%; p=0.005). OxLDL or CS did not alter vasodilation responses in aortas from WT-CD, or from both LOX-1KO groups postpartum.
Conclusion: Our preliminary data showed that the postpartum vascular dysfunction in WT mice that were fed a HCD in late pregnancy is mediated by LOX-1 activation and appears to involve the activation of the AT1 receptor. Our data suggest that LOX-1 could be a potential therapeutic target to prevent the development of cardiovascular complications in women that experienced preeclampsia.

This research has been facilitated by WCHRI through the generosity of the supporters of the Lois Hole Hospital for Women.

Participant #: 57
Presenter: Hannah Sell
Supervisor: MacDonald, Shannon
Title: The impact of the COVID-19 pandemic on school-based immunizations in Alberta
Authors: Hannah Sell, Don Voaklander, Shannon MacDonald

Theme: Children's health and well-being

Introduction
The implementation of physical distancing measures, school and clinic closures, and re-allocation of public health staff due to coronavirus disease 2019 (COVID-19) has meant that many Canadian children may have missed immunization doses. Immunizations for school-aged children have likely been significantly disrupted as school-based immunization programs were suspended due to school closures. Reduction in coverage for vaccines such as meningococcal (MenC-ACYW) or human papillomavirus (HPV) may increase Canadian children's susceptibility to vaccine-preventable diseases. Studies from outside Canada have shown significant declines in childhood immunizations following the onset of the COVID-19 pandemic, but the impact on immunization coverage for school children in Canada is unknown. As such, the objective of the current study is to determine the impact of the COVID-19 pandemic on school-based immunizations in Alberta, including HPV and MenC-ACYW.

Methods
The current study is a retrospective cohort study involving an analysis of immunization coverage in Alberta, Canada. This study will assess coverage of HPV and MenC-ACYW vaccines at the end of the 2019-2020 and 2020-2021 school years (i.e., pandemic), comparing to the 2017-2018 or 2018-2019 school years (i.e., pre-pandemic). Using multiple time points will allow us to evaluate the impact of evolving public health measures and determine whether coverage returns to pre-pandemic levels.

The cohorts will be created by linking population-based administrative data from the Alberta Ministry of Health and the Ministry of Education including vital statistics, Alberta Health Care Insurance Plan (AHCIP), Provincial School Immunization Record (PSIR), and Immunization and Adverse Reactions to immunization (Imm/ARI) data. Immunization status will be determined using the PSIR and Imm/ARI databases, which contain records of all children who received school-based vaccines in each school year, and which grade they were in.

Statistical comparisons between pandemic and pre-pandemic time periods will use Chi-square (independent) or McNemar (non-independent) tests for comparison of proportions and Poisson regression for comparison of rates. Multivariable logistic regression will be performed to test characteristics of children/families (e.g., rural/urban residence, attending school online/in-person) associated with immunization in the pandemic period in contrast to the pre-pandemic period.

Results
This study is in the introductory stages; therefore results are not yet available.

Conclusion
The knowledge that will be gained from this research can inform public health responses to address the effects of the pandemic on school-based immunization programs. Specifically, findings from this study can guide knowledge users at the Alberta Ministry of Health and the National Advisory Committee on Immunization regarding communication with key stakeholders, including physicians, public health nurses, and immunization program coordinators, with respect to identification of populations at risk of vaccine-preventable disease outbreaks and the need for catch-up immunization programs.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 158
Presenter: Jesus Serrano-Lomelin
Supervisor: Ospina, Maria
Title: Health Trajectories before Pregnancy in Gestational Hypertension and Preeclampsia
Authors: Jesus Serrano-Lomelin, Brittany Matenchuk, Graeme Smith, Sandra T. Davidge, Radha Chari, Meghan Riddell, Susan Crawford, Jeffrey A. Bakal, Maria B. Ospina

Theme: Pregnancy and developmental trajectories

Introduction. Gestational hypertension (GH) and Preeclampsia (PE) are major causes of mortality and morbidity. Type 2 diabetes mellitus (type 2 DM), maternal asthma, and stress-related illnesses have been recognized as independent risk factors for GH and PE. It is unclear how combinations of those risk factors diagnosed before or during pregnancy (health trajectories) may be related to GH and PE. We compared trajectories of type 2 DM, depression, anxiety, and asthma diagnosed before or during pregnancy in women with GH and PE. Results may inform the formulation of strategies to screen for GH and PE prior to or during pregnancy.

Methods. We conducted a case-control study using data from the Alberta Perinatal Health Program for the years 2010-2013. Cases were nulliparous women aged > 16 years having GH or PE during the study period. Controls were a random sample of pregnant women in their first pregnancy with no diagnosis of GH or PE, matched by gestational age for a ratio of 1:4 cases/controls. Both singleton and multiple pregnancies were included. Women diagnosed with hypertension prior to the pregnancy period were excluded. Diagnoses of type 2 DM, depression, anxiety, and asthma during pregnancy or in the five years before pregnancy were extracted from health administrative databases. Structural equation models were used for path analyses, with maternal age, overweight and socioeconomic status as covariates. We reported odds ratios (OR) with 95% confidence intervals (CI) for direct and combined (when applicable) effects of health trajectories on GH and PE.

Results: The study included a total of 18,381 mothers (controls=13,786; GH=3,443; PE=1,152). Combined depression and anxiety before pregnancy were associated only with GH (OR 1.8, CI 1.0, 3.0); type 2 DM was only associated with PE before (OR 1.9, CI 1.3, 2.6) or during pregnancy (OR 1.3, CI 1.0, 1.8); anxiety during pregnancy was associated with both GH (OR 2.1, CI 1.3, 3.5) and PE (OR 2.2, CI 1.1, 4.4); and asthma during pregnancy was only associated with PE (OR 2.7, CI 1.6, 4.5). Combined effects of conditions before and during pregnancy were not statistically associated with GH or PE.

Conclusion: Trajectories of type 2 DM, depression, anxiety, and asthma play a different role in the development of GH or PE. Our results may stimulate further research for the design of precision health approaches that incorporate clinical risk assessment into screening activities among women of childbearing age.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 150
Presenter: Md Nur Ahad Shah
Supervisor: Yokota, Toshifumi
Title: Antisense oligonucleotide-mediated exon 44 skipping to treat Duchenne muscular dystrophy
Authors: Md Nur Ahad Shah, Toshifumi Yokota

Theme: Children's health and well-being

Introduction: Duchenne muscular dystrophy (DMD) is the most common lethal genetic disorder affecting 20,000 children worldwide every year. The mean age of death is around 25 years. The DMD gene consists of 79 exons and encodes the protein Dystrophin that supports the muscle membrane. Out-of-frame mutations in this gene lead to the loss of dystrophin protein which predisposes muscle fibres to damage. While there are some relieving methods like corticosteroids and respiratory care, there is no cure for this disease. Exon skipping is a novel technique that employs antisense oligonucleotides (AOs) that act as a stitch to skip over the frame-disrupting part of the DMD gene. AOs bind to the critical splicing sequences in the DMD mRNA, excluding out-of-frame exons and restoring the reading frame. This allows for the production of truncated but functional dystrophin. In this study, we are developing a treatment using AOs to skip exon 44 that can effectively treat approximately 6% of DMD patients, the fourth most common target for exon skipping.

Methodology: We have evaluated the activity of multiple AOs designed based on our in silico analysis that can potentially be used for the treatment. We carried out in vitro experiments on immortalized DMD patient muscle cell lines (myotubes) that have an exon 45 deletion in the DMD gene resulting in the lack of dystrophin. The efficacy of exon 44 skipping and restoration of exons 44-45 skipped in-frame products were evaluated using RT-PCR analysis. Restoration of truncated dystrophin protein was further confirmed using Western blot analysis. Based on the results, the best AO will be further tested in humanized DMD model mice carrying the human DMD gene sequence with an exon 45 deletion.

Results: From our in silico analysis, we have selected 8 AOs that have a high potential for inducing successful exon skipping. From in vitro RNA analysis, 2 AOs were found to be highly efficient at skipping exon 44 (100% skipping) and restoring exons 44-45 skipped in-frame mRNA. Between them, one of the AOs has been shown to restore over 80% of the normal dystrophin protein levels according to the Western blot data.

Conclusion: We identified a promising AO that will be further evaluated in vivo. This study will lead to the identification of promising AOs for further pre-clinical testing.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 195
Presenter: Sumaiyah Shaha
Supervisor: Riddell, Meghan
Title: Atypical protein kinase Cs regulate trophoblast progenitor to extravillous trophoblast differentiation by modulating signalling
Authors: Sumaiyah Z. Shaha, Haley Frerichs, Josiah Kwong, Sareh Panahi, Meghan Riddell

Theme: Pregnancy and developmental trajectories

Introduction
The placenta is a fetally-derived organ allowing for the exchange of oxygen, nutrients, and wastes between the mother and fetus. Extravillous trophoblasts (EVT) are invasive placental cells responsible for remodelling uterine spiral arteries to allow for appropriate blood flow to the placenta. EVT develop from placental cell columns that are comprised of trophoblast stem cells (TSC) and progenitor cytotrophoblasts (pCT). EVT dysfunction has been linked to the development of common pregnancy disorders like preeclampsia. Thus, understanding how TSC to EVT differentiation is regulated is crucial. Atypical protein kinase Cs (aPKCs) are a family of kinases important for the regulation of stem cell differentiation, proliferation, and cell polarity. There are two major isoforms of aPKC: aPKC-ι and aPKC-ζ. Recently, aPKC-ι knockdown in TSC was shown to decrease syncytiotrophoblast formation, the other cell lineage derived from TSC. However, whether aPKCs regulate TSC to EVT differentiation has not been addressed. The Notch1 signalling pathway has been shown to be important for pCT maintenance and blocking pCT to EVT differentiation. APKC positively regulates Notch1 signalling in other cell types by controlling Notch1 intracellular trafficking. Therefore, we hypothesize that aPKCs play a role in EVT lineage differentiation by regulating Notch1 signalling.

Methods
First trimester human placental tissue was stained using immunofluorescence (IF) for aPKC-ι, aPKC-ζ, and HLA-G (EVT marker) to examine aPKC expression in EVT. An EVT outgrowth assay was carried out with six-week placental explants +/- aPKC inhibitor. Primary isolated human pCT were cultured in TSC medium +/- aPKC inhibitor and Notch1 localization was assessed by IF. Co-localization analysis of nuclear stains and Notch 1 was performed using Volocity imaging software. Students t-test was performed (n=3) for all experiments.

Results
Strong aPKC-ι and aPKC-ζ signal was seen cell column pCT but a low signal for both aPKC isoforms was observed in EVT, suggesting down-regulation of aPKCs may be important for EVT differentiaton. Total aPKC inhibition increased EVT outgrowth from cell columns by 3-fold ($p<0.01$). In primary pCTs aPKC inhibition led to a significant decrease in Notch1 nuclear localization, which would block the Notch1 signalling pathway ($p=0.0186$).

Conclusions
Our data shows that aPKC isoforms regulate pCT to EVT differentiation and suggest that this may be due to modulation of Notch1 activation. Future directions are to assess if there are isoform specific aPKC functions in Notch1 regulation and to identify whether aPKCs control Notch1 nuclear localization by modulating intracellular trafficking as in other stem cell populations. Our work delineating mechanisms of EVT differentiation will help identify novel pathways that may be disrupted in conditions such as preeclampsia and could lead to the development of treatments for these disorders in the future.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 70
Presenter: Tristan Sinnatamby
Supervisor: Funk, Gregory
Title: Inability of premature mammals to produce a sustained breathing response to hypoxia may reflect postnatal maturation of adenosine kinase
Authors: Tristan Sinnatamby, Robert Reklow, Daniel Zoccal, Detlev Boison, Gregory D Funk

Theme: Children's health and well-being

Introduction: Breathing in infants born prematurely is interrupted by frequent pauses (apneas) of variable duration because the brainstem network that generates and controls breathing is immature; a condition called apnea of prematurity (AOP). Long apneas cause the level of oxygen in the blood to fall (hypoxia), triggering the hypoxic ventilatory response (HVR) which comprises an initial increase in breathing followed by a centrally mediated secondary phase during which, in adults, breathing and metabolic rate decrease in parallel. Newborn mammals cannot sustain the breathing response during this secondary depression and ventilation falls more than metabolism. This creates a life-threatening positive feedback loop where apnea causes hypoxia, hypoxia depresses breathing, hypoxia worsens and so on, until an intervention interrupts this loop or it ends in death. Caffeine is the treatment of choice for infants with AOP. However, additional treatments are needed because caffeine is ineffective or associated with major side effects in ~20% of infants. These children will on average remain on pump ventilation for longer periods than caffeine-sensitive infants, have longer hospitalizations, and suffer increased risk of long term health problems like retinopathy and cerebral palsy. Understanding the mechanisms underlying this powerful hypoxic respiratory depression (HRD) could inform new therapies for AOP. The cause of this HRD is not known, but extracellular ADO (ADOe) is implicated because it increases in the brain during hypoxia and inhibits breathing. This is why caffeine, an ADO receptor antagonist, counteracts AOP. Removal of ADOe and cessation of its inhibitory actions depend on the enzyme adenosine kinase (ADK). However, in rodents the short isoform of ADK which affects brain ADOe levels is not mature until 2 weeks of age. We therefore hypothesized that the greater HRD seen in prematurity is due to minimal ADK activity.

