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Department of Pediatrics
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Celebrate Research Day 2024

Fellows Oral Competition

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Dr. Kayleigh Campbell

Prenatal Antidepressant Exposure and Neonatal Connectome Topology: A Neural Pathway for Early Social-Emotional Disturbances

Kayleigh Campbell[1,2], Colin Brown[3], Ghassan Hamarneh[3], Steven Miller[1,4], and Tim Oberlander[1,4]

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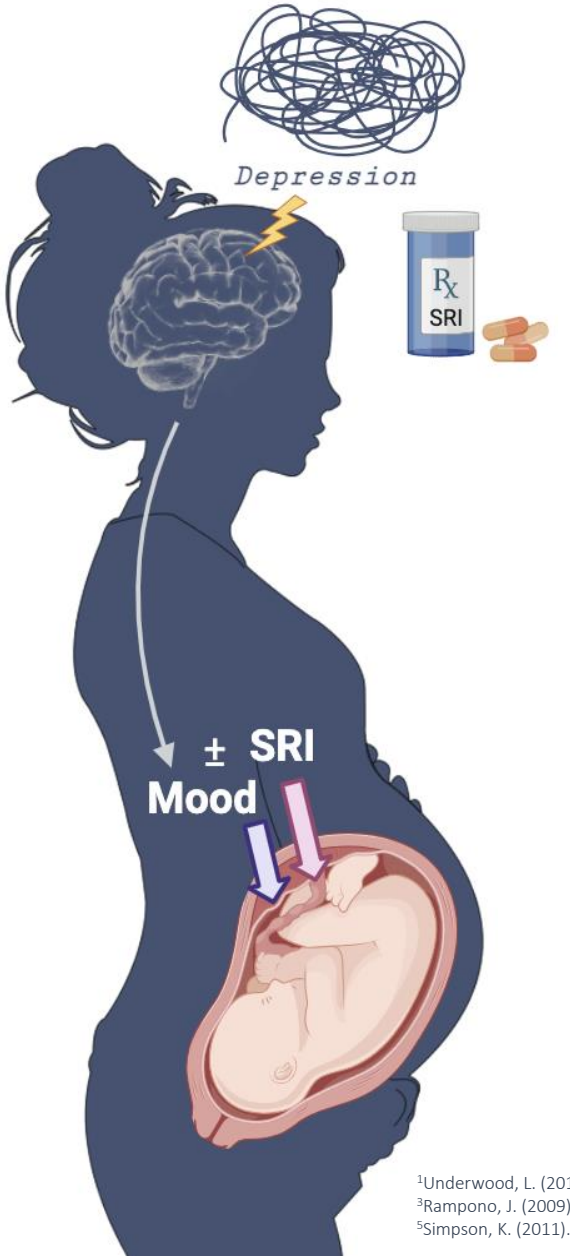
UBC Department of Pediatrics Research Day

Fellow / SSR Competition

April 12th, 2024

CLINICAL CONTEXT: *Maternal Depression during Pregnancy*



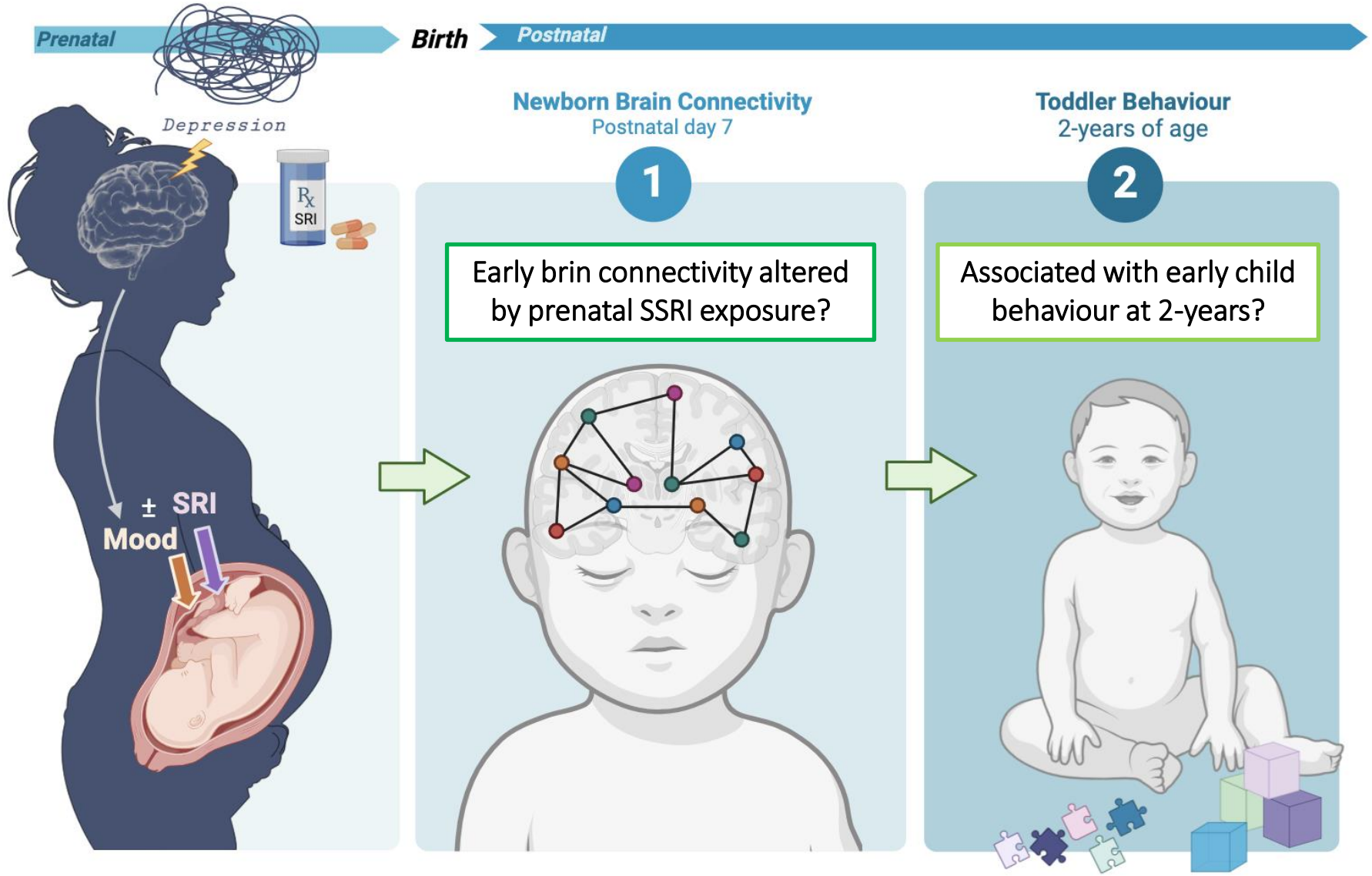
- 20% of women experience mood disturbances during pregnancy[1]
  - 1/3 are treated with **SSRI antidepressants**[2]
- SSRIs cross placenta[3]

- Rodents: widespread changes in brain morphology and circuitry[4,5]
- Humans: prenatal SSRI exposure associated with increased risk for mood disorders and anxiety into young adulthood[6]

- Unknown whether prenatal SSRI and/or depression alters early brain development, and whether this relates to subsequent behavioural outcome in infancy

[1]Underwood, L. (2016). *Arch Womens Ment Health., 19*:711-720. [2]Mitchell, J. & Goodman, J. (2018). *Arch Womens Ment Health., 21*:505-516.
[3]Rampono, J. (2009). *Pharmacopsychiatry, 42*(3):95-100. [4]Homberg, J.R. (2010). *Trends Pharmacol Sci., 31*(2):60-65.
[5]Simpson, K. (2011). *PNAS, 108*(45):18465-70. [6]Rommel, A. (2020). *J Clin Psychiatry., 81*(3): 19r12965.

RESEARCH QUESTIONS



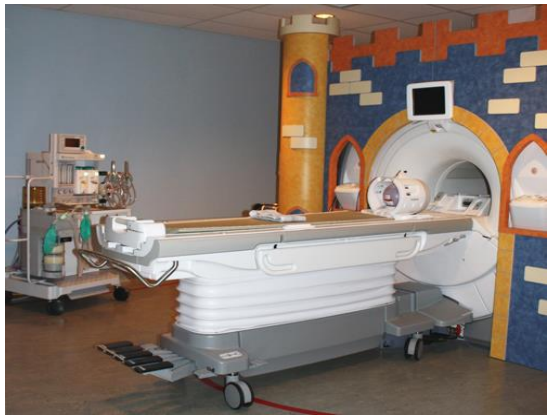
METHODS: *Structural Network Analysis*

Groups by Prenatal Exposure:

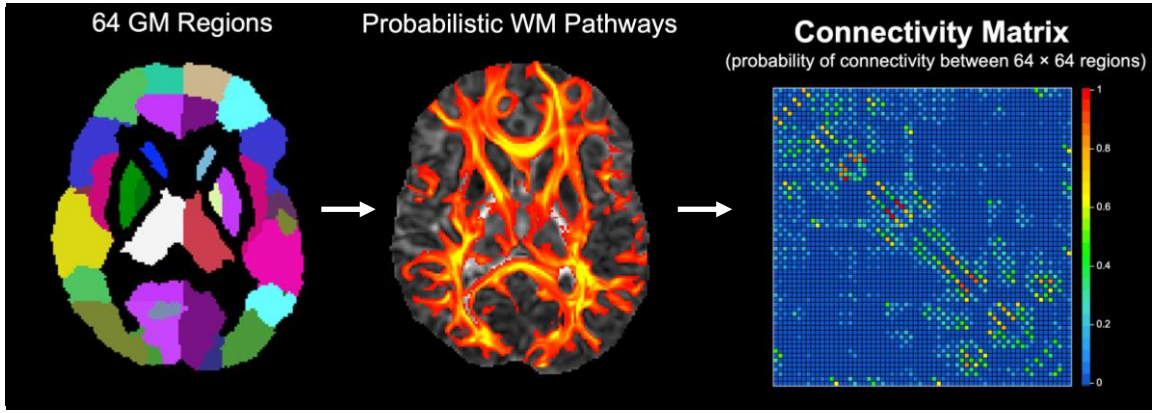
Control (*n* = 27) | **Depressed** (*n* = 23) | **SSRI** (*n* = 25)

Control	Depressed	SSRI
x depressive symptoms	✓ depressive symptoms	✓ depressive symptoms
x SSRI treated	x SSRI treated	✓ SSRI treated

Neonatal Brain Imaging → Diffusion MRI Data Processing → Whole-brain Connectivity → Connectome Topology



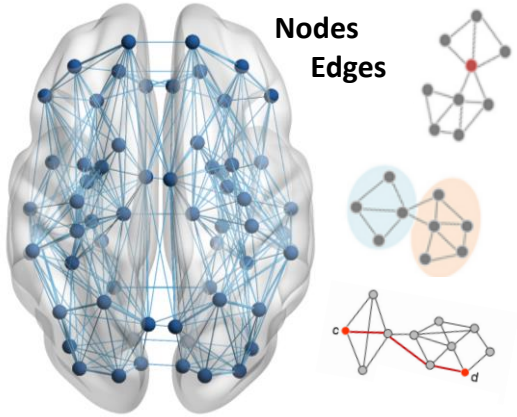
BC Children's Hospital Research MRI
GE Discovery MR750 3T Pediatric MRI Scanner



Atlas-Based Segmentation

Probabilistic Tractography

Structural Network Construction



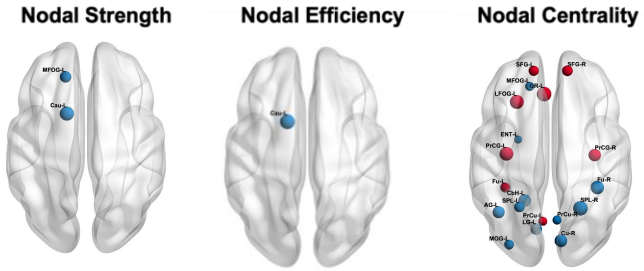
Graph Theory Analysis
Topological network properties

- *Connectivity strength*
- *Network segregation*
- *Network integration*

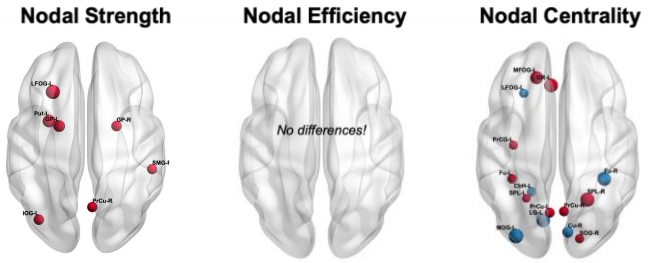
- General linear models testing group differences (Control, Depressed, SSRI)
  - Adjusted for *sex, gestational age at birth, infant age at MRI scan*
  - Significance determined from 10,000 permutations