Methods: To test this, we engineered ADKtg mice to have functional ADK from conception. Using a custom chamber to measure respiration, we compared the breathing and metabolic responses of ADKtg and wild-type (WT) mice to hypoxia (10 min, 8% O_2; 21% is normal) between postnatal days 0-14 (P0-14). We reported ventilation (VE) relative to metabolic rate (VO_2) because hypoxia affects ventilation and metabolism. An increase in VE/VO_2 represents an adaptive response to hypoxia.

Results: As predicted, at P0-2 hypoxia did not evoke a significant change in VE/VO_2 in WT mice, while in ADKtg mice hypoxia evoked a sustained, adult-like, 3-fold increase in VE/VO_2. At P6-8 and P12-14, strain differences disappeared; all mice responded to hypoxia with a sustained increase in VE/VO_2. Surprisingly, the VE/VO_2 response of P0-2 ADKtg mice did not reflect a greater increase in VE, but a greater decrease in VO_2. Similar responses were observed when mice were exposed to less severe hypoxia (10% O_2).

Conclusion: These data support our hypothesis that immature ADK is an important contributor to the powerful HRD seen in early life. However, data also suggest that the mechanism via which ADK prevents this HRD at birth is not by increasing breathing, but by depressing metabolism. Future work will explore mechanisms via which ADK affects metabolism.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 120
Presenter: Meghan Sit
Supervisor: Hartling, Lisa
Title: Youth mental health help-seeking information needs and experiences: a thematic analysis of Reddit posts
Authors: Sit, M., Elliott, S., Wright, K., Scott, SD., Hartling, L.

Theme: Children's health and well-being

Introduction: Adolescence is a formative time in which many physical, emotional, and social changes can make youth vulnerable to mental health challenges. These challenges can persist into adulthood and are associated with multiple maladaptive outcomes. Although in-person mental health support services exist for youth, there are many barriers youth face when accessing such services. Given the popularity of digital media, youth are increasingly turning to online sources for mental health information and support. Thus, social media presents a unique environment for evaluating an abundance of disinhibited mental health discourse and self-disclosure. The objective of this study was to explore reported experiences and information needs related to youth seeking support for mental health on the social media platform, Reddit.com.

Methods: We searched two subreddits: r/mentalhealth and r/teenagers on Reddit.com for posts made by youth (13-25 years) relating to mental health help-seeking behaviours and information needs. Posts were filtered using relevant flairs such as "need support", "question" and "serious" and by date category "this year" (2021). The first 1000 posts from each flair were extracted into Excel and screened by title for inclusion. Relevant data from included posts were then extracted, coded, and analysed using thematic analysis.

Results: 3000 Reddit posts were screened, and 98 were included. Thematic analysis of relevant posts yielded four overarching themes: 1) navigating mental health issues, 2) disclosing to others, 3) barriers to seeking care, and 4) experiences seeking care. Subthemes brought forth insights into how youth navigate through mental health challenges (information needs surrounding identifying, understanding, managing) and youth experiences disclosing mental health issues to others (social stigma, negative experiences, personal empowerment). Furthermore, analysis of Reddit posts revealed several barriers faced by youth when seeking care for mental health challenges including tangible barriers, psychological barriers, social barriers, knowledge barriers, and barriers related to accessibility. Additionally, youth reported several helpful (therapy, anonymous services) and unhelpful (feeling dismissed) experiences receiving care.

Conclusion: Information collected in this study suggests that youth have a diverse range of mental health help-seeking-related information needs and face several barriers throughout the process of seeking care. Future research should explore potential solutions to overcoming these barriers, and further investigate information preferences of youth concerning mental health resources.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 130
Presenter: Carina Siu
Supervisor: Adams, Kim D
Title: BCI-for-play: Development of interview questions to examine the experiences of play for children with severe physical disabilities when using brain computer interfaces (BCI)

Authors: Carina Siu, Matin Dokht Taghirad, John Andersen, Kim Adams

Theme: Children's health and well-being

Introduction:
Play is an essential aspect of cognitive, psychological and behavioural development in children. However, participation in playful activities is often significantly reduced in children with severe physical impairments, who often experience diminished voluntary control of movement. For these individuals, brain computer interfaces (BCI) provide a potential solution for greater engagement in play and other activities. BCI is a computer-based system that captures and translates brain signals to control external devices. BCI may allow children with disabilities to access play through commanding computer games and robots, thus providing newfound control over their environments. Currently there is little research and no established assessment procedures to guide BCI use with children and their families who would benefit the most from these technologies. Therefore, it is imperative to understand their experiences, needs and expectations concerning play and to examine to what extent BCI can support play and development. This project aimed to develop an interview questionnaire as a qualitative research tool to use with children who have severe physical disabilities. It aimed to answer two central research questions: 1) what are the current lived experiences of play for children with severe physical disabilities? 2) What are the play experiences for children with disabilities when using BCI?

Methods:
Interview questions were developed based on play theory and were refined in collaboration with team members from multiple disciplines and perspectives, including an adult with lived experiences of cerebral palsy and researchers with expertise in qualitative research and children's play development. In addition, a variety of adapted interview strategies for children with motor and communication impairments, such as photo and graphical elicitation, were incorporated into the generated interview questionnaire. To verify the child-centred nature of the questionnaire, a pilot interview was performed with a typically developing child.

Results:
The outcome of this project is a rigorous interview questionnaire that will be used in a qualitative study to evaluate BCI for play in children with severe physical disabilities.

Conclusion:
The next steps will be to collect pilot data using the generated interview questionnaire with four participants and their families (two participants without previous BCI exposure and two participants in the Glenrose Rehabilitation Hospital BCI program with extensive experience). The collected data will be transcribed, coded and analyzed for themes. Then the questionnaire will be used in a more extensive qualitative study to answer the above questions and to inform patient/family-oriented research in the BCI program.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 95
Presenter: Teri Slade
Supervisor: Gross, Douglas
Title: Consideration of gendered social factors in pain research
Authors: Teri Slade, Christine Guptill, Douglas Gross

Theme: Lifelong women's health

Introduction: In recent years, much research has been conducted on the differences in incidence, prevalence, and severity of pain between men and women. Countless studies have found that women report more neck pain, low back pain, facial pain, and pelvic pain than men. Many researchers have sought possible explanations for these differences using primarily biological and psychological factors but scientists have as yet been unable to explain the differences observed. Gender is a complex sociocultural construct and further inquiry is needed to understand the social factors that are relevant to the study of gender and pain.

Methods: We used a qualitative study design to identify social factors of gender that may be relevant to study of pain. Participants (n=18) were individuals with pain across many different experiences of gender, including two-spirit, transgender, non-binary, 2SLGBTQ+ cisgender individuals and non-2SLGBTQ+ men and women. We used a reflexive thematic analysis approach.

Results: The final thematic structure included five central themes: 1) societal expectations of gender and pain; 2) individual's position relative to social structures; 3) home as a restful place or not; 4) social connection/isolation; and 5) understanding self, understanding pain. The factors identified in these five themes were identified as relevant to the experience of pain, ability to cope with pain, and access to care.

Conclusions: There are many important considerations for the study of gender and pain. Researchers who include considerations of gender in their pain research should consider social factors at societal, interpersonal, and individual levels. Future research from this team will include the development of a questionnaire tool to address the relevant variables in this thematic analysis.

This research has been facilitated by WCHRI through the generosity of the supporters of the Lois Hole Hospital for Women.

Participant #: 87
Presenter: George Slim
Supervisor: Ali, Samina
Title: What Influences Canadian Pediatric Emergency Physicians When Prescribing Opioids for Children with Acute Pain?: A Qualitative Study
Authors: George Slim, MB BCh, Michael van Manen, MD PhD, Megan Fowler, MD, Naveen Poonai, MD MSc, Samina Ali, MDCM

Theme: Children's health and well-being

• Introduction: Pain is one of the most common symptoms requiring attention in the emergency department (ED), and opioids are amongst the top three medications used to treat pain in children. Recent pressures, including the ongoing Opioid Crisis, have compelled practitioners to consider the potential risk of misuse/addiction of opioids, and to balance this with the real consequences of undertreated pain. Understanding the reasoning behind physicians' opioid prescribing practices is vital to safe practice, as they are one of the main gatekeepers (along with parents) to optimal acute pain management in children. The primary objective of our study was to describe the pediatric emergency physicians' decision-making process when prescribing opioids for acute pain management.

• Methods: This study employed a qualitative methodology, using one-on-one semi-structured interviews within a grounded theory analytic framework. We used purposeful sampling to recruit pediatric emergency physicians practicing at pediatric tertiary care centers across Canada with a minimum of 1-year clinical experience. Our exclusion criteria included physicians not currently licensed to practice pediatric emergency medicine and lack of proficiency in spoken English. Interviews were conducted over telephone by a qualitative methods-trained interviewer. Transcript analysis occurred concurrently with data collection, allowing for considerations around data saturation and theory development.

• Results: A total of 11 interviews were completed. Participants represented the Canadian geographic regional distribution: Eastern, Central, and Western Canada. Interviews revealed nine major themes: 1) Treatment setting, 2) Medical considerations, 3) Physician confidence in the evidence, 4) Pain assessment, 5) Family-specific considerations, 6) Safety concerns, 7) Physician personal experiences, 8) Physician professional context, and 9) The Opioid Crisis and media influence. All participants identified challenges managing acute pain presentations in the ED, emphasizing the need for better guidance, evidence-based data, and knowledge translation. A family-centered approach was recognized as the current gold-standard of practice, especially in the midst of the current Opioid Crisis. However, after considering all other factors, most physicians indicated that the Opioid Crisis had minimal impact on their analgesic decision-making final outcomes. Suggestions for the future included addressing emerging challenges such as the management of opioid dependency and withdrawal in the pediatric setting.

• Conclusion: Our study explored the decision-making process for managing acute pain, isolating significant barriers, facilitators, and considerations when pediatric emergency physicians prescribe opioids. This can help inform knowledge translation strategies for safer practice and optimize acute pain management in pediatrics.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 107
Presenter: Frances Sobierajski
Supervisor: Conway, Jennifer
Title: Use of photovoice to explore pediatric hypertrophic cardiomyopathy patient and parent perceptions of a heart healthy lifestyle
Authors: Frances Sobierajski, Kate Storey, Melissa Bird, Samantha Anthony, Sarah Pol, Tara Pidborochynski, Diana Balmer-Minnes, Alliya Remtulla Tharani, Alyssa Power, Michael Khoury, Aamir Jeewa, Jennifer Conway

Theme: Children's health and well-being

Background: A heart healthy lifestyle, comprised of physical activity, healthy eating, and not smoking, is vital to promote long-term cardiovascular health. However, patients with hypertrophic cardiomyopathy (HCM) are often advised to avoid strenuous physical activity due to the risk of sudden cardiac death. Given activity restrictions and recommendations for patients with HCM, our objective was to explore youth and parent perceptions of a heart healthy lifestyle and the barriers and facilitators to this lifestyle.

Methods: Youth and their parents were purposefully recruited though outpatient clinics at two Canadian hospitals for participation in a photovoice project. Child-parent dyads were eligible to participate if the child was between 10 and 19 years of age and met diagnostic criteria for primary HCM. Participants (youth and parents) were given a camera and asked to take pictures of everyday heart healthy or unhealthy choices. Photos were then discussed during one-on-one qualitative interviews with youth and parents separately to understand the photos' meaning and significance. Inductive descriptive thematic analysis was employed.

Results: Sixteen youth (median: 14.4 [range: 10.5-17.7] years old, 10/16 [63%] male) and sixteen parents (100% female) participated. Fifteen youth were activity restricted. Data analysis revealed seven categories organized into: perceptions of healthy living (health is holistic and individualized) and factors influencing engagement in healthy living (self-awareness, ownership and autonomy, feeling restricted and peer pressure, support from parents, and support from the cardiologist). Specifically, participants had a complex understanding of health and discussed the importance of physical, mental and social well-being. They also perceived health as individualized and described tailoring their behaviours considering their unique health needs, especially their heart health. Youth described using self-awareness and taking responsibility as facilitators of healthy living. Healthy living behaviours were also shaped by peers, parent role-modelling and cardiologist recommendations.

Conclusions: This study depicts the everyday realities of youth with HCM and can be used to inform the development of tailored and responsive healthy living interventions. Our findings suggest that patient-specific interventions using a holistic approach are more likely to be successful. In addition, strategies like shared decision making may be important to promote self-awareness and patient autonomy.

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This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 73
Presenter: Shubham Soni
Supervisor: Dyck, Jason R.B.
Title: Gestational ketone supplementation during perinatal iron deficiency may improve cardiorenal damage in the neonatal offspring
Authors: Shubham Soni, Ronan Noble, Si Ning Liu, Claudia Holody, Jad Julian, Mourad Ferdaoussi, Stephane Bourque, Jason Dyck

Theme: Pregnancy and developmental trajectories

Introduction: Iron deficiency (ID) is the most widespread nutritional disorder in the world and commonly occurs during pregnancy. Recent evidence suggests that excess oxidative stress due to prenatal ID contributes to the cardiac and renal dysfunction and organ-specific mitochondrial dysfunction in the offspring. Interestingly, a noteworthy characteristic of ID neonates is an impaired ability to produce ketones. Ketones, namely β-hydroxybutyrate (BOHB), are molecules produced by the liver from fatty acids that can be used as a source of energy. However, ketones also have signaling properties that inhibit oxidative stress and inflammation. We hypothesized that gestational BOHB supplementation can reduce the cardiorenal impairments in ID neonates by favorably acting on metabolic, oxidative, and/or inflammatory pathways.

Methods: 6-week-old Sprague Dawley rats were fed an iron-restricted (3-10 mg/kg) or iron-replete (37 mg/kg) diet two weeks prior to and throughout gestation. Control dams were subcutaneously injected saline and ID dams were given saline or 300mg/kg body weight BOHB from gestational day 1 to 21. After birth, all dams were fed an iron-replete diet. Birth outcomes of the neonates were analyzed. Cardiac function (via echocardiography) was assessed on postnatal day (PD)1, PD4, and P14, and will be analyzed once all animals reach endpoint. Offspring hearts and kidneys were snap-frozen or preserved in OCT, and work is currently underway to measure protein and transcript markers of ketone metabolism, oxidative stress, inflammation, and organ damage by western blotting, various activity assays, mitochondrial respiration, immunofluorescence/histology, and qPCR. Data were analyzed with 2-way ANOVA.

Results: Perinatal iron restriction reduced maternal hemoglobin (Hb) in both ID and ketone-treated (KID) dams compared to control. Interestingly, despite the increased demands during pregnancy, ID and KID dams had higher blood glucose and lower blood ketone levels at the end of the 2nd trimester compared to control dams. Relative body weight of ID and KID dams changed at a similar trajectory throughout the pregnancy compared to controls.
Similarly, Hb was lower in ID and KID offspring at PD0, PD4, and PD14, and both ID and KID offspring were growth restricted relative to controls. ID and KID offspring also had greater heart:body weights at all timepoints. Interestingly, while liver weight was greater in PD4 ID males, ketone treatment blunted this effect. In addition, blood glucose was lower in PD4 KID offspring but not at PD0 or PD14. Nevertheless, work is currently under way to evaluate the cardiac and renal effects of ketones beyond these recently acquired data.

Conclusion: Altogether, these preliminary data suggest that ketone supplementation in ID mothers is safe for the ID mother and child, and it does not exacerbate ID-induced growth restriction. While it is expected that ketones cannot solely overcome ID-induced growth restriction, we have begun biochemical investigation into whether ketone supplementation can improve ID-induced cardiac and renal dysfunction via alterations in metabolism, oxidative stress, and inflammation.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 171
Presenter: Katherine Souter
Supervisor: Graf, Daniel
Title: Investigating fine control of cranial base development by Bmps
Authors: Souter, K., Roth, D.M., Graf, D.

Theme: Pregnancy and developmental trajectories

Introduction
The cranial base forms the lower enclosure of the brain and is important for craniofacial growth. It consists of several bones separated by cartilaginous growth zones. Conditions that affect these cartilages can lead to insufficient growth, midfacial hypoplasia, and airway obstruction. We recently characterized the first rodent model for midfacial hypoplasia and nasal airway obstruction. In this model, Bone Morphogenetic Protein 7 (Bmp7) was deleted from the anterior cranial base. While overall cranial base changes appeared minor, the structure was shorter, potentially contributing to airway obstruction. Bmp2 is another important growth factor controlling bone growth. In this project, we investigated how Bmp2 and Bmp7 control cranial base growth and formation, focusing on the sphenoid. We hypothesize that both proteins are expressed in overlapping regions but have independent, non-redundant functions.
Methods
This project involved histopathological characterization of bone and cartilage in Bmp-mutant mice. We studied global Bmp7-deficient (Bmp7 ko) and conditional neural crest-specific deletion of Bmp2 (Bmp2 ncko) or Bmp7 (Bmp7 ncko) in mouse embryos. We characterized the spatiotemporal distribution of Bmp2 and Bmp7 in the cranial base from embryonic day 13.5 (E13.5) to E15.5 using immunostaining. We performed 3D micro-CT analysis and skeletal preparations of E18.5 mutants to study bone and cartilage changes.
Results
Bmp2 had distinct, restricted expression in cranial base cartilage starting around E14.5. Bmp7 expression started earlier and was more widely distributed. Bmp7 expression was strong in cartilage, bone, and surrounding tissues early, but became more restricted to cartilage over time. Bmp ncko mutants showed variable severity of sphenoid bone malformation. The Bmp7 ncko had no obvious changes to sphenoid shape but the bone was shorter, contributing to a shorter cranial base. In Bmp7 ko mutants, the basisphenoid bone, a sub-structure of the sphenoid, had a notch. Bmp2 ncko embryos had smaller, disrupted bones of the sphenoid body, but lacked the basisphenoid notch in Bmp7 ko mutants. Bmp2 ncko/Bmp7 heterozygous ncko embryos were similar to the Bmp2 ncko while the Bmp2 heterozygous ncko/Bmp7 ncko pups were similar to Bmp7 ncko mice. Skeletal preparations supported these micro-CT findings. Histology revealed that in Bmp2 ncko embryos endochondral bone formation was strongly compromised in contrast to Bmp7 ncko mutants.
Conclusion
Using this developmental model, we have started separating the different roles of Bmp2 and Bmp7 in cranial base development. Our observations demonstrate that Bmp2 and Bmp7 have unique spatiotemporal roles in cranial base development, an important novel finding, as these two growth factors are often seen as interchangeable in bone formation.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 74
Presenter: Hyelin Sung
Supervisor: Scott, Shannon
Title: The use of arts-based knowledge translation tools in child health: a systematic review
Authors: Hyelin Sung, Arjun Bains & Shannon Scott

Theme: Children's health and well-being

Introduction

Knowledge translation (KT) is the process of taking research and presenting it in an easy way for everyone to understand. It is of particular importance in child health, due to the unique ethical situations and widely varying developmental stages of children. Arts-based KT approaches have the potential to overcome boundaries present in child health to increase understanding on complex health care topics. Drawing on a larger systematic review examining arts-based KT tools in the general population, this study seeks to elucidate the efficacy, function and nature of these tools within the distinct context of child health.

Methods

The larger systematic review searched 10 databases for English articles published between 1990-2020. The 212 included articles from the larger review were independently screened for title and abstract by 2 reviewers. The Archibald Classification Schema (ACS) was used to classify studies by narrative art form and participation type. Variables used to analyze studies were study method, country of primary author and study, age group of participants, study purpose, intervention classification and subclassification (description of art form), material type, ACS quadrant assignment, data collection and analysis methods, timing of data collection, a count and description of outcome measure types (categorized using "knowledge," "attitude," "behaviour," and "clinical" labels), and overall outcome effect.

Results

Eighty-seven articles were screened for full-text, with 64 included in our study. Included studies were of the following designs: quantitative (n=40, 62.5%), multi-methods (n=11, 17.2%), qualitative (n=9, 14.1%), and mixed-methods (n=4, 6.2%). 50 studies targeted children directly, 10 targeted parents or caregivers, 1 targeted health care professionals, and 3 had mixed target audiences. Intervention art forms included stories (n=31), theatre (n=19), first-person narratives (n=5), Illustrations or photographs (n=7), and videos (n=2). All four ACS quadrants were represented, with 34 studies in quadrant 1, 14 studies in quadrant 2, 9 studies in quadrant 3, 4 studies in quadrant 4, and 3 studies in multiple quadrants. 32 Studies (50.0%) reported overall positive effects, 7 (10.9%) reported overall mixed effects, 18 (28.1%) reported overall unclear effects, and 7 (10.9%) reported overall non-significant/negative effects.

Conclusion

This study identified 64 studies examining arts-based KT tools in child health. Our findings indicate a similar proportion of study designs in child health compared to that of the general population, while studies related to child health report more frequently unclear or negative outcomes. Moreover, studies in child health employ behavioural outcome measures more frequently compared to studies included in the larger systematic review. This study highlights the use of arts-based KT tools in child health, making clear their practical uses to healthcare professionals, patients, policymakers and researchers alike.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 145
Presenter: Yasser tabana
Supervisor: Barakat, Khaled H. S.
Title: Fishing the target of a potent small-molecule immunomodulator for cancer immunotherapy
Authors: Yasser Tabana, Jenny C.H. Lin, Dinesh Babu, Shaohui Yu, Ashley Ponich, Isobel S Okoye, R Piragasam, Marawan Ahmed, Richard Fahlman, Tae Chul moon, Shokrollah Elahi, Frederick G. West, Arno Siraki, Khaled Barakat

Theme: Lifelong women's health

Abstract
Background: T lymphocytes have been a major focus in the development of therapeutic agents as a mean to manipulate an infection or cancer response. T cells selectively recognize non-self peptides from cellular compartments and orchestrate diverse immune responses that lead to T cell-mediated killing of the infected cells. Our lab has identified a small molecule (Compound-A) that boost T-cell proliferation and cytokine production. Purpose: A comprehensive investigation is ongoing to identify and validate the target(s) and pathway(s) of this compound that contribute to its activity on T-cell proliferation and cytokine production. Methods: Effect of compound-A on its ability to produce cytokines (IFNγ and IL-2) and increase the T-cell proliferation in peripheral blood mononuclear cell (PBMCs) were measured by ELISA and CFSE staining, respectively. The genomic and proteomic changes were analyzed using RNA sequencing and label-free quantitative proteomics. Identification of the possible target(s) using pull-down was also conducted. Results: Compound-A increased T-cell proliferation and IL-2 secretion. After treating PBMCs with Compound-A for 12 h, a total of 792 differentially expressed genes (DEGs) were identified including 377 upregulated and 415 downregulated genes. Also, a total of 863 DEGs were identified after 24 h treatment, including 444 upregulated and 419 downregulated genes. GO and genome pathway analysis showed that these DEGs were enriched in signaling pathways associated with response to IFNγ. Plausible targets were obtained by pull-down assay, although they need further confirmation. Conclusion: Our study showed the immunostimulatory activities of Compound-A with possible immunological targets. A future direction will be to validate the molecular targets responsible for its immunological activities.

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Participant #: 177
Presenter: Rebecca Tan
Supervisor: Alexander, R Todd
Title: Can mutations in FAM111A cause autosomal dominant hypocalcemia?
Authors: Rebecca Tan, Christy Lee, Todd Alexander

Theme: Children's health and well-being

Introduction: Autosomal Dominant Hypocalcemia (ADH) is a childhood disorder resulting in low blood calcium and inappropriately low levels of parathyroid hormone (PTH), which functions to increase blood calcium. In 2014, a nine-year old female presented to the Stollery Emergency Department with seizures and was found to have low blood calcium levels (0.72 mM ionized), low PTH (1.2 nM) and increased urinary calcium excretion. She had no mutations in the genes (CASR and GNA11) known to cause ADH, although whole exome sequencing revealed a novel FAM111A gene mutation (c.1454G>A, p.C485Y). FAM111A mutations are known to cause Kenny Caffey syndrome and Gracile Bone disease, which are both characterized by low blood calcium levels, low PTH, short stature and bony abnormalities. The patient is normally grown, does not have bony abnormalities, but her other characteristics are consistent with a FAM111A gene mutation causing her disease. We therefore hypothesize that FAM111A mutations cause a range of diseases that all include low blood calcium and PTH levels.

Methods: We generated with CRISPR/Cas9 a mutant mouse carrying the same mutation as the patient. FAM111A heterozygous (HET; Female n=22, Male n=16), homozygous (HOM; Female n=12, Male n=10), and wild-type (WT; Female n=10, Male n=18) mice receiving a low calcium (0.01%) diet were placed in metabolic cages for 3 days to collect urine and feces every 24 hours, tissues (i.e. kidney, intestine) and blood before euthanasia.

Results: Blood calcium levels and PTH levels of all mice were within the normal physiological range and were not significantly different between WT and mutant mice. Additionally, there was no significant difference in the amount of intestinally absorbed calcium, fecal calcium excretion, or calcium balance. Urinary calcium excretion of females as assessed as a calcium/creatinine ratio (mM/mM) and 24-hour calcium excretion (mg/day) was significantly ($p<0.05$) lower in mutant HET (0.67 ± 0.13, 0.12 ± 0.03) and HOM (0.82 ± 0.18, 0.12 ± 0.03) than WT (1.15 ± 0.35, 0.19 ± 0.08). In females, the expression of intestinal genes involved in calcium absorption were not different among genotypes, however the expression of kidney genes (Cldn2, Cldn16, Cldn19, Pmca1b, Ncx1, Calb28k) involved in calcium reabsorption were significantly ($p<0.05$) decreased in HET compared to WT.

Conclusions: The mutant mice do not show an ADH phenotype. They may have increased activity of compensatory systems to normalize blood calcium levels. In HET females, this could include excreting less calcium into the urine, however, unexpectedly there was decreased expression of the kidney genes involved in calcium reabsorption. Overall, mice may not be a good model for studying FAM111A mutations due to species differences.