RESULTS: *Group Differences in Neonatal Connectome Topology*

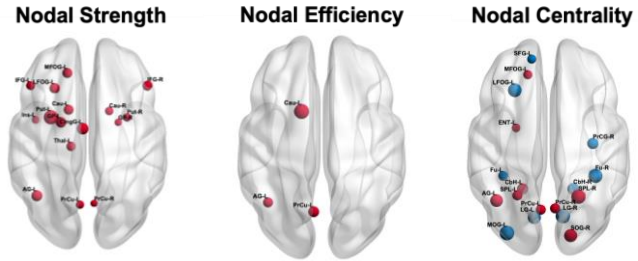
Control vs. Depressed



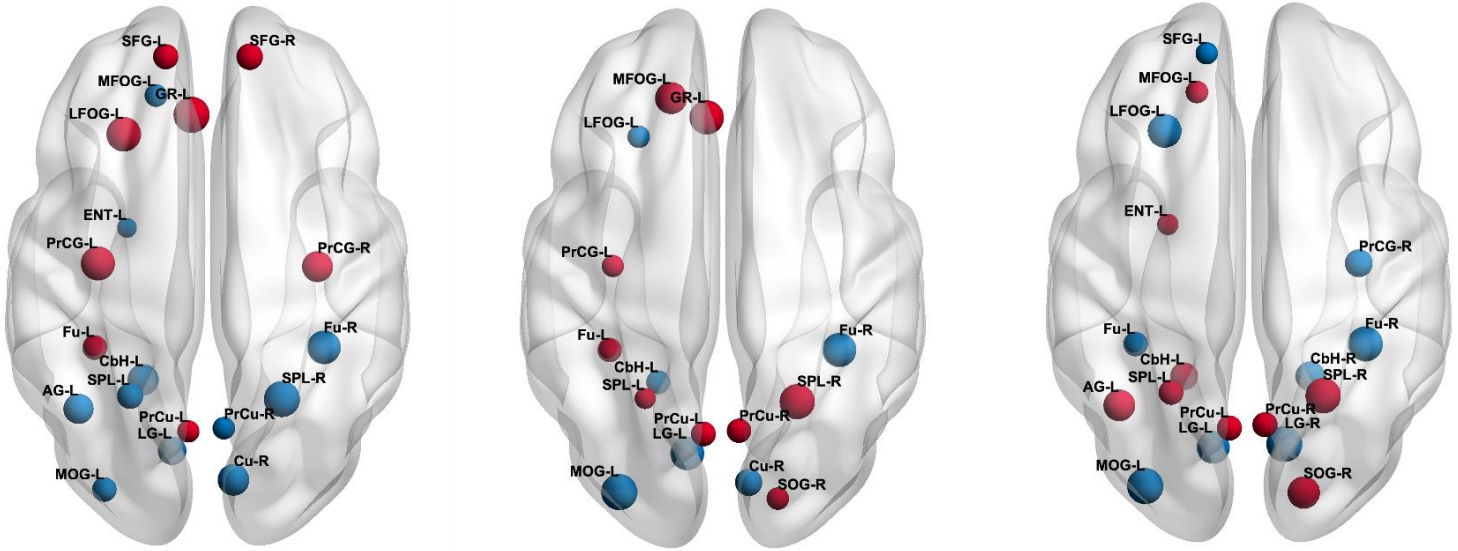
Control vs. SSRI



Depressed vs. SSRI



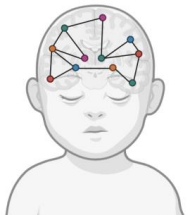
Nodal



Control > Depressed
Control < Depressed

Control > SSRI
Control < SSRI

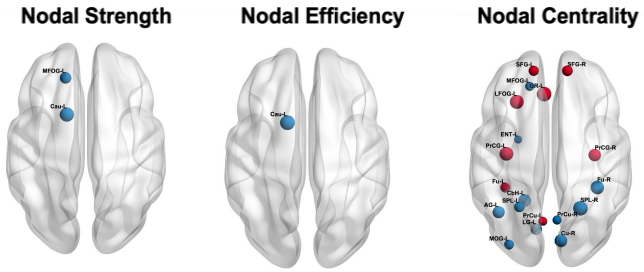
Depressed > SSRI
Depressed < SSRI

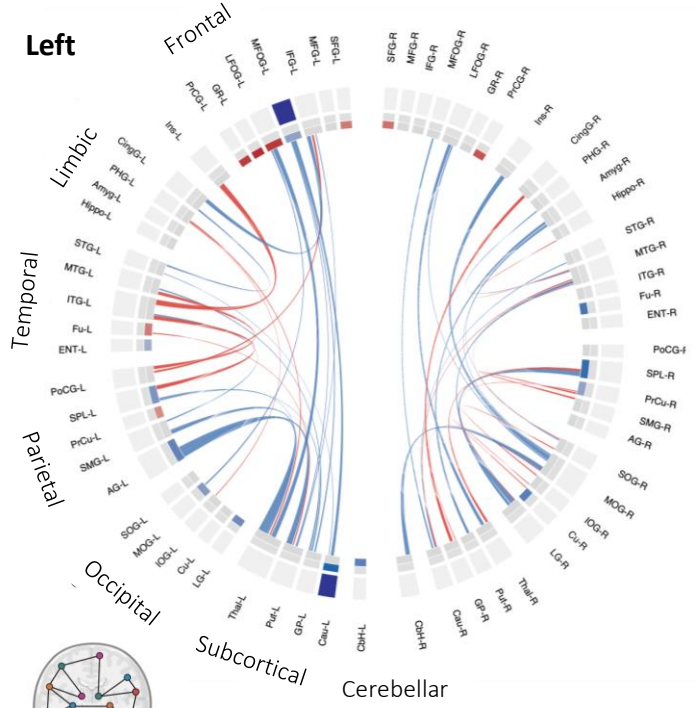


Nodal significance determined from 10,000 permutations of GLMs testing group differences, adjusted for sex, GA birth, age at MRI.

RESULTS: *Group Differences in Neonatal Connectome Topology*

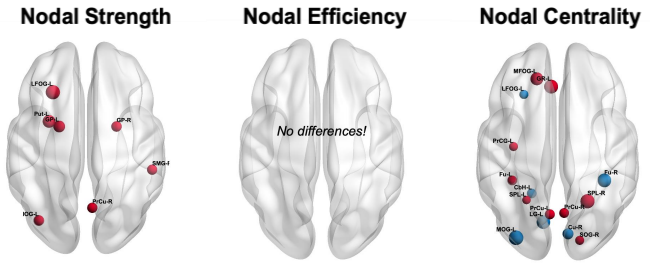
Control vs. Depressed

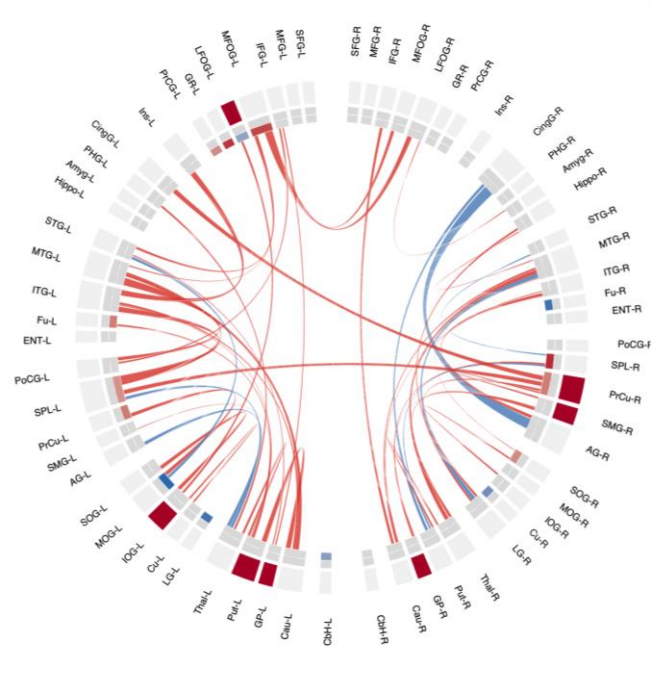




Control > Depressed
Control < Depressed

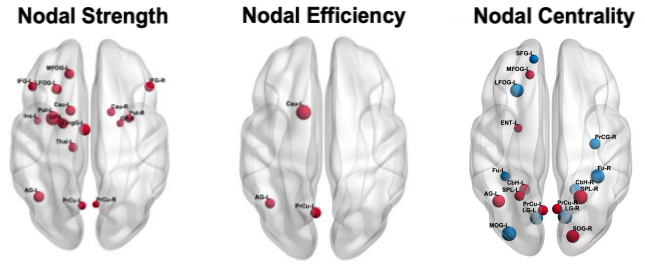
Control vs. SSRI

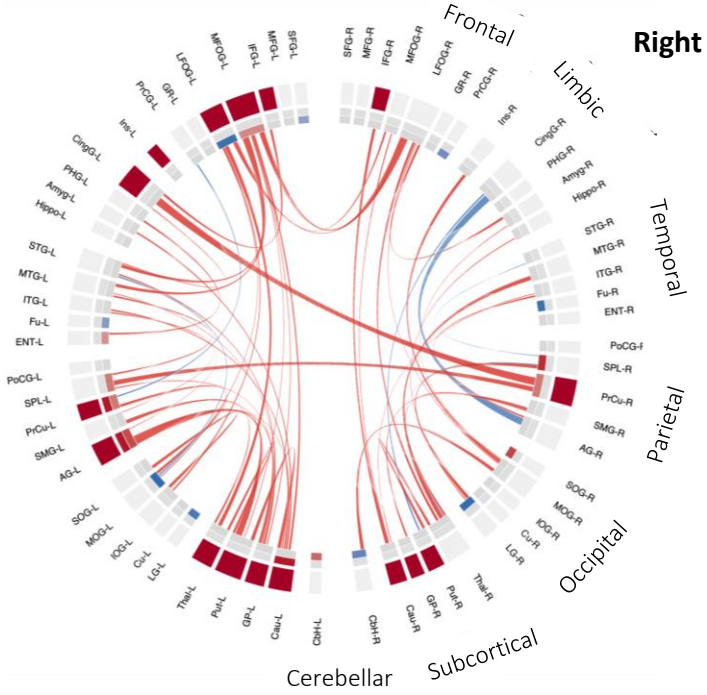




Control > SSRI
Control < SSRI

Depressed vs. SSRI





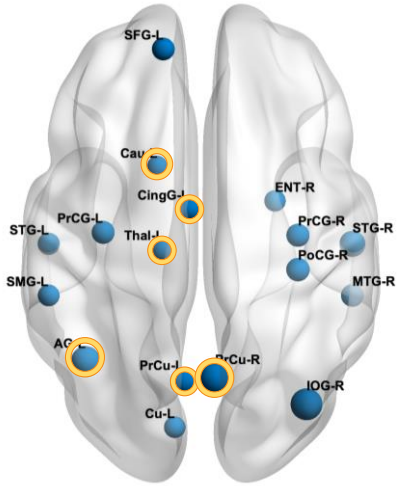
Depressed > SSRI
Depressed < SSRI

Edge-level significance determined from 10,000 permutations using the network-based statistic, testing group differences, adjusted for sex, GA birth, age at MRI.

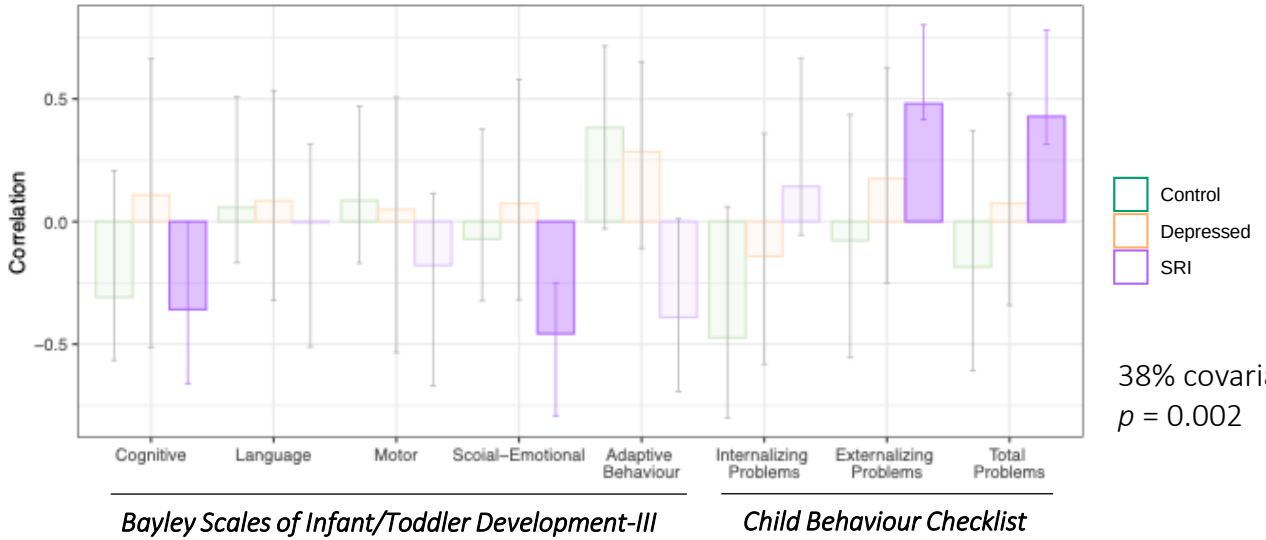
RESULTS: *Neonatal Brain Connectivity x Early Child Behaviour (2-years)*

Partial Least Squares Correlation

Neonatal brain regions significantly associated with Toddler Behaviour



Correlation: Neonatal Connectome Topology & Toddler Behaviour at 2-years

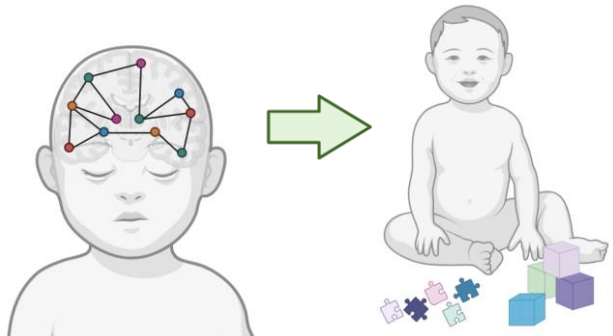


38% covariance
p = 0.002

Bayley Scales of Infant/Toddler Development-III

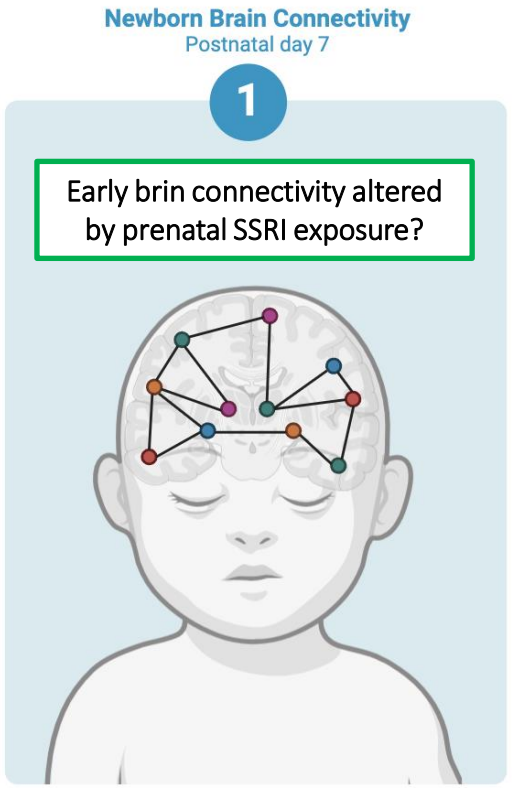
Child Behaviour Checklist

>> *Lower newborn brain connectivity across several regions associated with lower cognitive and social-emotional scores, as well as greater externalizing and total problem in SSRI-exposed toddlers.*



Significance determined from permutation and bootstrapping procedures (10,000 samples).

SUMMARY & CONCLUSIONS



Depression-exposed neonates:

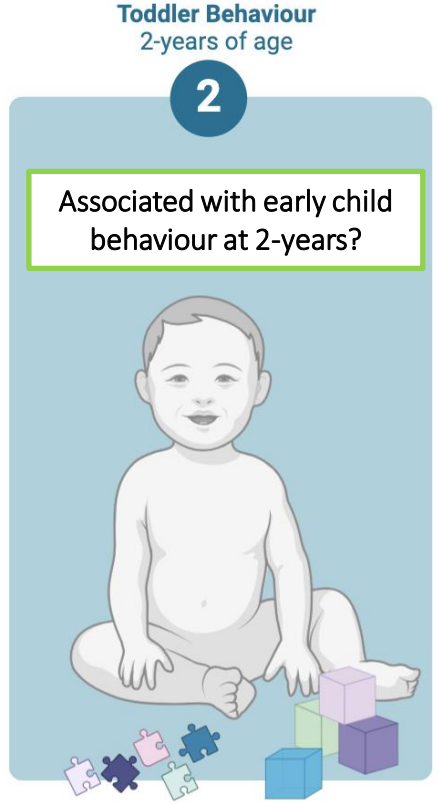
- Connectome topology did not greatly differ from non-exposed *Control* neonates, aside from greater nodal efficiency in the left caudate nucleus (esp. frontostriatal connectivity)

SSRI-exposed neonates:

- Widespread disruptions in frontal, parietal and subcortical connectome topology
  - *Regional consistencies with prior neuroimaging studies* [1–5]
- Lower interhemispheric orbitofrontal and superior parietal connectivity, as well as left cortico-subcortical connectivity
- Global pattern of ***less integrated*** connectome topology
  - *Phenotype of atypical development* [6–8]

Lower newborn brain connectivity across several regions associated with poorer **cognitive**, **social-emotional** and **externalizing behaviours** at 2-years of age

>> Bilateral PrCu, AG-L, Cau-L, Thal-L, CingG-L



Prenatal SSRI exposure associated with widespread disruptions in newborn brain topology, which may be a neural pathway for social-emotional disturbances in early childhood

[1]Jha, S. (2016). *Psychiatry Res: Neuroimaging, 253*:43-53. [2]Lugo-Candelas, C. (2018). *JAMA Pediatr 172*: 525-33. [3]Videman, M. (2017). *Cereb Cortex 27*: 3208-3216. [4]Moreau, A. (2023). *Biol Psychiatry Global Open Sci 3*(2): 232-245. [5]Koc, D. (2024). *Biol Psychiatry Cogn Neurisci Neuroimaging 9*(2):217-226. [6] Zhao, T. (2019). *NeuroImage 185*: 711-727. [7]Brown, C.J. (2014) *NeuroImage, 101*: 667-80. [8]Feldman, M. (2020). *Brain Comms., 2*(2): 1-15.

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Dr. Colin Brown

Medical Imaging Analysis Research Group

We are very grateful to the mothers and their infants for their participation!

QUESTIONS ?

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Dr. Rozalyn Chok

Infectious complications associated with treatment of children with relapsed acute lymphoblastic leukemia: a descriptive analysis

Rozalyn Chok, PGY-6 Peds Heme/Onc

Supervisor: Dr. Amanda Li

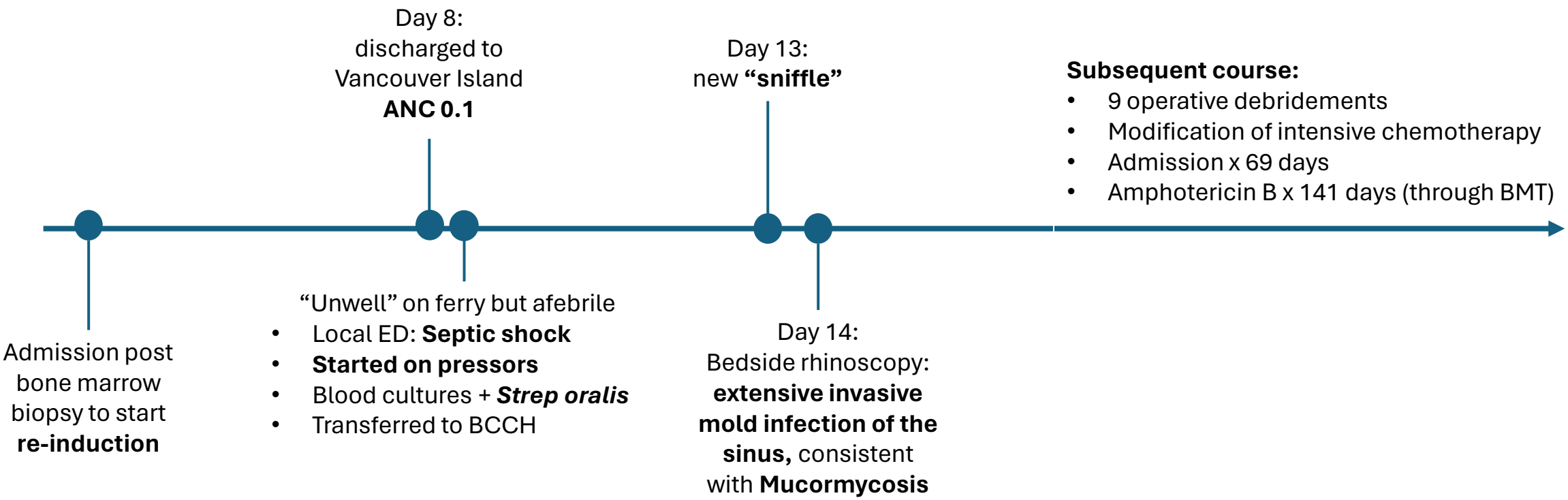
BCCH Department of Pediatrics Celebrate Research Day – April 12, 2024

Outline

- Rationale and objectives
- Patients and methods
- Results
- Conclusions and future directions

Why this project?

- 5-year-old male newly diagnosed with **first relapse of B-cell acute lymphoblastic leukemia** during maintenance therapy



What was our aim?

- **Primary objective:**
  - Describe the **incidence** and **pattern of infections** during **re-induction therapy** in children with **relapsed acute lymphoblastic leukemia (ALL)** at a single tertiary centre

- A deep understanding of the infectious complications seen during re-induction therapy for relapsed ALL may:
  - Improve our ability to **prevent and treat infections**
  - Help **reduce treatment delays**
  - **Guide novel approaches** for re-induction therapy

What do we already know?

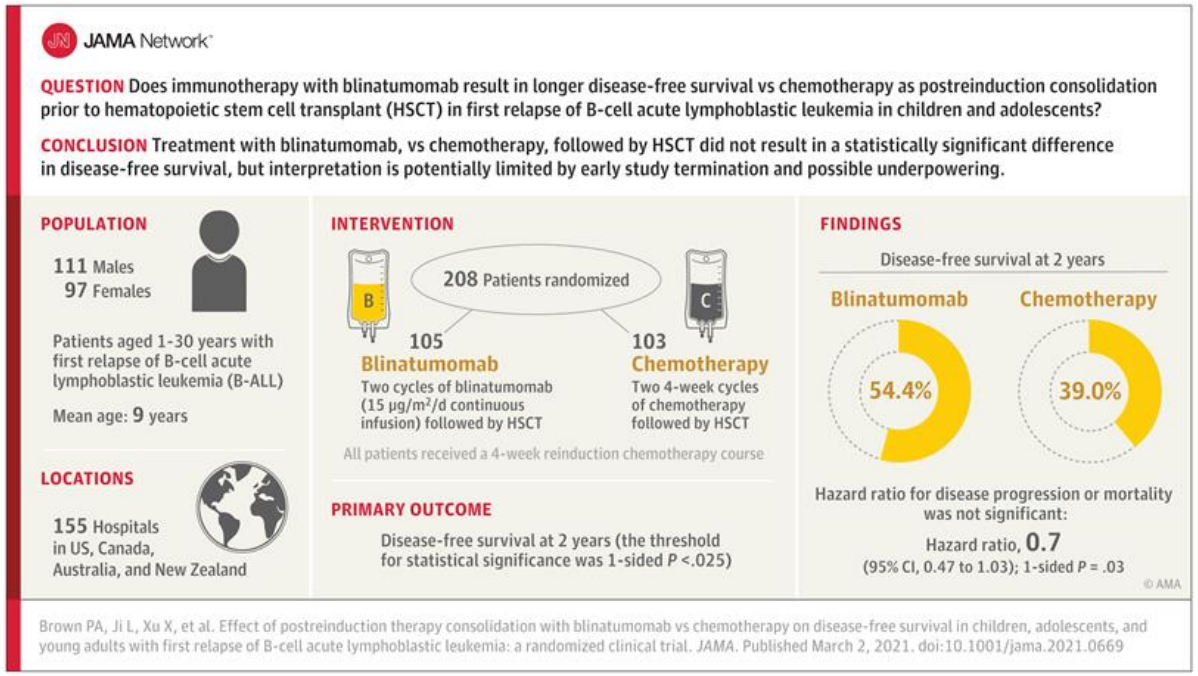
- Pediatric patients with **relapsed acute lymphoblastic leukemia** (ALL) have higher rates of **treatment related mortality (TRM)** than at initial diagnosis[1]

- **Infection** is the most common cause of TRM and affects **60-90% of patients with relapsed ALL**[2]

1. *Oskarsson T et al*. *Pediatr Blood Cancer*. Apr 2018;65(4)
2. *O'Connor D et al*. *Blood*. Aug 14 2014;124(7):1056-61.

Why study re-induction?

- The use of **immunotherapy** during ALL relapse has been shown to improve survival and decrease rates of infection[3]
- Intensive combination chemotherapy is still standard of care for **re-induction**
- Infection during re-induction can impair ability to proceed with curative therapy



3. Brown PA et al. JAMA. Mar 2 2021;325(9):833-842.

How did we do it?

- Study design: **Retrospective chart review**

- Analysis:
  - **Primarily descriptive**
  - Univariate and multivariate regression analysis is underway

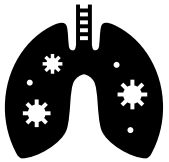
Who was included?

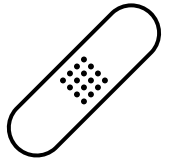
- **Inclusion criteria:**
  - **Pediatric patients** (age <18y years)
  - **First relapse** of acute lymphoblastic leukemia
  - Received **combination re-induction chemotherapy**
  - Treated at BCCH between **January 1, 2006 to Dec 31, 2022**

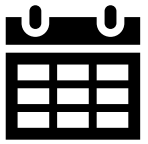
- **Exclusion criteria:**
  - Multiply relapsed patients

How did we define infection?

- **Infectious episode during re-induction** defined by:
  - Identification of a **microbiological pathogen**, or
  - **Radiographic evidence** of infection, or
  - **Clinical determination** of infection (i.e. cellulitis), **and**
  - Occurring from start of re-induction to end of induction marrow evaluation





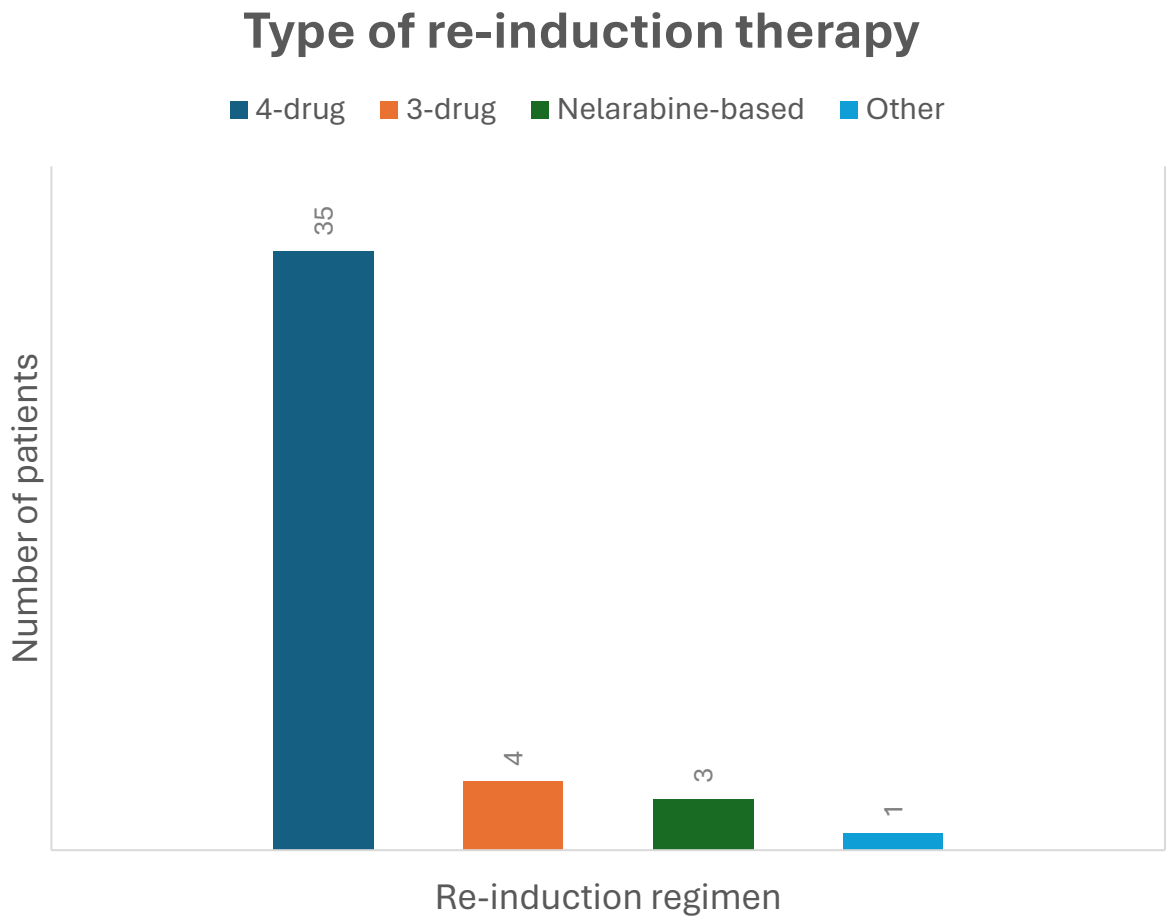


What did we find?