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Participant #: 134
Presenter: Lance Taylor
Supervisor: Aziz, Khalid
Title: Factors Associated with Severe Neurological Injury in Extremely Preterm Outborn Neonates
Authors: Lance Taylor, Dalal Abdelgadir, Mosarrat Qureshi, Khalid Aziz

Theme: Children's health and well-being

Introduction: Severe neurological injury (SNI), defined as neuroimaging-detected haemorrhage, ischemia, infarction, or cerebral ventricular enlargement, is common in extremely low gestational age neonates (ELGANs), and greatly increases the risk of adverse long-term neurodevelopmental outcomes. Being born outside a level III perinatal centre and then transferred to one (i.e., being "outborn") is associated with increased likelihood of SNI. We aim to describe the incidence and types of SNIs in outborn ELGANs.

Methods: We conducted a retrospective cohort study of 168 ELGANs born at <29 weeks GA, admitted to the Royal Alexandra Hospital Neonatal Intensive Care Unit (NICU) between 2010 and 2020, excluding neonates with congenital anomalies or unavailable neuroimaging. Patients were divided into 2 groups, with or without SNI. We collected infant demographics, ante-, intra-, and post-partum infant factors, and geographical measures. SNI included ventriculomegaly in the 1st week after birth with or without post-hemorrhagic hydrocephalus (PHHC), periventricular hemorrhagic ischemia or infarction (PVHI), cerebellar haemorrhage, or periventricular leukomalacia (PVL).

Results: Of 168 ELGANs, 38 (23%) had SNI: 23 out of 38 (61%) were <26w GA vs 15 out of 38 (39%) were 26-28w GA (p= 0.0023). The mean distance travelled during transport to level 3 NICU was not significantly associated with SNI. Male ELGANs had significantly higher rates of both PHHC and PVHI (p<0.05). ELGANs with SNI had significantly lower BW and Apgar scores, and were significantly more likely to have early cord clamping, >2 intubation attempts prior to level 3 admission, fluid boluses, and inotropic support in the first 72 hours. There was no significant difference in antenatal steroid use. We observed the following incidences of SNI: 50% (19/38) PVHI and PHHC together; 32% (12/38) PVHI alone; 13% PHHC alone (5/38); 5.3% (2/38) with PVL; and 5.3% (2/38) cerebellar haemorrhages. Delayed cord clamping for at least one minute was associated with lower rates of PHHC (OR= 2.25) but it was not associated with decrease in PVHI (OR= 0.32). Administration of fluid bolus and inotropes within the first 72 hours were associated with PHHC and PVHI, respectively (OR= 4.17 and 10.9). pCO2 levels outside 35-65 mmHg range in the 1st 72 hours after birth was significantly associated with SNI (p=0.0023). pCO2 levels outside the range of 35-65 mmHg in the 1st 72 hours of life was significantly associated with SNI (p=0.0023). Use of a Mean airway pressure (MAP) above 18mmHg was noticed more frequently among neonates with SNI but it was not statistically significant (p=0.08).

Conclusions: SNI, most commonly PVHI, is more frequent in more preterm and male outborn ELGANs and is unrelated to the distance transported or antenatal steroid use. SNI is associated with early cord clamping, multiple intubation attempts, fluid boluses, and inotrope use. Increasing early maternal transfers and implementation of a pre-transport bundle addressing peripartum interventions would be important quality improvement goals.

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Participant #: 160
Presenter: Nicole Tegg
Supervisor: Norris, Colleen M
Title: Improving Care for Women affected by INOCA
Authors: Nicole Tegg, BScN & Colleen M. Norris, PhD

Theme: Lifelong women's health

Introduction: There is an increasing prevalence of patients presenting with ischemia and no obstructive coronary artery disease (INOCA). It has been identified that women are disproportionately affected by INOCA and less likely to receive subspecialty care and targeted treatments compared to men. Evidence-based guidelines are lacking to assess, diagnose and manage patients with INOCA. Therefore, the purpose of this paper was to identify the proposed mechanisms of INOCA, contemporary diagnostic tests and treatments for INOCA.
Results: To date, there is no consensus on the exact mechanisms of INOCA. Proposed mechanisms include coronary microvascular dysfunction, vasospastic angina (VSA) and microvascular angina (MVA). Over 75% of patients with INOCA have MVA, VSA or both disorders. Epicardial adipose tissue thickness and volume, hypertension, and blood triglyceride levels are also significantly associated with INOCA. The vascular dysfunction in INOCA may be structural (remodelling of microvascular arterioles, capillary rarefaction and increased resistance in microvasculature) or functional (endothelial dysfunction). Given the lack of evidence, it is crucial to correctly identify the underlying disorder to tailor treatment plans for patients with INOCA. Non-invasive tests that identify potential causes for INOCA include nuclear myocardial perfusion imaging with coronary computed tomography angiography, positron emission tomography, cardiac magnetic resonance, and optical coherence tomography. Non-invasive tests assess perfusion during exercise or pharmacological stress through the use of adenosine (an indirect assessment of myocardial resistance). Invasive tests involve interventional diagnostic procedures (IDP) during an angiogram, including functional invasive coronary assessment, coronary reactivity testing and coronary function test. A guidewire assessment of blood flow is done at rest and under the influence of pharmacological agents such as adenosine and acetylcholine. Completing an IDP allows for the ability to discriminate between MVA, VSA and non-cardiac chest pain, which further allows for tailored treatment and provides prognostic value for physicians. There are as yet no clinical practice guidelines to treat and manage women with INOCA. In the interim, it is reasonable for therapeutic approaches to target lifestyle changes and optimized medical therapy. There is moderate quality evidence to suggest that quality of life may be improved through ACE inhibitors and ranolazine, and low quality evidence for the use of Beta blockers, CCB's and statins. There was no improvement of symptoms in single trials with irbesartan, ivabradine, metformin, omega-3 fatty acids, and trimetazidine. Low quality evidence proposes that ACE inhibitors Beta blockers, CCBs, nicorandil, ranolazine, and statins may decrease the frequency of angina and possibly delay ischemia on stress tests.
CONCLUSION: Women presenting with INOCA, often viewed as "low risk" have been recognized as high risk for major adverse CV events. This review has identified that there is a heightened need for high quality research to address the gaps in the diagnostic criteria, treatment and management of this underserved population.

Keywords: ischemia and no obstructive coronary arter

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Participant #: 64
Presenter: JuliAnn Thai
Supervisor: Hocking, Jennifer
Title: Using a zebrafish model to characterize photoreceptor degeneration in a congenital ocular disease.
Authors: JuliAnn Thai, Karen Attia, Nathan Nadolski, Jennifer Hocking

Theme: Children's health and well-being

Introduction:
KCNV2 Retinopathy is an eye disease caused by defective photoreceptors, which are light-detecting retinal cells. Diagnosed in early childhood, patients with this disease possess poor central vision, aversion to bright light and night blindness. Research has shown that mutations in a single gene, KCNV2, underlie the disease. KCNV2 codes for a potassium channel protein subunit, called Kv8.2, that resides on photoreceptor membranes. This protein contributes to sensing light and converting light into signals that can be sent to the brain. Mutations in the KCNV2 gene create dysfunctional Kv8.2 protein subunits, leading to abnormal photoreceptor responses to light and photoreceptor death. Currently, the mechanisms involved in photoreceptor death are not understood. The Hocking lab created a zebrafish model of KCNV2 Retinopathy to learn more about the disease. Zebrafish eyes are very similar to human eyes. So far, research has shown that juvenile mutant zebrafish possess enlarged yet functioning photoreceptors, with evidence of degeneration in 5-month-old fish. The functioning photoreceptors in young fish provide the potential for intervention at this stage.
Methods:
The aim of this project was to compare photoreceptors between larval and adult 16 month old fish in the zebrafish KCNV2 Retinopathy model. In this project, we characterized aged cone photoreceptors of both control and mutant 16 month adult zebrafish by assessing photoreceptor response to light using electroretinography. We additionally observed cone photoreceptor morphology using the following microscopy methods: transmission emission microscopy, immunofluorescence and hematoxylin staining.
Results:
Compared to the wild type response, mutant adult zebrafish electroretinography results revealed a delayed and diminished photoreceptor response to light. Additionally, mutant cone photoreceptors were significantly larger than age-matched controls and outer segments, the light sensing parts of the photoreceptors, were extremely disorganized.
Conclusion:
While young zebrafish models of KCNV2 Retinopathy contain functioning photoreceptors, degeneration and dysfunction of these photoreceptors in the adult stage were evident in data collected in this project. Our results have allowed us to successfully assess photoreceptor degeneration across the zebrafish lifespan. This will be extremely useful in developing treatment and intervention for patients with this disease.

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Participant #: 174
Presenter: Alexa Thompson
Supervisor: Charlton, Carmen L
Title: Investigating the adherence to HCV screening guidelines for prenatal women and infants in Alberta: a retrospective population-level analysis from 2015-2019
Authors: L. Alexa Thompson & Carmen L. Charlton

Theme: Pregnancy and developmental trajectories

Introduction
Hepatitis C (HCV) is a bloodborne virus that can cause severe liver complications. Guidelines recommend risk-based screening in pregnant women, which includes submitting one blood sample for antibody testing and, if positive, a second sample for RNA testing. Infants are recommended for HCV screening if they are born to an HCV positive mother, which involves RNA testing at 2 months old and antibody testing at 18 months old. We aimed to investigate adherence to these guidelines in Alberta.

Methods
The Public Health Laboratory database (ProvLab LIS) was retrospectively reviewed for HCV testing in prenatal women and infants under the age of 2. Data from 2015-2019 was extracted for analysis. Prenatal data was analyzed to determine the proportion of all pregnant women receiving HCV testing. For those antibody positive, the proportion of pregnant women receiving follow-up RNA testing was evaluated. All infant data was analyzed to determine the proportion of babies receiving RNA testing at 2 months and antibody testing at 18 months old.

Results
Over the study period there were 226,549 prenatal women in Alberta; only 19,393 (8.56%) had record of being risk-based screened for HCV. From those antibody positive (n=311), only 209 (67.2%) received follow-up RNA testing. From 2015-2019, there were 2,477 infants under the age of 2 that were tested for HCV. In total, 2,352 received antibody testing, while 125 received RNA testing. From those with antibody testing, 1,570 tests (66.8%) were performed before 18 months. Out of all infants 2 months or younger that were tested (n=295), 44 (14.9%) received RNA testing and 251 (85.1%) received antibody testing.

Conclusion
Adherence to HCV screening guidelines is lacking for prenatal women and infants in Alberta. Almost one-third of all antibody positive pregnant women did not receive follow-up testing, preventing proper diagnosis and linkage to care. The majority of infants were tested for HCV antibodies before recommended timelines and could receive false positives due to maternal antibodies. Universal screening programs coupled with HCV reflex testing could increase adherence to guidelines and help properly diagnose more women and infants with HCV in Alberta.

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Participant #: 207
Presenter: Courtney Tromburg
Supervisor: Ospina, Maria
Title: Association between Social Determinants of Health and Emergency Department Utilization in Pediatrics: A Systematic Review
Authors: Courtney Tromburg, Sana Amjad, Maryam Adensunkanmi, Sandra Campbell, Maryam Adesunkanmi, Brian H. Rowe, Radha Chari, and Maria B. Ospina

Theme: Children's health and well-being

Aim: To describe and evaluate the evidence of the association between social determinants of health factors (SDOH) and emergency department (ED) outcomes in pediatric populations. We hypothesize that SDOH drives inequalities in the frequency, characteristics, and outcomes of ED visits.

Methods: This systematic review was conducted in accordance with PRISMA guidelines. Databases searched include: MEDLINE, EMBASE, CINAHL, SCOPUS, ProQuest Dissertations and Theses Global, PROSPERO, and Cochrane Library from inception to June 2021. Citations were included if they: 1) contained primary research; 2) included participants below 18 years of age who have accessed the ED; 3) examined at least one of the following social determinants of health (SDOH) according to the PROGRESS-plus framework: place of residence, race/ethnicity/culture/language, occupation, gender and sex, religion, education, socioeconomic status, social capital, immigration status, and disability; and, 4) reported ED utilization and/or outcomes such as ED wait time, length of stay, investigations, treatment, discharge plan, leaving the hospital against medical advice, and leaving without being seen.

Results: Of the 6,567 titles and abstracts screened, 131 are being included for a full-text review. Full-text review is ongoing. Of these studies, 98 have examined >1 SDOH. The most commonly investigated SDOH was socioeconomic status (92), followed by race/ethnicity/culture/language (86), gender and sex (52), and place of residence (42). Less commonly investigated SDOH were social capital (10), immigration status (8), education (6), disability (3), and religion (0).