Patient Demographics (N=43)	
Characteristics	**Number of patients N, (%/Range)**
Male sex	25 (58%)
Trisomy 21	2 (5%)
Age at relapse (years)	10.2 (0.1-16.7)
Disease type	
• B-ALL	36 (84%)
• T-ALL	6 (14%)
• Mixed lineage	1 (2%)
Timing of relapse	
• Early	23 (53%)
• Late	20 (47%)
Site of relapse	
• Isolated Bone Marrow	31 (72%)
• Isolated Extramedullary	7 (16%)
• Combined	5 (12%)

Treatment

- Most patients (81%) received standard **four-drug regimen**
- 3 patients received **nelarabine-based regimen** for T-ALL
- 1 patient had individualized regimen due to toxicity
- 6 patients received concomitant **targeted therapy**



Clinical features

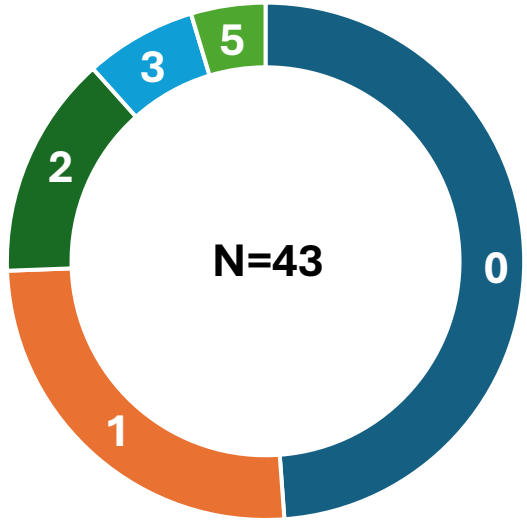
- There were **no deaths** due to infection in our study population
- Median duration of severe neutropenia was **21 days** (*4-40 days)*
  - *High risk for development of invasive fungal infection*[4]
- **51%** of patients experienced **hyperglycemia**
- Use of **antimicrobial prophylaxis was variable**:
  - Bacterial: 0/43 (0%)
  - Fungal: 13/43 (30%)
  - *Pneumocystis jirovecii:* 43/43 (100%)

4. Freifeld AG et al. *Clin Infect Dis*. Feb 15 2011;52(4):e56-93.

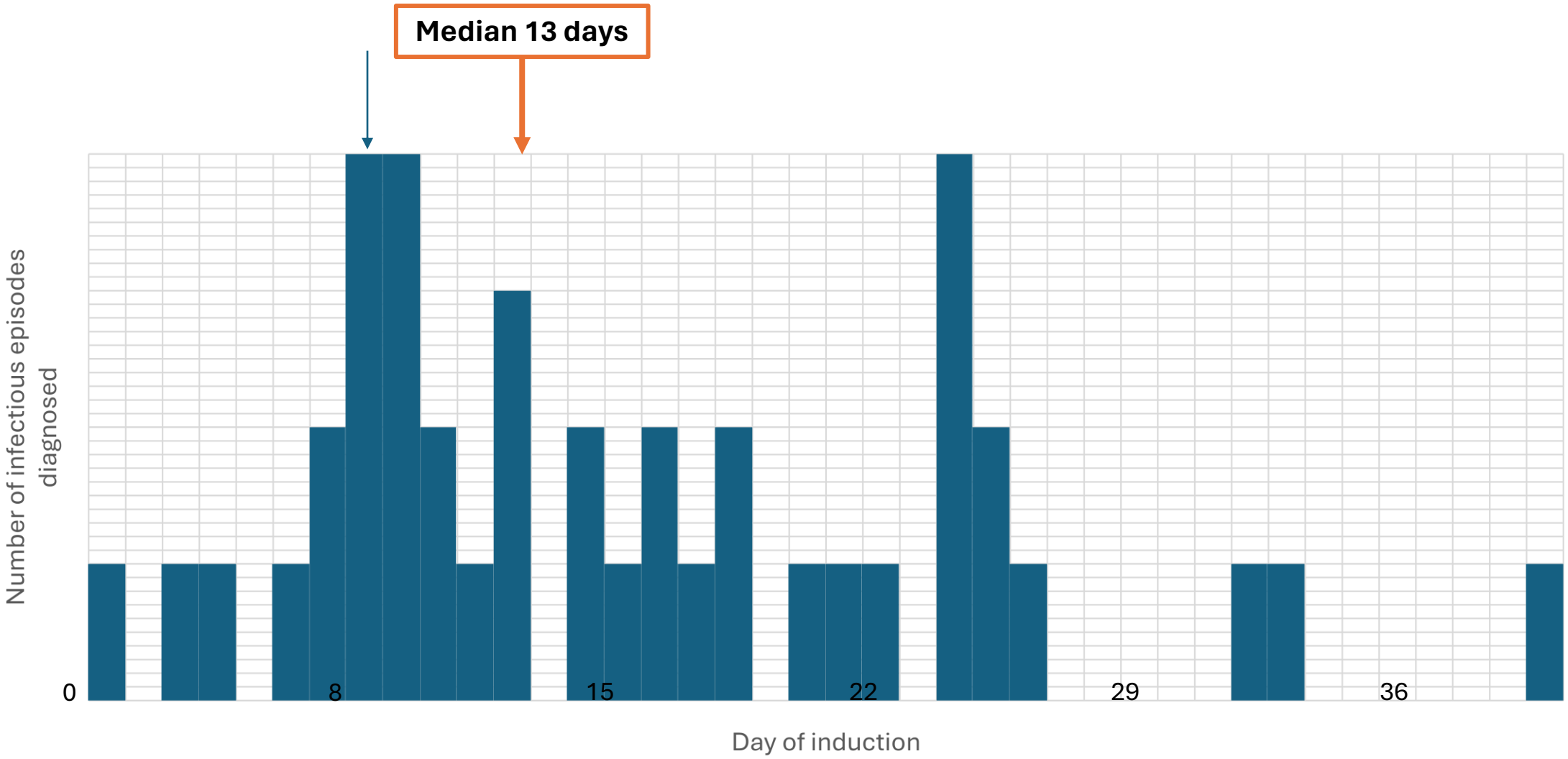
Infections

- There were **42 clinically significant infectious episodes** diagnosed in **22 patients**
- **18 episodes (42%)** were diagnosed in outpatients and required **readmission to hospital**
- **2 episodes (5%)** were severe enough to warrant PICU admission
- There were no deaths due to infection

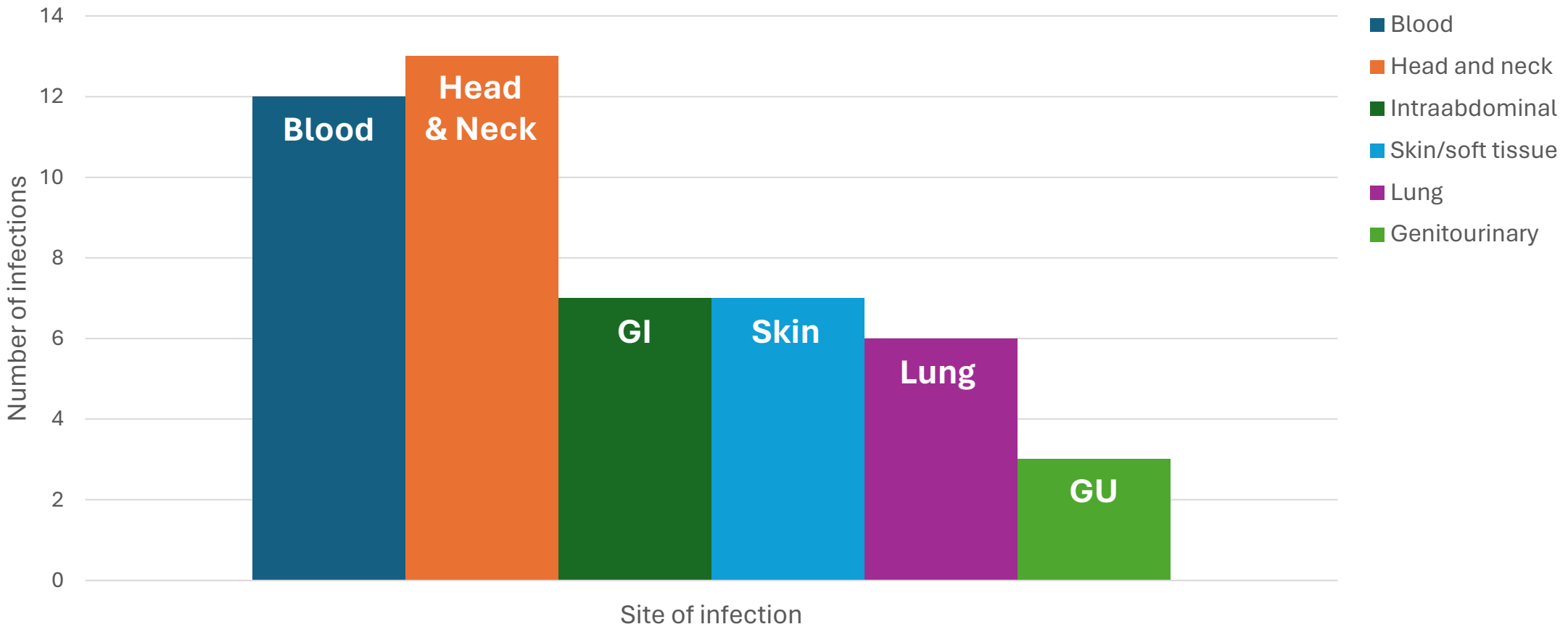
Number of infectious episodes per patient



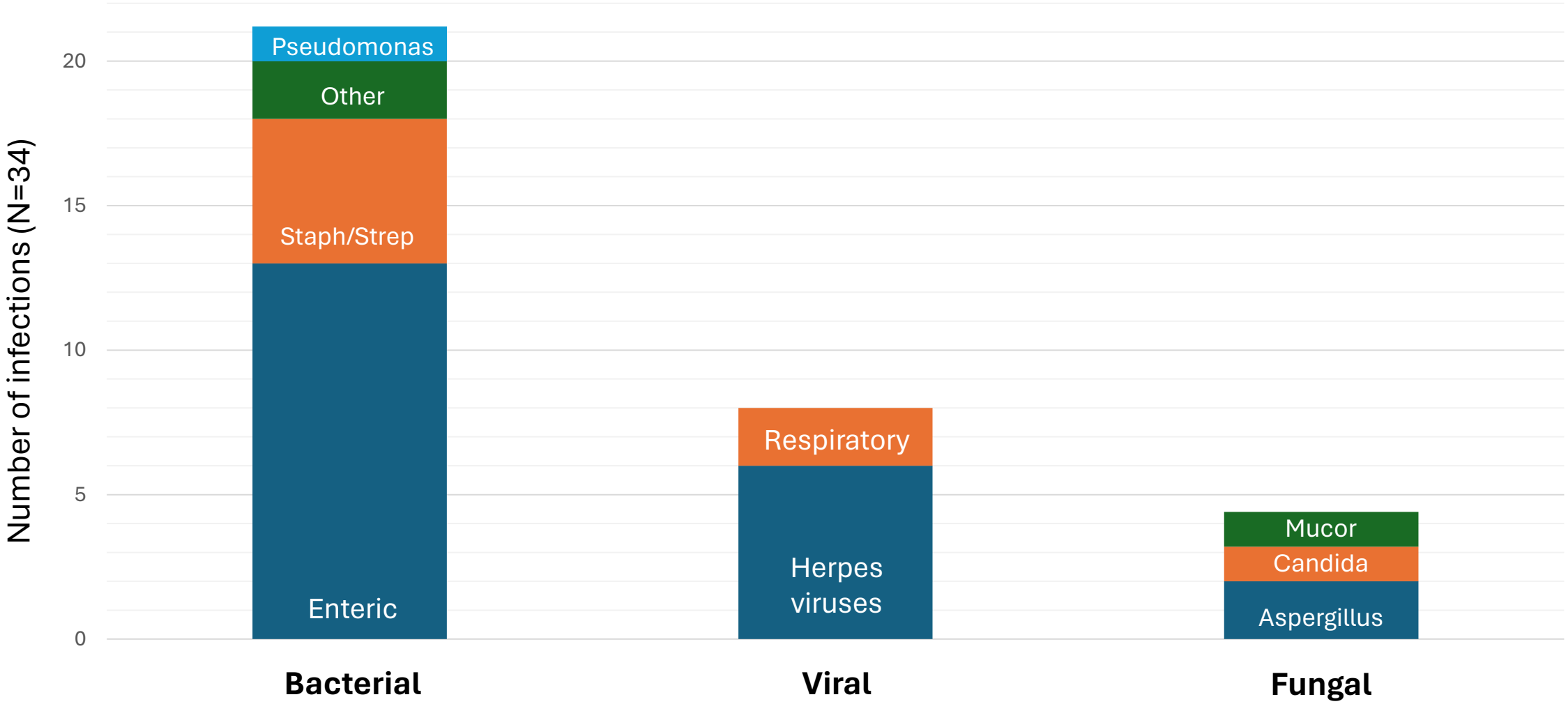
Timing of infection onset



Site of infection



Type of microbiologically confirmed infection



Conclusions

- In our study, **51% of patients with relapsed ALL had clinically significant infections** during re-induction chemotherapy

- Preventive measures such as **admission** and **antimicrobial prophylaxis** during periods of severe neutropenia should be considered in this high-risk population

- Future directions may include implementation and prospective evaluation of a **uniform enhanced antimicrobial prophylaxis regimen** in children with relapsed ALL at our centre

Acknowledgements

- Our patients and families
- Dr. Amanda Li
- Dr. Rebecca Deyell
- Mr. Jim Potts

References

1. Oskarsson T, Soderhall S, Arvidson J, et al. Treatment-related mortality in relapsed childhood acute lymphoblastic leukemia. *Pediatr Blood Cancer*. Apr 2018;65(4)doi:10.1002/pbc.26909
2. O'Connor D, Bate J, Wade R, et al. Infection-related mortality in children with acute lymphoblastic leukemia: an analysis of infectious deaths on UKALL2003. *Blood*. Aug 14 2014;124(7):1056-61. doi:10.1182/blood-2014-03-560847
3. Brown PA, Ji L, Xu X, et al. Effect of Postreinduction Therapy Consolidation With Blinatumomab vs Chemotherapy on Disease-Free Survival in Children, Adolescents, and Young Adults With First Relapse of B-Cell Acute Lymphoblastic Leukemia: A Randomized Clinical Trial. *JAMA*. Mar 2 2021;325(9):833-842. doi:10.1001/jama.2021.0669
4. Freifeld AG, Bow EJ, Sepkowitz KA, et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the infectious diseases society of america. *Clin Infect Dis*. Feb 15 2011;52(4):e56-93. doi:10.1093/cid/cir073

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Faculty of Medicine

BC Children's Hospital Research Institute

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Dr. Jad El Maamari

Harmonizing Age Pathology Parameters In Kids Study

HAPPI KIDS

Jad El Maamari

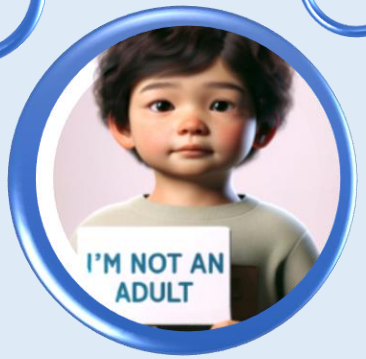
Pediatric Hematology Oncology, BC Children's Hospital, Vancouver BC Canada

Disclosures

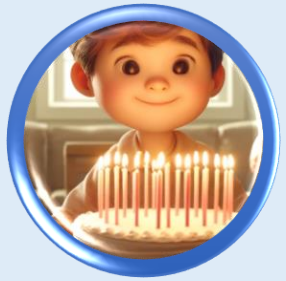
- Grant and sponsorship: ISTH-INVENT-VTE training fellowship

HAPPI KIDS Objectives

Risks of Inappropriate Norms



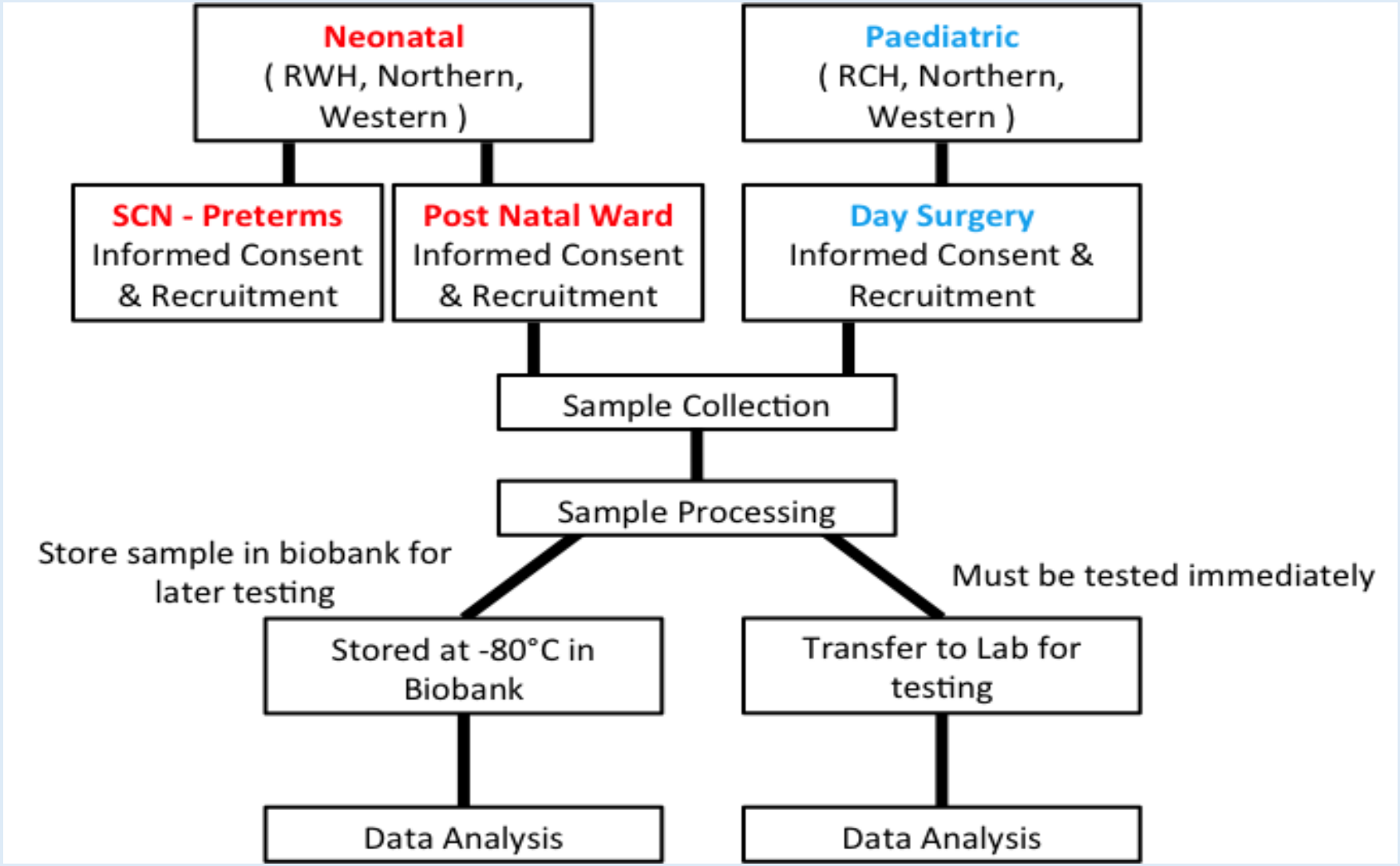
Gap in Paediatric Data



Necessity of Age-Appropriate Reference Ranges

Prospective cross-sectional study, collecting pediatric blood samples for analysis of commonly requested biochemical, immunological and hematological tests

Study Design



RCH	Roche Cobas
Melbourne Pathology	Roche
RMH	Architect
Dorevitch/ACL	Siemens
Monash	Beckman

Eligibility Criteria

	Neonate	Paediatric
Inclusion	• Healthy term babies (>37 weeks), birth weight ≥ 2.5kg • APGAR Score ≥7 at 5 mins	• Healthy children aged 1 month to 18 years • Minor day procedure requiring general anaesthetic • E.g. tonsillectomy, circumcision, grommets • Specific haematology, immunology and biochemistry related q's
Exclusion	• Babies with systemic abnormalities	• Complex medical history • Blood sample unable to be obtained from same cannula used for anaesthetic.

Collection Statistics

	Days	Approached	Consented		Sample Obtained		Mean Sample Per Day
RWH Neonates	881	6818	1220	18%	860	70%	1.0
Sunshine Neonates	274	2108	236	11%	170	72%	0.6
Northern Neonates	233	1288	235	18%	159	68%	0.7
RCH Theatre	1403	7028	5882	84%	5179	88%	3.7
Sunshine Theatre	265	834	705	85%	641	91%	2.4
Northern Theatre	39	126	99	79%	87	88%	2.2

	Days	Eligible	OK'd by NUM/Nurse	Approached	Consented	Obtained Sample
RWH Pre-term	109	33	20	14	6	4

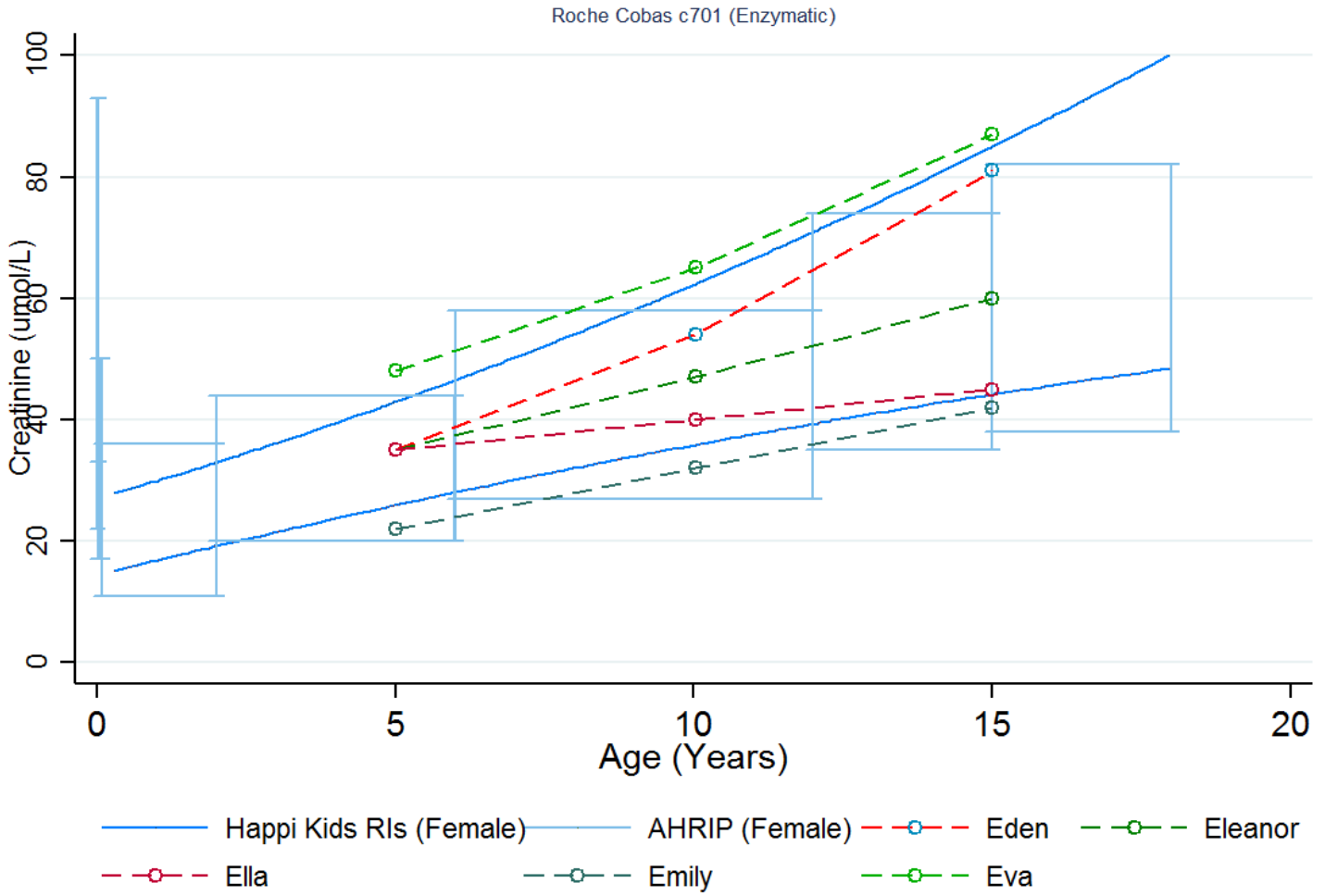
Total Numbers of Samples Collected

- **18,202** families have been approached
- **8,377** have consented to participate
- **7,055** samples have been collected

	Total	Female	Male
Neonate	1253	585	668
1 year	429	134	295
2 year	504	167	337
3 year	400	158	242
4 year	395	151	244
5 year	436	187	249
6 year	418	178	240
7 year	362	150	212
8 year	317	134	183
9 year	274	120	154
10 year	269	122	147
11 year	223	93	130
12 year	251	117	134
13 year	246	120	126
14 year	253	116	137
15 year	272	116	156
16 year	257	120	137
17 year	239	94	145
18 year	178	81	97
Adult	79	38	41
TOTAL	**7055**	**2981**	**4074**

Reference Ranges – Aged Partitions VS Continuous Variables

- Continuous reference intervals accurately represents the complex relationship between pediatric age and analyte concentration
- Reduced false abnormal results around partition breakpoints
- Ability to monitor patient trends over time
- Clinical care implications
- Cost implications
- Increased sensitivity to disease onset



Methods- Ex: Haptoglobin

Venous blood collected into S-Monovette serum gel tubes, centrifuged at 5000 rpm, 6°C, for 5 min, aliquoted into 400 µL, and stored at -80°C for up to 24 months.

Samples transported on ice, processed in batches alongside routine clinical analysis between Dec 2015 - Dec 2017

Uniform thawing, mixing, and quality control protocols across laboratories, following accredited procedures.

Sample analysed on Roche Cobas c501/c502, Cobas c701, and Beckman Counter Unicel DXL 600/800.

Direct comparison of patient results across different analyzers and labs

Statistical methods- Ex: Haptoglobin

Scatterplots of haptoglobin and age were used to visually inspect for outliers.

Age-specific RIs for pediatric cases were generated after removal of outliers by applying a fractional polynomial regression model of age separately for each laboratory

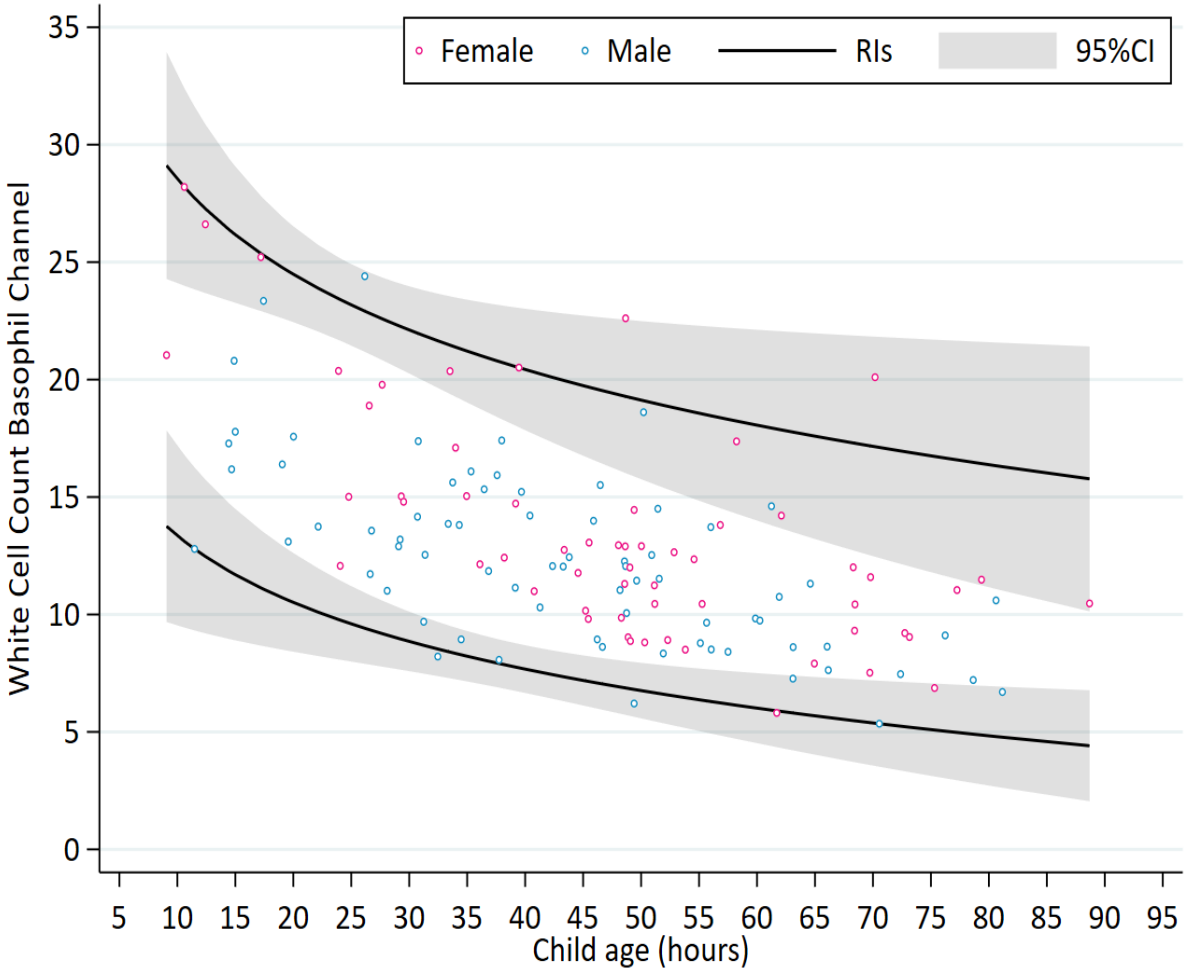
Quantile regressions estimated 2.5th and 97.5th centiles, and the 95% CI of these centiles were estimated based on the fitted model for the RI.