Conclusion: It is widely accepted that various SDOH contribute to health inequity: differences in care between privileged and disadvantaged groups. How health inequity presents in pediatric populations who access the ED has not been well described. An understanding of the associations and impact of various SDOH on ED utilization and outcomes will help to identify areas for targeted intervention to improve ED care for vulnerable pediatric populations.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 123
Presenter: Kimberly Tworek
Supervisor: Macala, Kimberly
Title: Developing a novel scoring system for the longitudinal clinical evaluation of sepsis in newborn rats
Authors: Kimberly Tworek*, Forough Jahandideh*, Ronan Noble, Stephane L. Bourque, Kimberly F. Macala

* Equal contribution

Theme: Children's health and well-being

Background:Neonatal sepsis is a leading cause of mortality and may burden survivors with lifelong morbidity. Animal models of neonatal sepsis can be used to explore pathophysiological mechanisms, but require extensive characterization to maximize clinical relevance. Notably, tools to assess severity of sepsis and evaluate well-being in neonatal rats are lacking. An ideal scoring system would be minimally disruptive, limit subjectivity, and be effective with narcotic use. To address this paucity of data, we tested a scoring system designed for newborn septic rats on post-natal day (PD) 3-10 that relies on clinical observation and examination used with sustained release (SR) buprenorphine for pain management.
Methods:Our study complies with the University of Alberta Animal Care Committee and CCAC guidelines. Our neonatal Rat Sepsis Score (nRSS) was developed based on mobility, response to touch, respiration, skin temperature, skin color, feeding behaviour, and scattering. Scoring was based on examination of above parameters to assess the categorical aspects of health. To study effects of SR buprenorphine on the nRSS, pups were randomized to 0 (control), 0.125mg/kg, 0.25mg/kg, and 0.5mg/kg of SR buprenorphine injected subcutaneously (SC) in male and female Sprague-Dawley rats on PD 3. Controls received saline. nRSS was assessed 4 hours post injection and then every 8 hours for 24 hours. nRSS was further validated in PD 3 pups after intraperitoneal injection of fecal slurry (0.75-1.25 mg/kg). Controls received sterile saline. We used antibiotics based on fecal slurry culture and antibiotic sensitivity (Prairie Diagnostic Services Inc., Saskatoon, SK). Ampicillin (20mg/kg, SC, every 12 hours) and gentamicin (4mg/kg, SC, every 24 hours) were administered starting 4 hours post fecal slurry injection. Saline was also injected SC every 12 hours for a total fluid volume of 5mL/kg/day. nRSS was measured every 4 hours during the first 24 hours and every 12 hours thereafter until PD 10. SR buprenorphine 0.5mg/kg SC was administered if nRSS was ≥2.
Results:Key aspects of neonatal sepsis severity were time to complete the righting reflex, work of breathing, response to touch, skin temperature, skin color, and feeding. To correlate severity of sepsis and mortality, our nRSS ranged from 0 (robust) to 4 (unwell, requiring euthanasia). SR buprenorphine resulted in no mortalities and maximum dosing of 0.5 mg/kg did not interfere with scoring of sepsis as no pups scored >1 after injection. All sepsis related mortalities occurred within the first 24 hours post sepsis induction. Septic pups scoring ≥3 on the nRSS experienced 88% mortality compared to 7% for those scoring ≤2.
Conclusion:We developed a scoring system for neonatal rats that included observation and minimal physical examination. Despite the small size of pups (PD 3-10), designing a preclinical sepsis scoring system incorporating pain management was accomplished. We discovered our nRSS serves as a reliable indicator of sepsis severity in both sexes and maximum dosing of SR buprenorphine does not interfere with this sepsis scoring system. With all mortality occurring within the first 24 hours, this demonstrates a critical time period where pain management and non-invasive assessment are imperative.

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Participant #: 191
Presenter: Kazuki Ueda
Supervisor: Simmonds, Andrew
Title: A neuroprotective role of select peroxisome proteins at the fat body of Drosophila melanogaster
Authors: Kazuki Ueda
Matthew Anderson-Baron
Nathan Hoeven
Julie Haskins
Andrew Simmonds

Theme: Children's health and well-being

Introduction:

A systemic lipid homeostasis is crucial in proper functioning and development of organ systems. Peroxisome is a membrane-bound organelle and is one of the central hubs of lipid metabolism. A congenital, autosomal recessive disorders affecting one of 14 core peroxisome genes, Peroxins (Pex), lead to spectrum of peroxisome biogenesis disorders (PBDs) exhibiting neurological deficits and developmental delays in children currently with no effective treatment options. Our lab has identified a peroxisome-independent function of two Pex proteins, Pex13 and Pex14, in promoting lipid storage at lipid droplets (LDs) (cellular fat storage site) in Drosophila melanogaster. Our objective is to identify how these new roles of Pex proteins contribute to pathologies observed in PBD patients.

Methods:

Fruit fly is an established model organism used to investigate both PBD and lipid-associated metabolic diseases. Various Pex mutant and fat body(human adipose tissue and liver equivalent)-specific Pex knockdown (Pex FKD) flies were prepared to recapitulate patient symptoms and investigate how PEXs in tissues central to lipid metabolism influences overall animal development, respectively. i) The 3rd instar (L3) larvae with Pex FKD were challenged with a high-fat (holidic+lard) or fed a low-fat (holidic) diet and the survival rate to adult was measured. ii) The size of the brain of Pex FKD L3 larvae raised on high-fat diet were compared iii) The fat storage (LDs) in the fat body of Pex mutant larvae raised on regular diet were compared.

Results:

i) When wild type (WT) and Pex FKD (Pex1, Pex13, and Pex14) were fed on holidic food, they remained relatively stable and exhibited similar survival rates. When raised on holidic+lard food, the survival rate of both WT and Pex1 FKD larvae remained similar to the previous feeding condition while Pex13 or Pex14 FKD displayed reduction in their survival rates. ii) Compared to the WT larvae, Pex13, Pex14, and Pex16 FKD showed reduced brain size while Pex11 and Pex19 did not seem to be affected. iii) Compared to the WT larvae, only Pex13 and Pex14 mutants displayed reduced fat storage in the fat body indicated by reductions in size and quantity of LDs while Pex1 and Pex5 mutants seemed to display increased fat storage.

Conclusion:

Overall, these evidence seem to support the unique roles of both Pex13 and Pex14 in promoting lipid storage in the fat body of Drosophila melanogaster. Moreover, these roles seem to be independent of peroxisomes as other Pex FKD and mutants that also similarly affect peroxisome functions were seemingly unaffected. When the function of Pex13 or Pex14 was interrupted at the fat body it had a systemic effect which negatively impacted brain development. Further research is required to interrogate the mechanism of this delayed brain development and to investigate the impact on other organ systems affected in PBDs including the gut, oenocytes (liver equivalent), and Malphigian tubule (kidney equivalent).

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 151
Presenter: Roberto Villalobos-Labra
Supervisor: Davidge, Sandra
Title: Comparison of the Effects of Placenta-Derived Extracellular Vesicles from Preeclamptic and Healthy Pregnancies on Vascular and Endothelial Function
Authors: Roberto Villalobos-Labra, Floor Spaans, Tamara Sáez, Anita Quon, Christy-Lynn M. Cooke, Sandra T. Davidge.

Theme: Pregnancy and developmental trajectories

Introduction: Preeclampsia (PE) is a pregnancy complication affecting ~5% of all pregnancies in Canada, characterized by new-onset hypertension during pregnancy and end-organ damage. It is thought that maternal vascular/endothelial dysfunction is central to the development of PE, which may be due to a poorly developed placenta releasing damaging factors into the maternal circulation, such as syncytiotrophoblast-derived extracellular vesicles (STBEVs). Literature shows that STBEVs from PE differ in protein composition, and are potentially more damaging to vascular function, compared to STBEVs from normal pregnancies (NP). NP STBEVs were previously shown to impair vascular function, but the effects of PE STBEVs on vascular function are still unknown. Thus, we hypothesized that PE STBEVs have a more adverse effect on endothelial/vascular function than NP STBEVs.
Methodology: STBEVs were collected by perfusion of placentas and pooled (n=3 NP or PE placentas). Human umbilical vein endothelial cells (HUVECs) isolated from NP umbilical cords (n=5) were treated with or without NP or PE STBEVs (10, 50, 100, 200 µg/mL for 24h), and levels of reactive oxygen species (ROS; by DHE staining) were assessed as an endothelial dysfunction marker. In addition, mesenteric arteries isolated from pregnant rats on gestational day 20 ([term=21 days]; n=7-9) were incubated overnight with or without NP or PE STBEVs (10, 100, 200 µg/mL). Endothelium-dependent vasodilation to methylcholine (MCh) was evaluated by wire myography. Nitric oxide (NO) contribution was determined by incubating vessels (treated with 100 µg/mL of NP or PE STBEVs) with or without L-NAME (inhibitor of NO synthases) 30 min before adding MCh. Endothelium-independent vasodilation was assessed by evaluating the response to sodium nitroprusside (SNP, a NO donor). Data were analyzed by ANOVA with Sidak's posthoc test and is presented as the mean±SEM; $p<0.05$ was considered significant.
Results: Both NP and PE STBEVs increased ROS levels in HUVECs at 100 and 200 µg/mL compared to the untreated cells, but there were no differences in effect between NP and PE STBEVs (fold increase vs. untreated cells: NP STBEVs at 100 µg/mL: 1.28±0.07 fold, 200 µg/mL: 1.38±0.06 fold; PE STBEVs at 100µg/mL: 1.23±0.08 fold, 200 µg/mL: 1.34±0.08 fold). NP and PE STBEVs reduced max. vasodilation to MCh at 100 and 200 µg/mL (% reduction vs. untreated vessels: NP STBEVs at 100 µg/mL: 16.8±2.97%, 200 µg/mL: 16.2±4.86%; PE STBEVs at 100 µg/mL: 12.26±3.11%, 200 µg/mL: 12.64±3.79%). Both NP and PE STBEVs reduced NO contribution to vasodilation (% reduction vs. untreated vessels: NP STBEVS: 62.67±7.28%; PE STBEVs: 41.98±9.23%), without differences between NP and PE STBEVs. SNP-induced vasodilation was similar between all conditions.
Conclusions: Our data suggest that NP and PE STBEVs impair endothelial function via increased oxidative stress and reduced NO bioavailability. However, in contrast to our hypothesis, there appeared to be no differences between PE and NP STBEVs. Our future studies are focused on the potential mechanisms, and if the effects of PE STBEVs would be different in PE compared to healthy vessels. Our data contributes to the development of potential targets to prevent and treat women affected by preeclampsia.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 97
Presenter: Maggie Wang
Supervisor: Zhang, Dawei
Title: Multiple site cleavage on LDLR by MT1-MMP increases risk for high plasma cholesterol.
Authors: Adekunle Alabi, Maggie Wang, Hongmei Gu, Dawei Zhang

Theme: Children's health and well-being

Introduction: The Low-density lipoprotein receptor (LDLR) which mediates cellular uptake of LDL is the main pathway for plasma LDL cholesterol (LDL-C) clearance. Membrane type 1-matrix metalloproteinase (MT1-MMP) is a Zn2+ - dependent endopeptidase that can cleave extracellular matrix and non-matrix substrates. We have previously demonstrated that MT1-MMP promoted ectodomain shedding of LDLR, reducing LDLR-mediated LDL-C clearance. The aim of this study was to understand the cleavage pattern of MT1-MMP on LDLR.

Methods: We made cDNA with deletions in regions coding for different parts of the LDLR protein. Each deletion mutant was co-expressed with MT1-MMP in HEK293 cells. To determine the importance of the catalytic region of MT1-MMP, we also deleted specific regions of MT1-MMP with an HA tag and then co-expressed the mutant with WT LDLR.

Results: MT1-MMP cleaved all LDLR mutants tested in a similar manner to the wild-type protein, indicating that the regions in LDLR we tested are not required for MT1-MMP's cleavage of the LDLR. It also indicates that MT1-MMP has multiple cleavage sites on the protein. The cleavage property was lost with the catalytic region deletion of MT1-MMP, reinforcing the importance of the catalytic property of the proteinase for LDLR cleavage. In addition, deletion of the MT-loop in MT1-MMP led to a loss of the cleavage property of MT1-MMP even though the protein still retained its catalytic property as indicated by its autocatalysis to generate a 44 KDa fragment of the protein. All other deletion within the MT1-MMP protein did not affect its ability to cleave LDLR.

Conclusions: MT1-MMP promotes ectodomain shedding of hepatic LDLR by cleaving at multiple sites. The catalytic activity and the MT-Loop are essential for MT1-MMP's action on LDLR. Our studies indicate that the MT-Loop is a promising target for inhibiting MT1-MMP-promoted LDLR degradation, reducing the risk for atherosclerotic cardiovascular disease.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 203
Presenter: Shi Wang
Supervisor: Li, Xingyu
Title: Feasibility of applying deep learning on EEG data for ADHD children identification
Authors: Shi Wang, Xingyu Li

Theme: Children's health and well-being

Introduction: Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common neuropsychiatric disorders in childhood. The traditional diagnosis of ADHD includes clinical interviews, symptom questionnaires, and neuropsychological testing. Prior research effort has shown the usefulness of neurophysiological signals such as electroencephalogram (EEG) data in this diagnostic process. As EEG recording is very data-intensive, this preliminary study evaluates the feasibility of using deep learning models to analyze EEG data for ADHD children identification.

Methods: We use a public event-revoke EEG dataset collected from 100 ADHD children and 44 normal kids in this study. For data quality, EEG data was collected using 56 electrodes; furthermore, multiple trials of EEG recordings from the same kid are included in this dataset. We design the evaluation protocol with two settings: subject-independent and subject-dependent tests. The subject-independent test can be used for a patient's regular follow-up check, and the subject-dependent test is more suitable for new patient examination. We first apply a deep convolutional neural network (CNN), EEGNet, to our problem, where the CNN architecture consists of five convolutional layers with a SoftMax layer for classification. In addition, we design a self-supervision contrastive learning model for EEG numerical feature representation. Particularly, we incorporate subject IDs and their health conditions in contrastive learning so that EEG recording trials from the same kid are clustered together in the low-dimensional feature domain. We assess the performance of the proposed contrastive learning model using the same evaluation protocol as EEGNet.