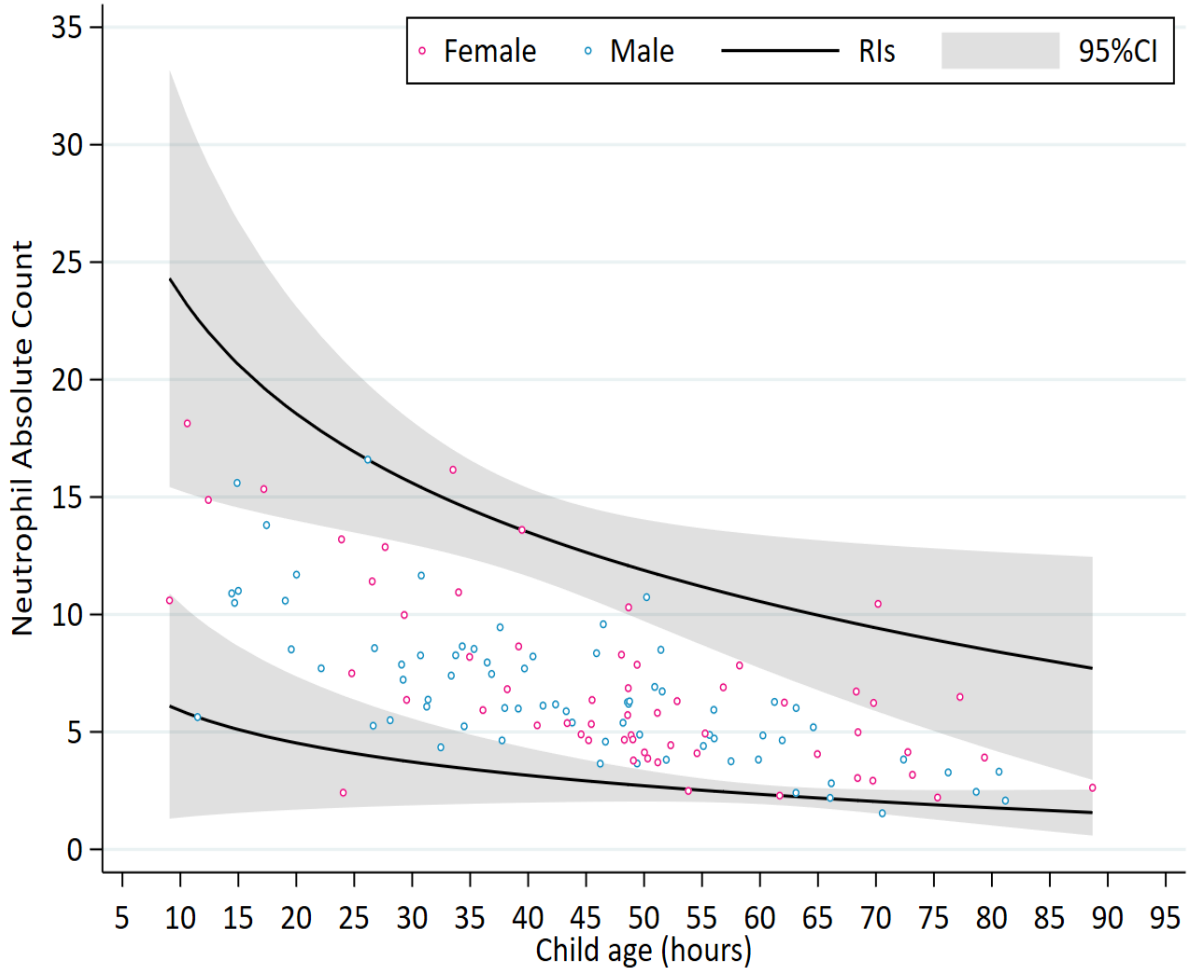
The sample size calculation is based on the publication by Royston et al.

Bland-Altman analyses were carried out to determine agreement between the 3 analytical platforms. Mean difference (and 95%CI) and limits of agreement were presented on plots of differences for each pairing.

White Blood Cell Count- NEONATE

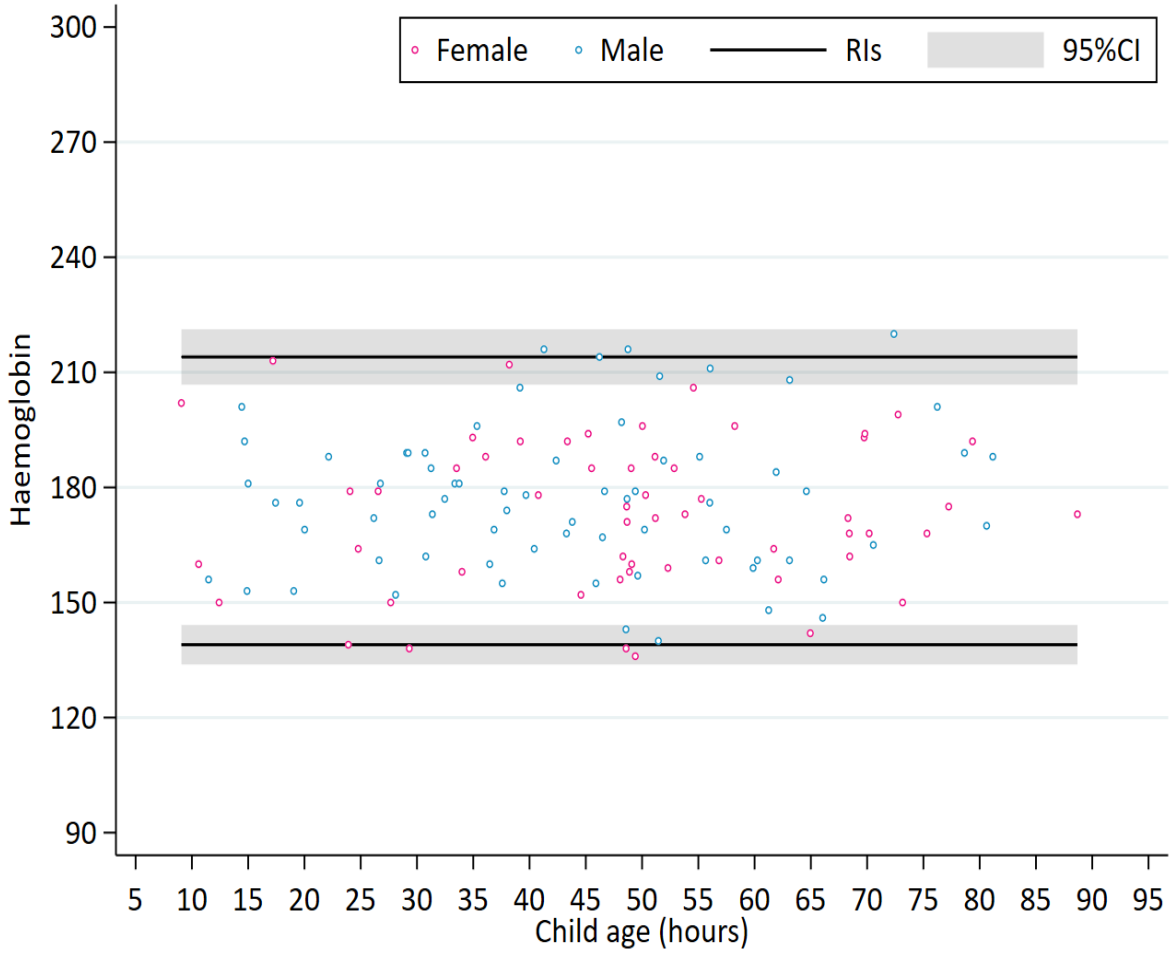
Advia 2120i automated analyser system- Siemens

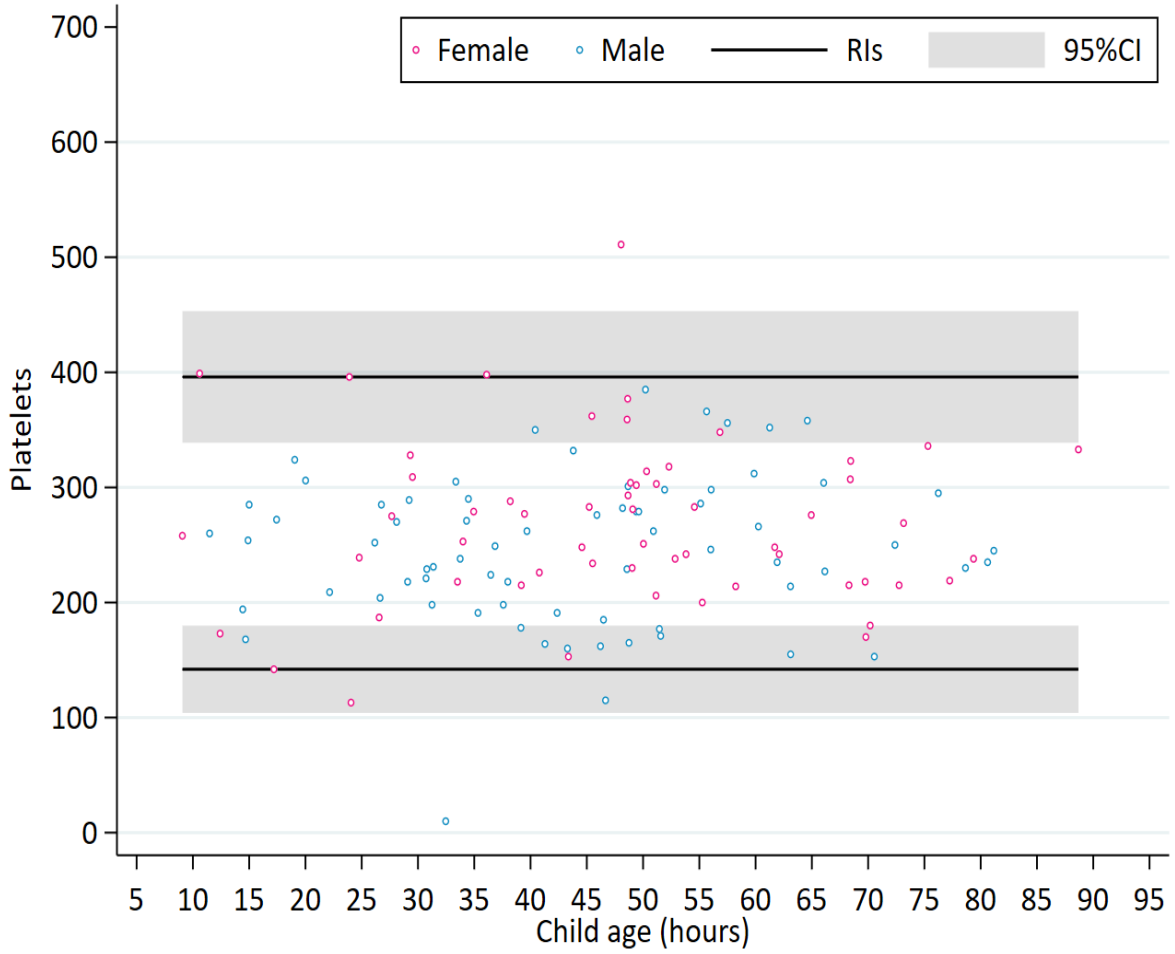




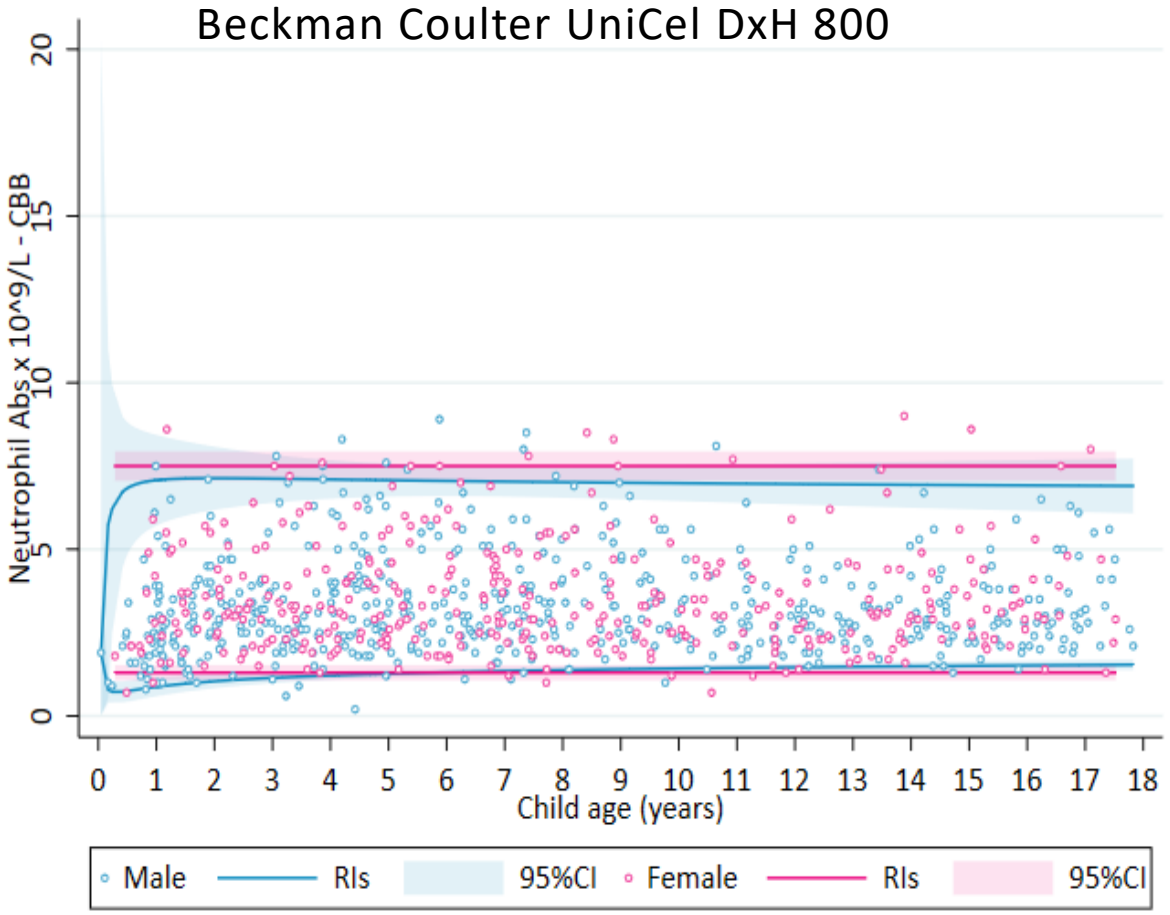
Haemoglobin & Platelets -NEONATE

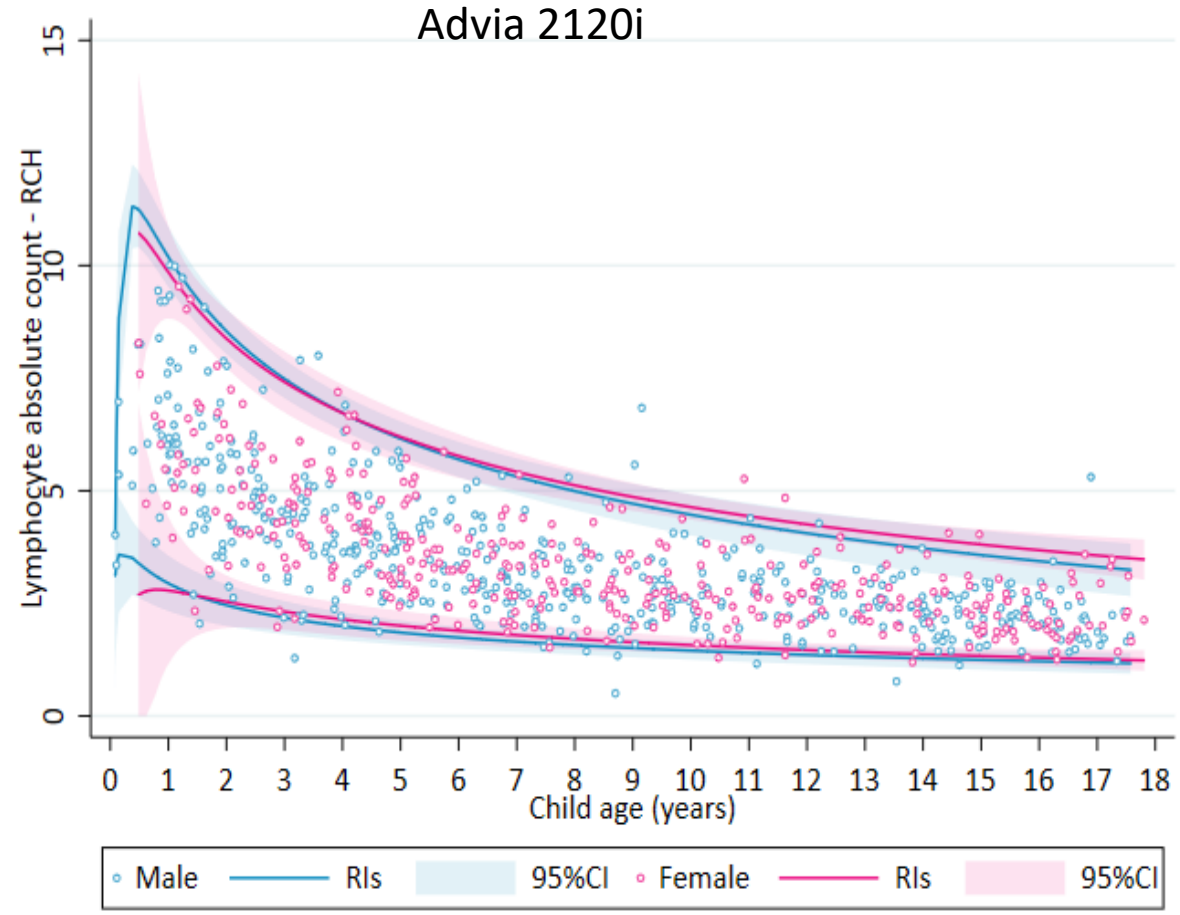
Advia 2120i automated analyser system- Siemens