Results: Over the event-evoked EEG dataset, EEGNet achieves 90% and 24% diagnosis accuracy in the subject-independent and subject-dependent settings, respectively. The surprisingly low diagnosis accuracy suggests that EEGNet fails to identify new ADHD kids. Compared with EEGNet, the contrastive learning model achieves better performance under both settings. Specifically, the subject-independent diagnosis using contrastive learning can reach up to 99% accuracy, and the subject-dependent classification accuracy is improved to about 70%.

Conclusion: The proposed deep contrastive learning method achieves plausible results in this study. This indicates that deep learning, especially contrastive learning, is a promising means to support clinical diagnosis in ADHD. However, more work needs to be done to improve the diagnosis performance.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 100
Presenter: Adrianne Watson
Supervisor: Voronova, Anastassia
Title: The role of fractalkine signalling in neural stem cells during brain development
Authors: A. Watson, M. Almeida, N. Dittmann, Y. Li, P. Torabi, T. Footz, G. Vetere, D. Galleguillos, S. Sipione, A. Cardona, A. Voronova.

Theme: Children's health and well-being

INTRODUCTION: During brain development, neural stem and precursor cells (NPCs) generate diverse progeny, including neurons, astrocytes and oligodendrocytes. Oligodendrocytes are glial (non-neuronal) cell types that generate myelin, a fatty substance that coats and protects nerve projections. The ability to form healthy myelin, which comprises white matter, is critical for proper brain development and cognition; however, in children with neurodevelopmental disorders, white matter formation is abnormal. NPCs in the subventricular zone (SVZ) of mammalian brain have the ability to produce oligodendrocytes throughout life. If we can identify the signals that instruct NPCs to become oligodendrocytes, we may be able to utilize this information to engage endogenous NPCs to regenerate oligodendrocytes and myelin for proper brain development and function. My project focuses on chemokine fractalkine (FKN). Mutations in FKN receptor (CX3CR1) are present in patients with autism spectrum disorder and schizophrenia. While CX3CR1 is highly expressed in brain immune cells (microglia), recent reports suggest NPCs also express this receptor, although at a lower level. However, the role of FKN-CX3CR1 signalling axis in postnatal and adult NPCs is not known.
METHODS: To address this knowledge gap, we analyzed oligodendrogenesis from NPCs isolated from postnatal SVZ niche in the presence of FKN or FKN function-blocking antibodies. We then infused FKN into murine brain and analyzed its in vivo ability to engage NPCs for oligodendrocyte formation.
RESULTS: We show postnatal NPCs express Cx3cr1 and bind FKN in vitro and in vivo. When FKN is added to microglia-free NPC cultures, it 1) enhances NPC to OPC commitment; and 2) accelerates OPC to oligodendrocyte differentiation without affecting neurogenesis, astrogliogenesis, precursor proliferation or survival. Importantly, itracrerebral infusion of FKN enhances OPC and oligodendrocyte genesis from SVZ NPCs in vivo. Inhibition of FKN signalling with function-blocking antibodies inhibits neuron and oligodendrocyte differentiation from NSCs (Watson et al. 2021 Stem Cell Rep). To confirm this finding, we cultured primary NPCs from mice that express a human pathogenic variant of CX3CR1 (hM280/I249), which is known to disrupt proper FKN signalling. Our preliminary data show NPCs and OPCs that express pathogenic CX3CR1 show increased proliferationI am currently corroborating these results in vivo and expanding them to oligodendrocyte differentiation analysis.
CONCLUSIONS: Taken together, these data show i) FKN-CX3CR1 signalling is critical for oligodendroglial cell formation from neural stem cells in the developing brain; and ii) mutations in FKN-CX3CR1 signalling axis may lead to dysfunctional neural stem cells, which may contribute to aberrant brain development seen in autism and schizophrenia patients. Finally, our results identify FKN as a potential therapeutic target for enhanced oligodendrocyte genesis.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 185
Presenter: Olivia Weaver
Supervisor: Proctor, Spencer
Title: Elevated non-fasting remnant cholesterol is associated with increased odds of incident cardiovascular events in Canadian women
Authors: Olivia Weaver, Jacqueline Krysa, Ming Ye, Jennifer Vena, Dean Eurich, Spencer Proctor

Theme: Lifelong women's health

Introduction
Fasting low-density lipoprotein cholesterol (LDL-C) is the traditional lipid marker used in cardiovascular disease (CVD) risk screening in Canada. However, even after reducing fasting LDL-C to recommended levels residual CVD risk remains. Non-fasting remnant cholesterol (RC) is an emerging marker that may better predict CVD risk compared to fasting LDL-C. Despite this, data in Canadian populations does not exist to support clinical implementation of non-fasting RC as a marker for CVD risk. In addition, women have unique CVD risk factors and outcomes compared to men, warranting sex-specific investigations into novel lipid screening methods. Previously, unadjusted results from this analysis were presented. Therefore the current analysis aimed to determine the adjusted relationship of non-fasting RC (versus LDL-C) with CVD incidence in a Canadian, female population.

Methods
Female participants of the Alberta Tomorrow Project/Canadian Partnership for Tomorrow Project (a prospective cohort study of chronic disease, 2000-present) were selected for the current analysis if they had a complete non-fasting lipid profile with non-negative lipid values, provided their personal health number and consented to data linkage with Alberta Health administrative databases (n=10,957). Non-fasting RC was calculated as: total cholesterol - LDL-C - high-density lipoprotein cholesterol. LDL-C was calculated via Friedewald equation. Data linkage was used to obtain individual-level data on CVD outcomes, statin use and comorbidities. The primary outcome of interest was a composite variable of incident CVD events (ischemic heart disease, myocardial infarction, angina, heart failure, transient ischemic attack, acute ischemic stroke). Multiple logistic regression was used to analyze the relationship between non-fasting lipids (LDL-C, RC) and composite CVD incidence while adjusting for age, Elixhauser comorbidity index, statin use and RC/LDL-C).

Results
Women were on average 61.48±9.71 years of age with a mean Elixhauser score of 3.12±2.42. Non-fasting lipid levels included mean LDL-C of 2.88±0.85mmol/L and mean RC of 0.75±0.36mmol/L. Incident CVD events occurred in 6.2% of participants and mean RC was significantly higher in these women compared to those without incident events (0.85±0.39mmol/L vs 0.74±0.36mmol/L, $p<0.0001$). Mean LDL-C was not different between groups. Odds of incident composite CVD events per mmol/L increase in RC were significantly increased (adjusted OR: 1.64, 95% CI: 1.34-2.02), whereas odds of incident CVD events per mmol/L increase in LDL-C were significantly reduced (adjusted OR: 0.81, 95% CI: 0.73-0.89). Similarly, odds of incident composite CVD were significantly increased with increasing quartiles of RC, but were significantly decreased with increasing quartiles of LDL-C.

Conclusion
Increased odds of incident CVD events were associated with elevated non-fasting RC but not LDL-C in this sample of Canadian women. Further research in a wider Canadian population is warranted to investigate the RC/CVD relationship in the context of comorbidities presenting increased CVD risk (eg Type 2 Diabetes, Polycystic Ovarian Syndrome) and to develop sex-specific RC reference ranges which may help improve CVD risk screening for women in Canada.

This research has been facilitated by WCHRI through the generosity of the supporters of the Lois Hole Hospital for Women.

Participant #: 147
Presenter: Alyssa Wiedemeyer
Supervisor: Bourque, Stephane
Title: Macrophage polarization as a mechanism of altered kidney growth and dysfunction in perinatal rats exposed to iron deficiency
Authors: Wiedemeyer, A., Holody, C., Bourque, SL.

Theme: Pregnancy and developmental trajectories

Introduction: Stressors during early development can increase the risk of chronic diseases later in life. Iron deficiency (ID) is the most common nutritional deficiency worldwide, affecting approximately 38% of pregnant women. Our lab has shown that maternal ID impacts fetal kidney development, characterized by reduced nephron endowment and impaired growth and maturation. However, the cellular mechanisms that drive altered renal development in ID are not known.
Macrophages are important immune cells within the kidney. During kidney development, alternatively activated M2 macrophages promote growth by mediating cell turnover and tissue remodelling. Conversely, classically activated M1 macrophages mediate inflammatory responses, and in turn, can damage organs when inappropriately activated. Further, macrophages can switch phenotypes between M1 and M2 in response to microenvironmental cues and energy substrate availability. Polarization towards the inflammatory M1 phenotype is implicated in many disease pathologies. We hypothesized that perinatal ID impairs nephrogenesis by causing a phenotypic switch from M2 to M1 macrophages in neonatal kidneys.
Methods: Female Sprague Dawley rats were fed an iron-restricted diet prior to and throughout gestation to induce maternal ID. Dams at gestational day (GD) 21 were euthanized, and tissues and hemoglobin (Hb) values from fetal offspring were collected for analysis. Kidneys were homogenized and subjected to flow cytometry to evaluate M1 and M2 macrophages. M1 populations were defined using CD68+CD86+ staining, while M2 populations were defined by CD68+CD163+ markers. Further, fluorescence activated cell sorting will be utilized to separate M1 and M2 phenotypes, and single cell RNA sequencing will be performed to examine M1/M2 genes that are altered due to ID. Immunofluorescence (IF) will also be performed to assess M1 and M2 proportions based on intracellular markers; CCR7 for M1 and arginase-1 for M2 cells.
Results: Hb levels were reduced in ID pups at GD21 for both males and females ($P<0.001$ for both). ID resulted in decreased birth weight compared to control pups in both male and female pups ($P<0.001$ for both). Preliminary flow cytometry data demonstrate a 29% decrease of M2 macrophages in males ($P=0.004$) and a 24% decrease in females ($P=0.02$), compared to their respective controls. Males ID fetuses had a 12% decrease of M1 cells ($P=0.04$) while female ID fetuses exhibited a 17% decrease of M1 cells ($P=0.01$). Currently, IF is being performed to validate these results with cytoplasmic markers.
Conclusion: This study will provide new insights into the mechanisms by which ID affects kidney development. Understanding macrophage biology during kidney development may lead to novel therapeutic targets to prevent long-term kidney diseases associated with ID. Drugs such as atorvastatin can be explored to correct for M1 polarization in ID kidneys, preventing renal damage. By preventing organ damage during early development, we hope to prevent the development of diseases later in life.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 121
Presenter: Jessica Wijesundera
Supervisor: Ball, Geoff DC
Title: Associations between social determinants of health and preschool children's weight status: A population-based study
Authors: Jessica Wijesundera, Anamaria Savu, Sunjidatul Islam, Douglas C. Dover, Linn E. Moore, Andrea M. Haqq, Padma Kaul, Geoff DC Ball

Theme: Children's health and well-being

Background: Unhealthy child weights can lead to serious chronic conditions. Social determinants of health (SDH) may influence children's weight status. Our objective was to examine relationships between key SDH, including ethnicity, immigrant status, income, setting, material and social deprivation, and weight status in preschoolers in Alberta, Canada.

Methods: In this retrospective, population-based cohort study, children's anthropometric measurements were taken during preschool (4-6 years old) immunization visits in Edmonton and Calgary (Alberta, Canada) from 2009 to 2017. Children were categorized into weight status categories (underweight, normal weight, at risk of overweight/overweight, obesity) using body mass index z-scores (zBMI) based on World Health Organization criteria. Maternal data were linked to child data. Material and social deprivation indices were calculated using the Pampalon Index. Our first multinomial logistic regression model used relative risk ratios (RR) to estimate the association of maternal ethnicity, maternal immigrant status, annual neighborhood-level household income, geographic setting at birth, and preterm birth status with child preschool weight category. Our second and third models estimated material and social deprivation associations, separately, with child weight category at preschool age (using RR). All models were adjusted for child sex and age at anthropometric measurement.

Results: Our first model analyzed data from 168,383 children. Children of Chinese ethnicity (versus 'General Population') were less likely to have at risk of overweight or overweight status (RR, 0.63; 95% confidence interval (CI) [0.60, 0.67]) and less likely to have obesity (RR, 0.47; 95% CI [0.39, 0.57]), whereas South Asian children were more likely to have underweight (RR, 3.95; 95% CI [3.40, 4.59]) and more likely to have obesity (RR, 1.38; 95% CI [1.21, 1.57]). Children with maternal immigrant status were less likely of having underweight (RR, 0.70; 95% CI [0.62, 0.79]) and having obesity (RR, 0.70; 95% CI [0.65, 0.75]). Children were less likely to have at risk of overweight or overweight (RR, 0.94; 95% CI [0.94, 0.95]) and less likely to have obesity (RR, 0.87; 95% CI [0.85, 0.88]) for every $10,000 increase in neighborhood-level household income. Relative to the least deprived quintile, children in the most materially deprived quintile were more likely to have underweight (RR, 1.98; 95% CI [1.67, 2.34]), more likely to have at risk of overweight or overweight (RR, 1.56; 95% CI [1.51, 1.63]), and more likely to have obesity (RR, 3.32; 95% CI [2.99, 3.69]). Children in the most socially deprived quintile were more likely to have at risk of overweight or overweight (RR, 1.15; 95% CI [1.11, 1.18]) and more likely to have obesity status (RR, 1.28; 95% CI [1.18, 1.39]).

Conclusions: The weight status of preschoolers varied across several key SDH, namely ethnicity, maternal immigrant status, and material and social deprivation. Interventions designed to address these differences are needed to minimize inequities across SDH and optimize healthy weights in young Canadian children.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 175
Presenter: Harry Wilton-Clark
Supervisor: Yokota, Toshifumi
Title: Competition between dystrophin isoforms causes a Duchenne muscular dystrophy-like phenotype
Authors: Harry Wilton-Clark, Md Nur Ahad Shah, Kenji Rowel Lim, Toshifumi Yokota

Theme: Children's health and well-being

Introduction
Duchenne muscular dystrophy (DMD) is one of the most lethal genetic diseases affecting children, with an average lifespan in the early-mid 20's. DMD is caused by a mutation in the DMD gene encoding for dystrophin, a protein critical for muscle repair, and the loss of which leads to progressive systemic muscle deterioration. Various isoforms of dystrophin are naturally expressed in a tissue-specific manner throughout the body; however, DMD mutations can alter this regulation and cause over- or under-expression of specific dystrophin isoforms. In this study, we aimed to characterize an unexpected dystrophic phenotype in a mouse model, a humanized exon 52 deleted mouse (hDMDdel52;C57BL/6J), containing two copies of the DMD gene: one mutated, one wild-type. Despite the presence of a healthy wild-type gene, the mouse displayed a DMD-like cardiac phenotype. While we discovered this phenotype incidentally, the same interaction could impede the treatment of DMD patients. We hypothesized that this dystrophic phenotype was due to competition between the products of the short DMD isoform (DP71) and the healthy DMD gene (DP427m).

Methods
To analyze the connection between isoform expression and muscular dystrophy, dystrophin protein isoforms from skeletal and cardiac muscle were quantified with western blot, RNA expression was qualified with RT-PCR, and immunohistochemistry was performed to visualize the localization of dystrophin in muscle fibres. Heart function was also assessed through echocardiography. Data in all tests was compared to data from wild-type control mice, and statistical analysis was performed with either Student's t-test or ANOVA and post hoc Tukey's HSD test. Our humanized mouse model was selected as it allows us to study the human dystrophin gene in vivo outside of clinical trials, providing a robust and translatable platform for our research.

Results & Conclusion
We found that compared to healthy wild-type mice, our dual-copy mice had significantly increased cardiac DP71 protein levels ($P<0.05$), significantly reduced cardiac cell size when measured with minimal Feret's diameter ($P<0.001$), and significantly reduced cardiac ejection fraction ($P<0.05$). These data suggest an important association between DP71 overexpression, reduced cardiac cell growth, and reduced cardiac performance, laying the groundwork for future studies which will broaden our understanding of muscular dystrophy and how best to treat it. Specifically, these findings indicate a need to explore how the presence of host mutant dystrophin isoforms might disrupt the effect of dystrophin-producing therapy options for patients, and how best to avoid this.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 183
Presenter: Jason Wong
Supervisor: Lou, Edmond HM
Title: Applying machine learning to semi-automatically measure the Cobb angle on ultrasound images for adolescent idiopathic scoliosis
Authors: Jason Wong, Marek Reformat, Eric Parent, Edmond Lou

Theme: Children's health and well-being

Introduction
Scoliosis is a three-dimensional spinal curvature condition that affects 1-3% of adolescents. The Cobb angle measured on radiographs quantifies curve severity. To minimize radiation exposure, ultrasound has been investigated for imaging scoliotic spines and has been found to be comparable to radiography in terms of accuracy and reliability. However, measuring the Cobb angle on ultrasonographs requires identifying the centers of laminae (COL), which is more time-consuming than on radiographs and subject to human error. The purpose of this study was to develop a machine learning algorithm to semi-automatically measure the Cobb angle on ultrasonographs and report the validity of the developed method.

Methods
The spines of 130 children with idiopathic scoliosis who had a Cobb angle below 45° and no prior surgery were scanned by an ultrasound imager with consent. Among those, 70 ultrasonographs were selected for lamina segmentation machine learning training and 60 for semi-automatic Cobb measurement testing. The training set comprised of 1,186 lamina pairs, or 157 curves with Cobb angle of 20.2°±8.4°. A convolutional neural network (CNN) was trained to identify lamina pairs for all vertebrae. The test set consisted of 118 curves with Cobb angle of 20.4°±8.2°, manually measured by two raters with more than three years of experience. The test images were input into the CNN to automatically predict the COL. The COL were then automatically paired up for each vertebra. A rater with two years of x-ray Cobb angle measurement experience interacted with the program to confirm the relevant lamina pairs for measurement. Then, the Cobb angles were automatically calculated. The standard error of measurement (SEM) and inter-method intraclass correlation coefficient (ICC3,1) between the manual and semi-automatic measurements were calculated. Results were analyzed by curve region, with main thoracic (MT) and thoracolumbar/lumbar (TL/L) groups. This is because TL/L curves are harder to measure since their vertebrae have a larger surface area that creates extra ultrasound reflections, generating more noise.

Results
Out of the 118 curves manually measured, 107 (91%) were detected by the semi-automatic method. The SEM of these 107 paired Cobb measurements was 1.1°, with 81 curves (76%) measured within the clinically accepted error (5°). The semi-automatic measurements also demonstrated good reliability (ICC3,1 = 0.87), performing the best for MT (ICC3,1 = 0.91) but less reliably for TL/L (ICC3,1 = 0.81). This approach reduced the Cobb angle measurement time from 5 minutes (manual) to an average of 29 seconds (semi-automatic), with the CNN generating lamina predictions in under 1 second.

Conclusion
Using machine learning to assist Cobb angle ultrasound measurements provided good inter-method reliability. This is a promising result since the reliability of manual ultrasound with x-ray measurements is good (ICC2,1 = 0.86). A 76% clinical acceptance measurement rate and a quicker measurement time were achieved with this semi-automatic procedure. Future work includes fully automating Cobb angle measurements on ultrasonographs so that the risk of cancer in these children can be reduced by further validating ultrasound as a viable imaging method for AIS.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 71
Presenter: Amy Wooldridge
Supervisor: Davidge, Sandra
Title: Advanced maternal age impairs pregnancy-induced adaptations of the rat main uterine artery
Authors: Amy L. Wooldridge, Mazhar Pasha, Raven Kirschenman, Floor Spaans, Christy-Lynn M. Cooke, Sandra T. Davidge

Theme: Pregnancy and developmental trajectories

Introduction: Almost a quarter of live births in Canada are to women of advanced maternal age (>35 years). Advanced maternal age is a risk factor for pregnancy complications such as preeclampsia. We previously showed that ex vivo uterine artery constriction in response to increasing intraluminal pressures (myogenic tone) was greater in arteries of aged compared to young pregnant rats. Aging impairs vascular reactivity and increases vascular stiffness, however, the impact of aging on uterine artery adaptations to pregnancy are not known. Thus, to assess pregnancy adaptations, the current study included non-pregnant controls. We hypothesized that the functional and structural adaptations to pregnancy in the uterine artery (non-pregnant vs pregnant) are reduced in aged rats compared to young rats.
Methods: Pregnant young (4 months) and aged (9 months; ~35 years in humans) rats were studied on gestational day 20 (term=22 days) with age-matched non-pregnant rats. Pregnancy outcomes were recorded, and uterine arteries were isolated and mounted in a pressure myograph. The effect of pressure on vessel diameter was assessed under active (calcium present, n=6-10) and passive (calcium absent, to assess mechanical properties of circumferential stress and strain, n=10-24) conditions. Myogenic tone, circumferential stress and strain of the vessels were calculated from data from active and passive curves. Data are mean area under the curve (AUC)±SEM; analyzed by two-way ANOVA with Sidak post-hoc tests (significance at $p<0.05$).
Results: Aged dams had more reabsorptions ($p<0.005$), and greater placental weights, with smaller litter sizes and fetal weights ($p<0.0001$ for all) than young dams. Between 4-100 mmHg, we observed no differences in myogenic tone with age or pregnancy. However, uterine arteries from young pregnant rats displayed forced vasodilation at higher pressures (100-160 mmHg) due to a reduction in myogenic tone that did not occur in arteries from any of the other groups (AUC of % myogenic tone; young non-pregnant: 3261±248; young pregnant: 751±244; aged non-pregnant: 2700±175; aged pregnant: 2616±259; young non-pregnant vs. young pregnant, and young pregnant vs. aged pregnant, $p<0.0001$). Pregnancy increased uterine artery circumferential stress (AUC non-pregnant 217±5 vs. pregnant 272±9; $p<0.0001$), without effects of aging. Circumferential strain increased with pregnancy (AUC non-pregnant 98±3 vs. pregnant 128±4; $p<0.0001$), and was reduced with age in vessels from pregnant (AUC young pregnant 116±5 vs. aged pregnant 104±4; $p<0.05$), but not non-pregnant rats.
Conclusions: As hypothesized, our study indicates that uterine arteries do not adapt to the same extent with pregnancy in aged rats as in young rats. Uterine arteries of aged pregnant rats were less compliant, which may contribute to the lack of forced vasodilation at high pressures in these arteries. These age-related changes may impact uteroplacental blood supply, consistent with the reduced fetal and increased placental weights (suggesting placental insufficiency). Thus, impaired uterine artery adaptations may contribute to an increased risk of pregnancy complications at an advanced age.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 155
Presenter: Samuel (Suk-Min) Yang
Supervisor: Storey, Kate E
Title: Sleeping Soundly: Strengthening school-based sleep promotion through diverse perspectives
Authors: Samuel (Suk-Min) Yang, Pamela Mellon, Genevieve Montemurro, Kate Storey

Theme: Children's health and well-being

Introduction:
Sleep serves as a foundation for healthy living in children; the consequences of insufficient sleep in children are broad and include both physical and psychosocial impacts. Inadequate sleep can also impair learning through behavioural changes such as daytime sleepiness, hyperactivity, attention, and memory. Because the school setting plays a pivotal role in influencing children's health behaviors, school-based sleep promotion is vital for children's wellbeing. Comprehensive School Health (CSH) is an internationally recognized framework utilized to build healthy school communities through its integrative and holistic approach. Where CSH has proven effective in enhancing healthy behaviours among students, research on school-based sleep promotion is sparse. Greater understanding is needed on how sleep promotion can be strengthened through alignment with the CSH approach.

Purpose:
The purpose of this research was to conduct a secondary analysis of student, parent/guardian, and teacher interviews regarding sleep through the CSH framework. The overarching goal was to incorporate diverse perspectives to improve and strengthen the practice of school-based sleep promotion and guide ongoing knowledge mobilization.

Methods:
A secondary qualitative analysis of student (n=45), parent/guardian (n=25), and teacher (n=19) interviews from participants representing schools and communities in Alberta, Canada was completed. This provided an understanding of diverse perspectives on student and family sleep behaviours as well as existing school-based sleep promotion practices. The secondary analysis involved re-analyzing the data through a process of inductive content analysis using an a priori framework in which the data were examined for their alignment with the four components of the CSH framework: social and physical environment, teaching and learning, policy, and partnerships and services.

Results:
Preliminary findings identified key learnings related to all components of the CSH framework. Students described healthy bedtime routine practices learned from school and some shared these tips with friends and families ('social and physical environment'). Teachers sparked conversations surrounding sleep through school and classroom-wide activities (e.g., announcements, bulletin boards, monthly campaigns) ('teaching and learning'). While participants rarely referenced school policy, teachers highlighted the importance of sleep education in school curriculum to support healthy sleep habits ('policy'). Additionally, parents/guardians and teachers both expressed that home-school collaboration would support families with resources to guide healthy sleep behaviours for children ('partnerships and services').

Conclusions:
By exploring students, parents, and teachers' perspectives on school-based sleep promotion through the CSH framework, this research lays the foundation for improving school-based sleep promotion in practice. Alignment with the CSH approach will allow the development of knowledge products that will support practitioners and decision-makers, ultimately improving sleep health for the whole school community.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 198
Presenter: Vasyl Yavorskyy
Supervisor: Wilbur, Colin
Title: Medical Investigations in Paediatric First Episode Psychosis
Authors: Vasyl Yavorskyy, Erin Stolte, Francois-Dominique Morneau-Jacob, Colin Wilbur

Theme: Children's health and well-being

Introduction: Children presenting with a first episode of psychosis (FEP) often represent a diagnostic challenge, as symptoms may result from many pathophysiologic processes including primary psychiatric disorders and treatable medical conditions. A protocol was recently developed at the Stollery Children's Hospital to standardize the initial investigations in children presenting with FEP with attention to identifying treatable conditions. The aim of this retrospective study was to evaluate current clinical practice in comparison to this proposed protocol.
Methods: Children less than 18 years of age admitted to the Royal Alexandra Hospital or Stollery Children's Hospital with discharge diagnoses corresponding to psychosis or encephalitis were identified through the Discharge Abstract Database for the period January 1, 2019 - December 31, 2020. Retrospective chart review was performed and those with an admission diagnosis of psychosis were included, provided there was no previous documented episode of psychosis or an admission diagnosis of substance-induced psychosis.
Results: 23 children (12 female) were identified with a median age of 16.4 years (range 13-17 years) at admission. 16 children (70%) had neuroimaging (MRI or CT) performed during their primary admission, all with normal results. 9 children (39%) had at least one metabolic investigation and 8 (35%) had cerebrospinal fluid testing, with no abnormalities identified. Brain positron emission tomography (PET) scan was performed during the initial admission in 5 children, all of which reported an abnormal pattern of brain metabolism that included encephalitis as a potential etiology. Four of these children received immunotherapy with methylprednisolone and intravenous immunoglobulin. Discharge diagnosis was documented as a primary psychiatric illness in 13 (57%) and undetermined in 10 (43%); an organic etiology of psychosis was not specifically identified in any children.
Conclusions: We identified variability in the medical work-up for FEP. Dissemination of the proposed protocol may help improve screening for organic causes of FEP, particularly for metabolic aetiologies. The role of PET in the investigation of FEP needs to be further investigated.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 143
Presenter: Elnaz Yazdanbakhsh
Supervisor: Sharifzadeh-Amin, Maryam
Title: Trends of Dental Treatments Under General Anesthesia in Pediatric Patients in Alberta
Authors: Elnaz Yazdanbakhsh, Babak Bohlouli, Steven Patterson, Maryam Amin

Theme: Children's health and well-being

Introduction
Dental caries continues to be one of the most prevalent chronic diseases, affecting more than half of children in Canada. Pediatric dental treatment under general anesthesia (DGA) is often warranted to provide optimal dental care in a single visit when extensive treatment is needed or conventional and advanced behavior guidance techniques (e.g., conscious sedation) are not indicated or are ineffective. It is the most frequent and the number one surgical procedure performed on children in Canadian hospitals. Few Canadian studies have explored the trends, demographic and clinical characteristics of pediatric patients undergoing DGA. The aims of this study were to determine trends in pediatric dental surgeries over a 9-year period in Alberta, Canada, identify the characteristics of patients undergoing DGA and to describe the distribution of dental procedures under GA.

Methods
A retrospective analysis of all children (age≤12, and ASA-1 classification) underwent DGA with primary diagnosis of dental caries, at hospital- and community-based outpatient clinics in two of the largest cities of Alberta, Canada between June 2010-May 2019 was conducted. The Alberta Health Services (AHS) administrative database was used to extract patients' information including demographics, socioeconomic status (SES), dental diagnoses and procedures. Descriptive statistics were performed using STATA16.1 software.

Results
There were 10,536 DGAs identified during the 9-year study period with 9,955 individuals having these visits. 94.6% of patients had only one DGA and 5.4% had 2 or more DGAs. The mean (SD) age at time of service was 4.64 (2.29), and over 70% of the children were less than 6 years of age, with 3-6-year-old's representing the largest group (54.6%). Children with most SES deprivation had 1.9 times higher number of DGA than those with least SES deprivation (29.5% vs.15.2%). Though the annual number of DGA increased from 1189 in 2010/11 to 1316 in 2018/19, the number of DGA per 1000 children appear to decrease over time. Additionally, annual number of DGA by age group, revealed a 14.5% decrease in 3-6-year-old's (from 6.9 to 5.9 per 1000). Fillings were the most common procedure performed under GA which increased over the given period (38.1% to 48.5%), followed by extractions and Crowns.

Conclusion
The relatively high visits of DGA in children under the age of 6 due to caries remains as a serious public health problem in Alberta. The high utilization of dental surgeries among children with lower SES supports the need for effective community-based preventive strategies.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 133
Presenter: Camille Yearwood
Supervisor: Wilbur, Colin
Title: Trends in the epidemiology and treatment of pediatric-onset multiple sclerosis in Alberta
Authors: Camille Yearwood, Colin Wilbur

Theme: Children's health and well-being

Introduction: Multiple sclerosis (MS) is an autoimmune disease affecting the central nervous system. Approximately 2-5% of cases have onset in childhood and are associated with a high rate of clinical relapse, cognitive impairment, and the occurrence of disability and progressive disease at a younger age than those with adult-onset MS. In this study, the aim was to describe trends in the incidence, prevalence, and treatment of MS in Albertan children over the past 10 years.
Methods: This study entailed a retrospective review of administrative health databases. We compared two administrative case definitions of MS and included those with a date of diagnosis from January 1, 2011 - December 31, 2020 (defined as the earliest hospital visit/physician claim associated with a CNS demyelinating diagnosis). Crude incidence and prevalence estimates were calculated and stratified by sex and age cohort, as well as age-standardized. Pharmacy dispenses of MS disease modifying therapies (DMTs) were identified by Anatomical Therapeutic Chemical classification and grouped as injectables (glatiramer acetate, interferon-beta) or newer agents (all others).
Results: 106 children met one or both of the MS case definitions. In 2020, the age-standardized incidence was found to be 0.57 (95% confidence interval [CI] 0.21-1.26) per 100,000 and the age-standardized prevalence was 3.41 (95% CI 2.37-4.75) per 100,000 using the Marrie definition. 61 children (57%) filled a prescription for at least one DMT. Injectables accounted for all DMT dispenses prior to 2015, while by 2020 injectable DMTs only accounted for 11/49 dispenses (22%). 19/28 (68%) incident cases initially dispensed an injectable DMT were later dispensed an alternate agent compared to only 3/16 (19%) initially dispensed a newer agent ($p<0.001$). Children diagnosed with MS from 2016-2020 were first dispensed a DMT a median 186 days (interquartile range [IQR] 133-417) from the date of diagnosis compared to 424 days (IQR 142-1409.5) in those diagnosed from 2011-2015 ($p=0.06$).
Conclusion: The treatment of children with MS in Alberta has evolved, with earlier treatment and the increasing initial use of newer agents, which are associated with a lower rate of subsequent therapy changes.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 118
Presenter: Kennedi Young
Supervisor: Alexander, R Todd
Title: Claudin-2 and Claudin-12 DKO mice display vitamin D resistance
Authors: Kennedi Young, Megan R. Beggs, R. Todd Alexander

Theme: Children's health and well-being,Lifelong women's health

Introduction:
Infants and children require a net positive calcium (Ca^{2+}) balance to achieve optimal bone mineral density by early adulthood. A failure to do so results in decreased bone mineral density and increased fracture risk. In both the kidney and intestine, Ca^{2+} is absorbed both paracellularly, through claudin proteins that make up the tight junction, and transcellularly, through Ca^{2+} specific transporters and channels. Claudins-2 and -12 are tight junction proteins that mediate calcium permeability across renal and intestinal cell culture epithelial layers. However, knockout of either of these genes did not result in a negative Ca^{2+} balance, suggesting compensation of one by the other.
Methods:
To test this hypothesis, we generated claudin-2 and claudin-12 double knockout (DKO) mice for use in metabolic cages. Urine and serum ion concentrations were measured using ion chromatography and iSTAT blood analyzer, respectively.
Results:
Unlike the single KO models, DKO mice displayed a decreased Ca^{2+} balance. This was due to reduced intestinal Ca^{2+} absorption and reduced renal reabsorption. This resulted in hypocalcemia, hypercalciuria and decreased bone mineralization. Interestingly, DKO mice did not have an increase in serum 1,25(OH)2-vitamin D levels or upregulation of the genes regulating serum 1,25(OH)2-vitamin D, despite a significant increase in serum PTH levels compared to WT mice. Both claudins localized to colonic epithelial crypts and renal proximal tubule cells, but they did not physically interact in vitro. Over-expression of either claudin increased Ca^{2+} permeability in cell models with endogenous expression of the other claudin.
Conclusion:
We find claudin-2 and claudin-12 form partially redundant, independent Ca^{2+} permeable pores in renal and colonic epithelia. Additionally, DKO mice have an inability to respond adequately to low serum Ca^{2+} and increased PTH to produce 1,25(OH)2-vitamin D. The reason for this is the focus of future work. Thus, the loss of claudin-2 and claudin-12 contribute to a negative calcium balance that negatively affects mineralization of bone and highlights the essential role of the paracellular pathway in maintaining a positive calcium balance.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation and supporters of the Lois Hole Hospital for Women.

Participant #: 59
Presenter: Aran Yukseloglu
Supervisor: Ali, Samina
Title: Association between pharmacogenomic profile and both pain relief and adverse events in children treated with oxycodone and ibuprofen
Authors: Aran Yukseloglu MD, Bruce Carleton PharmD, Colin Ross PhD, Robin Manaloor MD, Rhonda J. Rosychuk PhD, Amy L. Drendel DO, MS, David W. Johnson MD, Sylvie LeMay RN, PhD, Samina Ali MD

Theme: Children's health and well-being

INTRODUCTION: Ibuprofen and opioids are two of the most commonly used pain medications for children, worldwide. In order to personalize and best treat pain, we must understand how CYP2D6, CYP3A4, and CYP2C9 polymorphisms influence clinical effectiveness and safety. Our primary objectives were to explore how allelic variations of CYP2D6, CYP3A4, and CYP2C9 affected both pain relief and adverse events for ibuprofen and oxycodone. We further explored the degree to which genomic and clinical factors were influenced analgesic effectiveness and safety.

METHODS: This prospective, observational cohort included children aged 4-16 years who were treated at the Stollery Children's Hospital emergency department (between June 2010 - July 2014) with an acute fracture and were prescribed ibuprofen OR oxycodone for at-home pain management. Saliva samples were obtained, and telephone follow-up collected self-reported pain scores, medication use, adverse events, and functional limitations for three consecutive days. Pain was measured using the Faces Pain Scale-Revised. Genotyping identified allelic variants of CYP2D6, CYP3A4, and CYP2C9. Regression analyses were employed to determine relationships between clinical and genomic patient characteristics, pain relief, and adverse events.

RESULTS: We included 210 children (n=140 ibuprofen, n=70 oxycodone); mean age was 11.1 (±3.5) years, 66.2% were male, and 79.5% self-identified as Caucasian. 97.1% of individuals used non-pharmacologic adjuncts on Day 1. The median pain reduction was 4 (±2.0) in the ibuprofen group and 4 (±3.5) in the oxycodone group on Day 1 ($p = 0.69$). Adverse events were experienced by 53.2% of the ibuprofen group and 78.3% of the oxycodone group ($p < 0.001$). Classifying CYP2D6 phenotypes, 7.5% were Poor Metabolizers, 26.4% Intermediate Metabolizers, and 66.0% Extensive Metabolizers. The Intermediate Metabolizers reported less pain relief when oxycodone was used compared to the Extensive Metabolizers ($p = 0.04$). CYP3A4 variants were not associated with differential pain relief or adverse events. For ibuprofen, the decreased functioning CYP2C9*2 allele was associated with fewer adverse events compared to the normal functioning allele CYP2C9*1 ($p = 0.003$). Male sex ($p = 0.035$) and use of non-pharmacological adjuncts ($p = 0.02$) was associated with less pain relief for the oxycodone group.

CONCLUSION: Oxycodone and ibuprofen provided similar pain relief with significantly more adverse events with oxycodone use. Decreased metabolism phenotype for CYP2D6 was associated with decreased analgesic effectiveness for oxycodone, while CYP2C9 hypofunction was associated with fewer ibuprofen-related adverse events. Male sex and use of non-pharmacologic adjuncts were associated with less pain relief with oxycodone, warranting further study.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.

Participant #: 104
Presenter: Zhiguang Zhang
Supervisor: Carson, Valerie
Title: Demographic Correlates of Movement Behaviours in Infants: A Longitudinal Study
Authors: Zhiguang Zhang, Madison Predy, Kylie D Hesketh, Lesley Pritchard, Valerie Carson

Theme: Children's health and well-being

Introduction: There is limited evidence on demographic correlates of movement behaviours (i.e., tummy time, restrained time, reading time, screen time, sleep time) in infants. Therefore, this study aimed to examine the longitudinal associations between demographic correlates and movement behaviours in this age group.
Methods: Participants were 411 parents of typically developing infants from the Early Movers project in Edmonton, Canada. Movement behaviours, infant and parental age, and non-parental care time were assessed using a parental questionnaire at 2, 4, and 6 months of age. Other infant and parental demographic variables were assessed at 2 months of age. Due to distribution, tummy time and restrained time were square root transformed, while reading time and screen time were dichotomized as participating or not participating in the behaviour. Linear and generalized linear mixed models were conducted.
Results: Infant age (days) or age squared was positively associated with tummy time, reading time, and screen time, as well as negatively associated with sleep time. Caucasian infants and those with older parents had less tummy time and increased odds of having reading time. Infants of the most educated parents also had lower tummy time. Higher parental education and more siblings were associated with no screen time and longer infant sleep time. Infants with immigrant parent(s) were less likely to have reading time. No associations were found for child sex, time spent in non-parental care, and parental marital status.
Conclusion: Movement behaviours changed throughout the first 6 months of infancy and no single demographic group demonstrated healthy patterns for all movement behaviours. Therefore, a healthy balance of movement behaviours should be promoted universally for all infants.

This research has been facilitated by WCHRI through the generosity of the Stollery Children's Hospital Foundation.