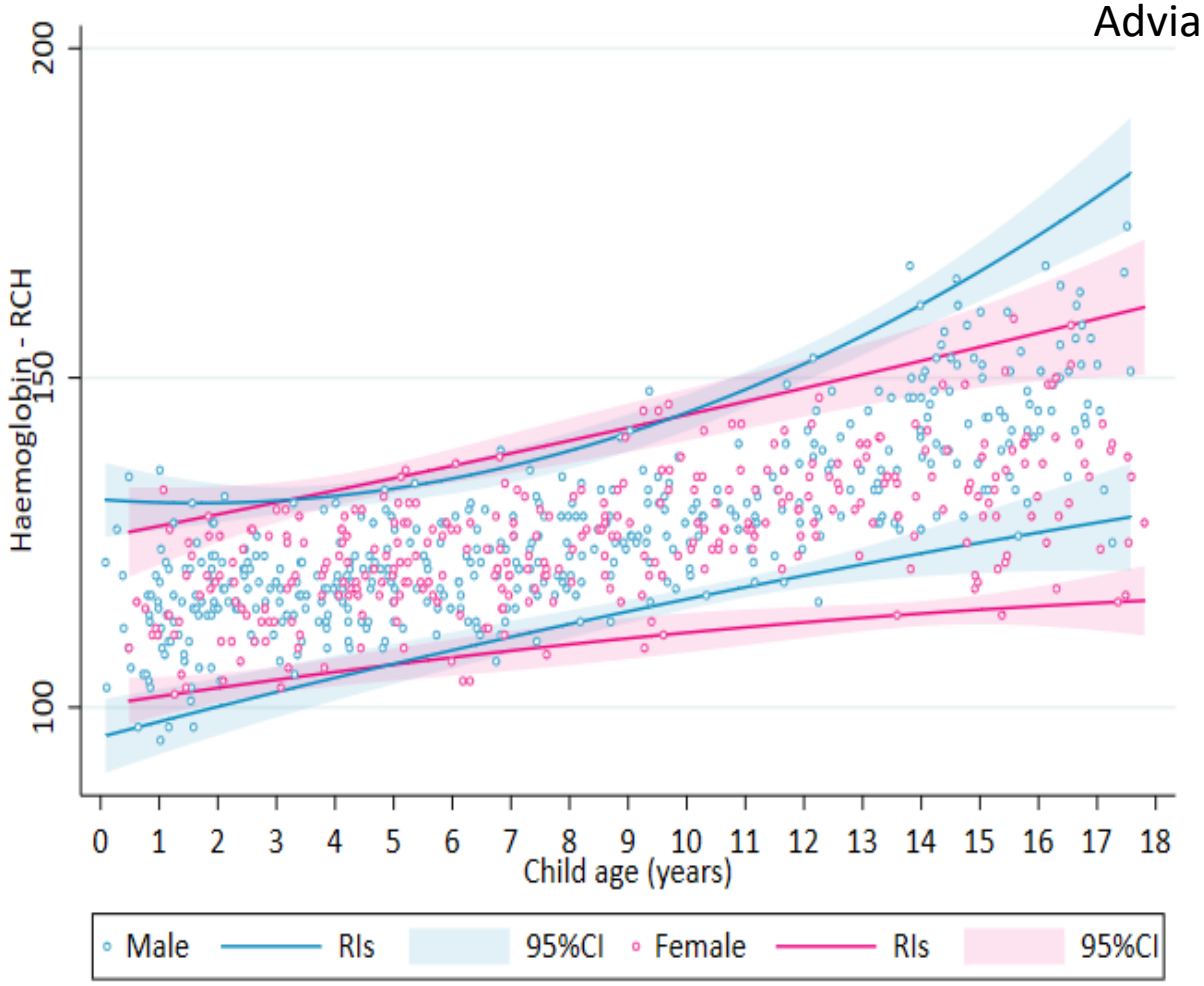
Neutrophil & Lymphocyte -PED

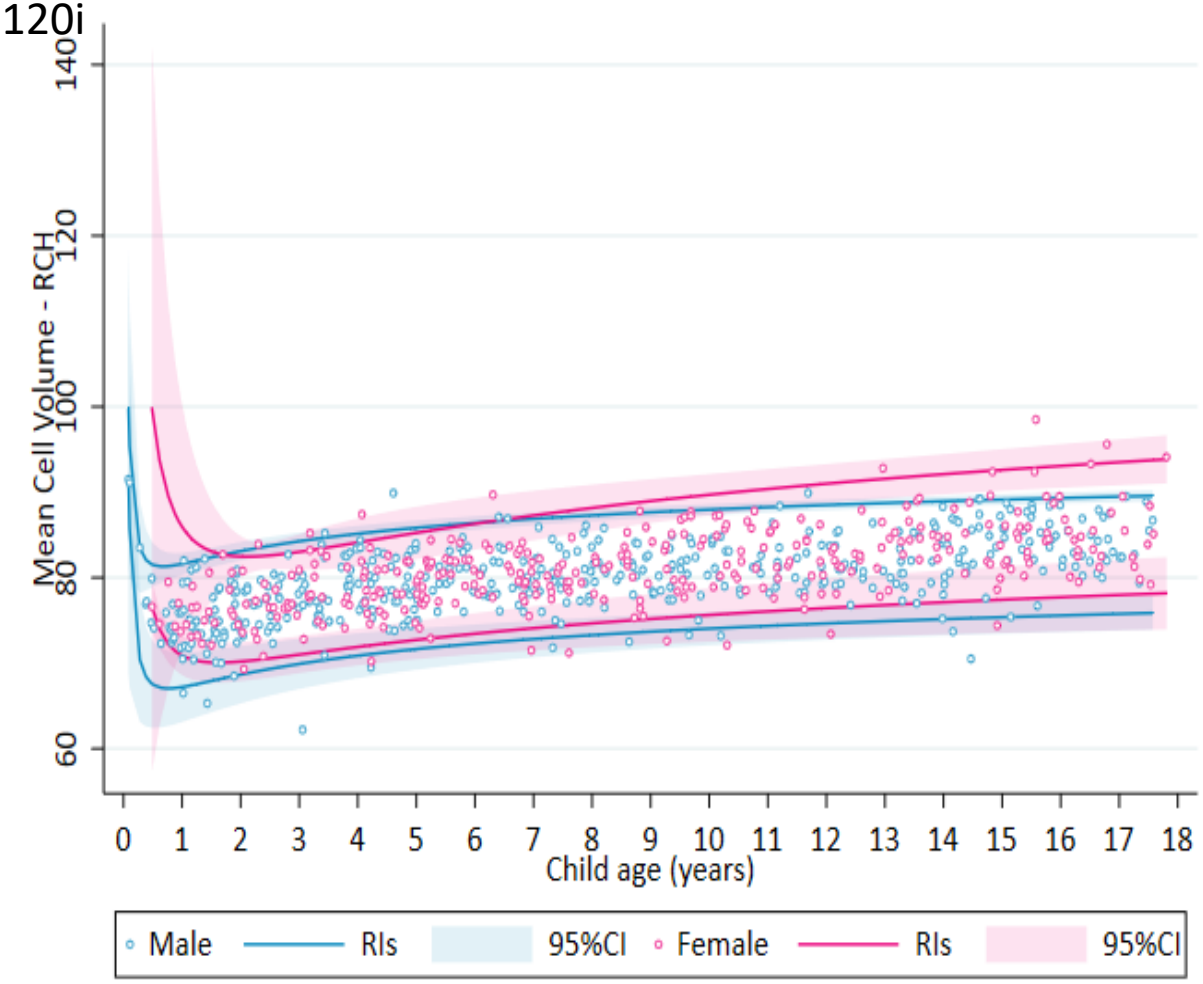




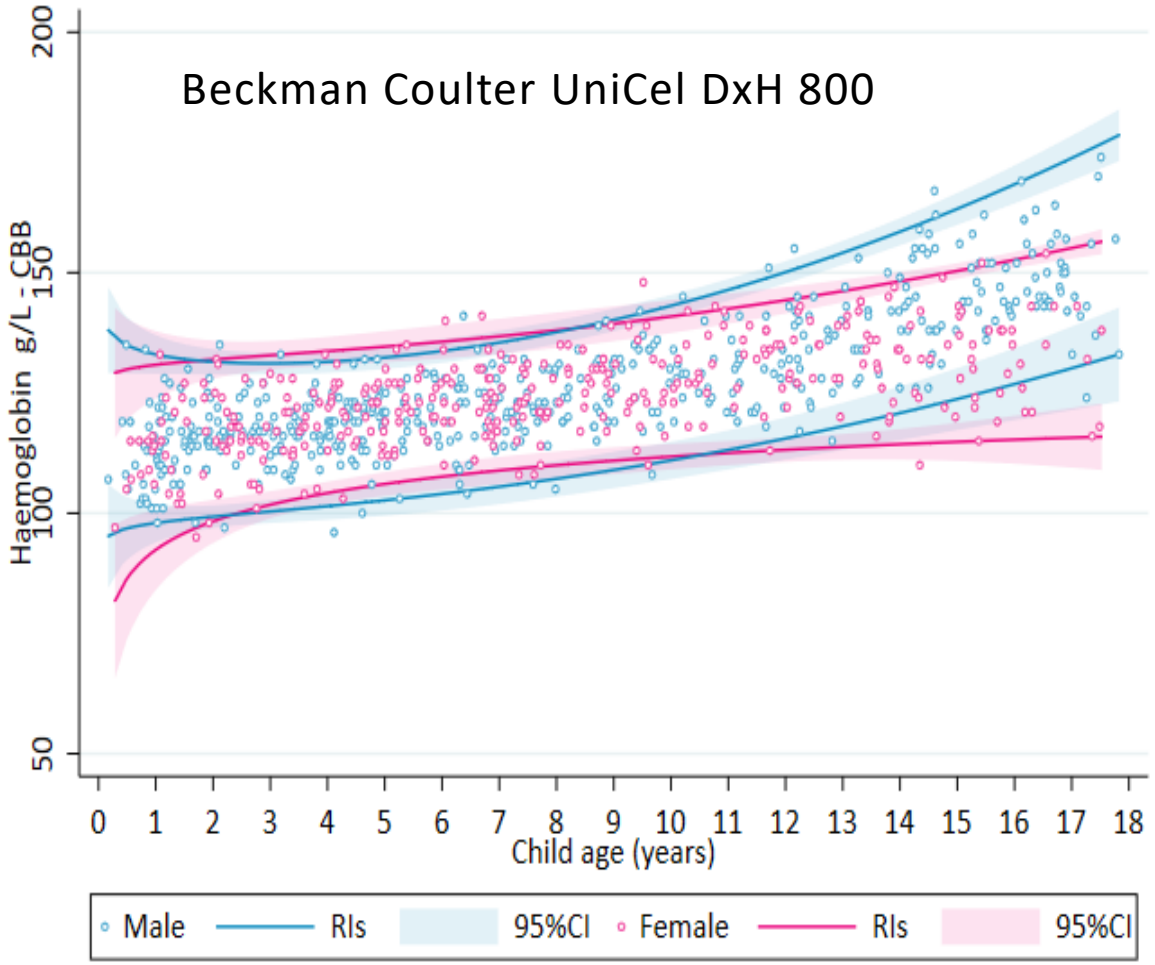
Haemoglobin& MCV -PED

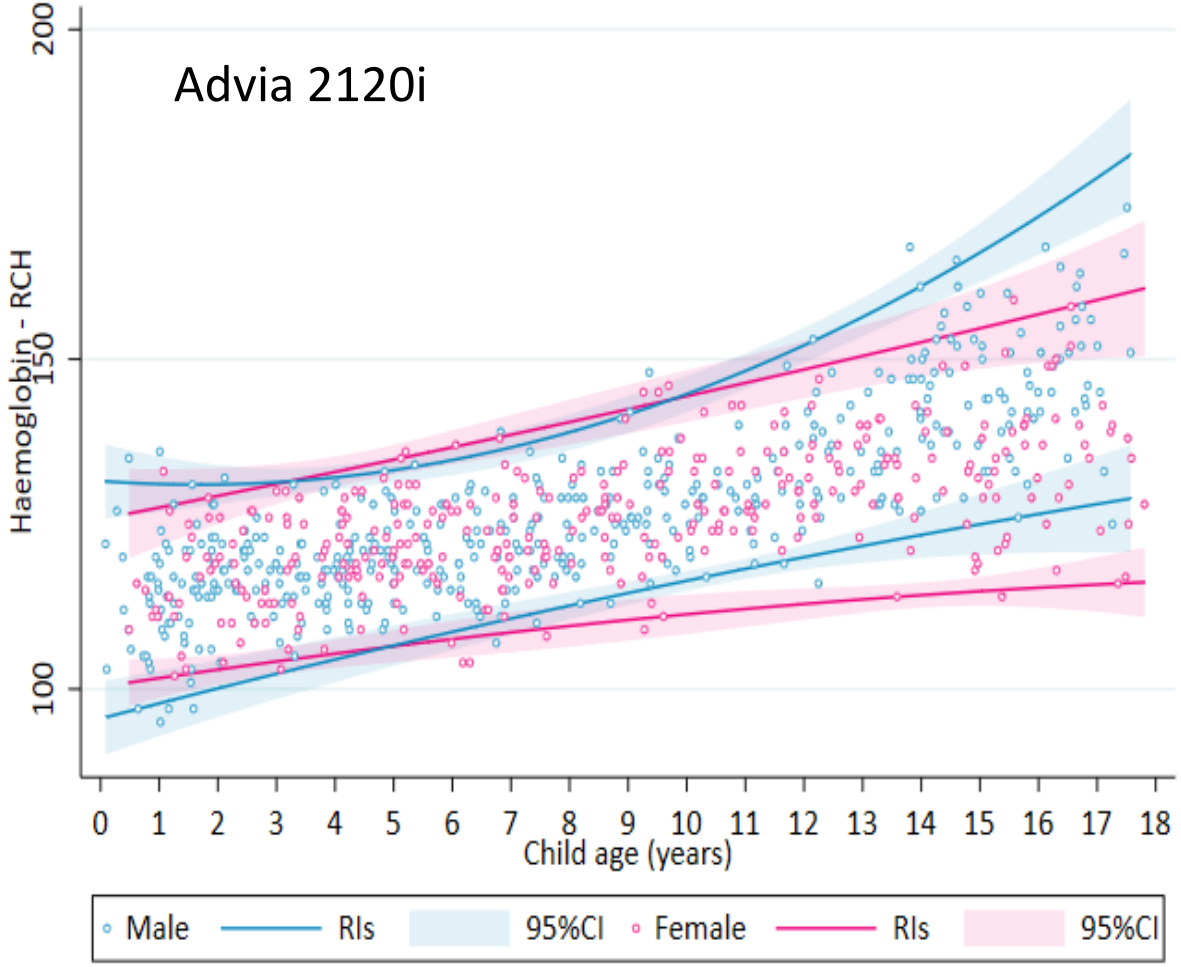
Advia 2120i



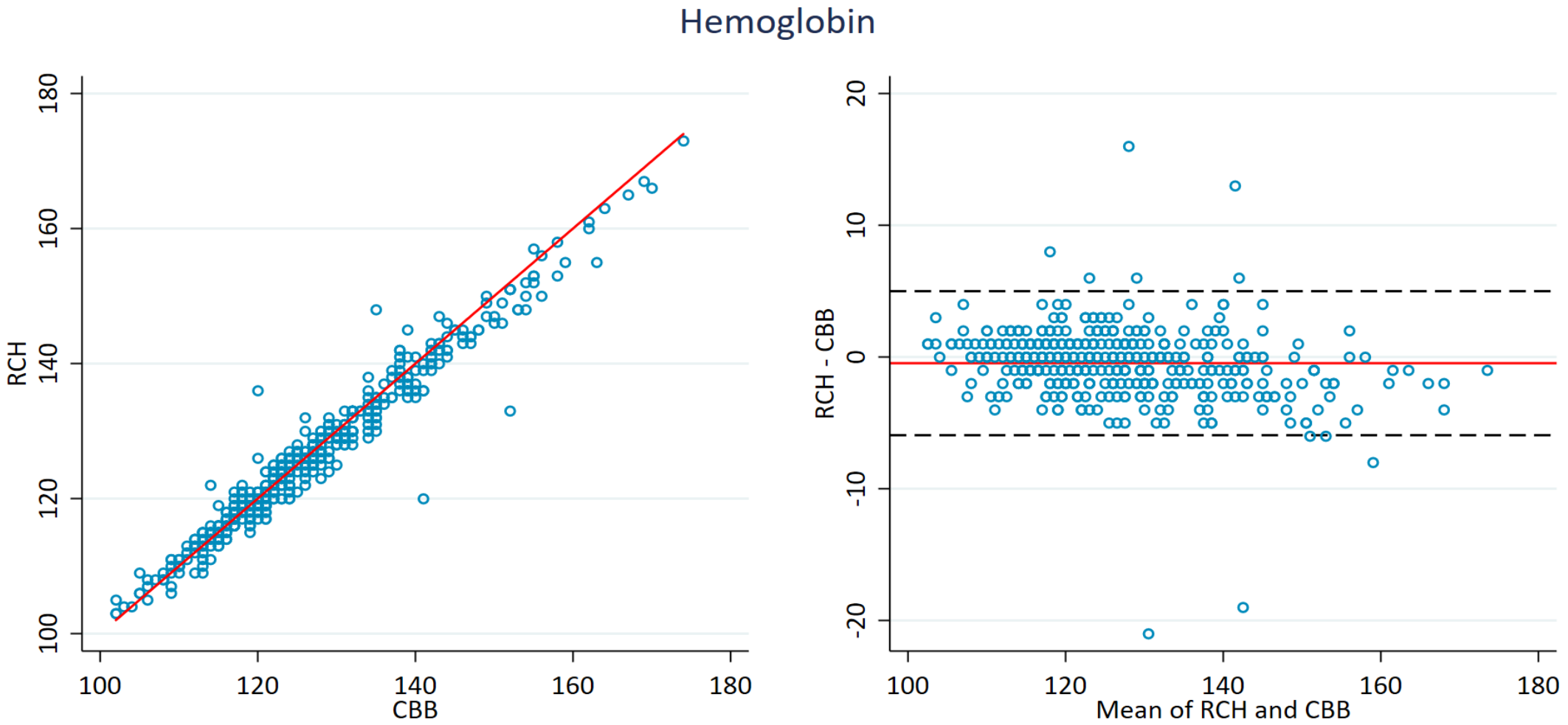


Analyzer comparison





Analyzer comparison

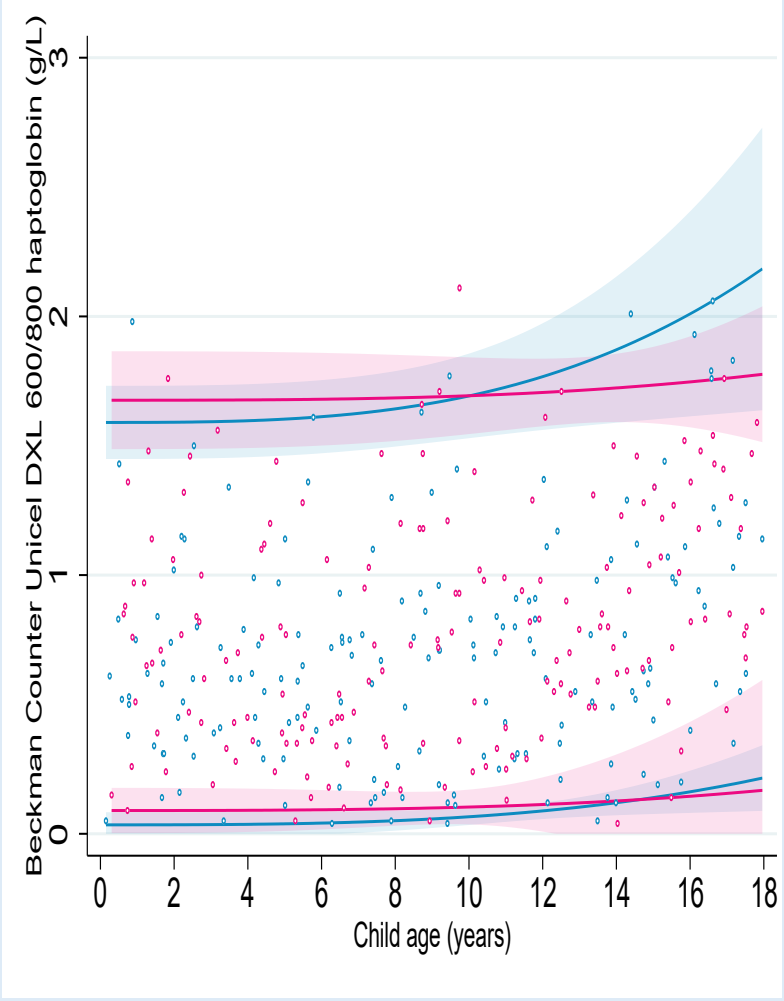


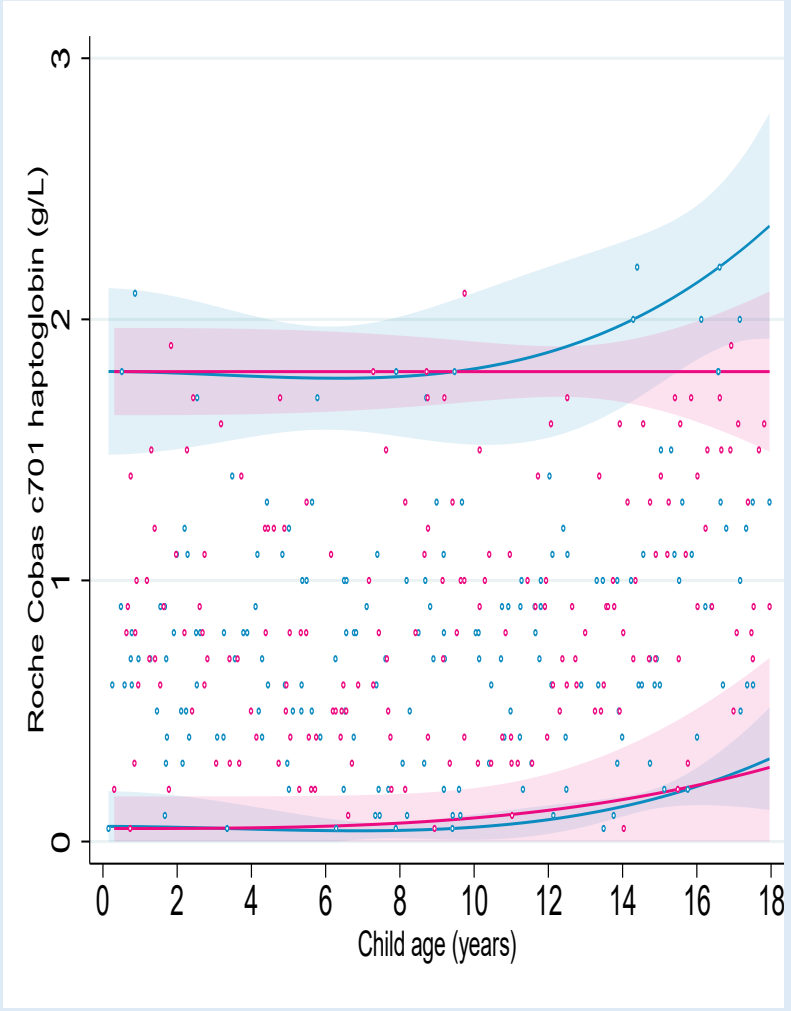
Correlation and agreement between RCH and CBB measurements.

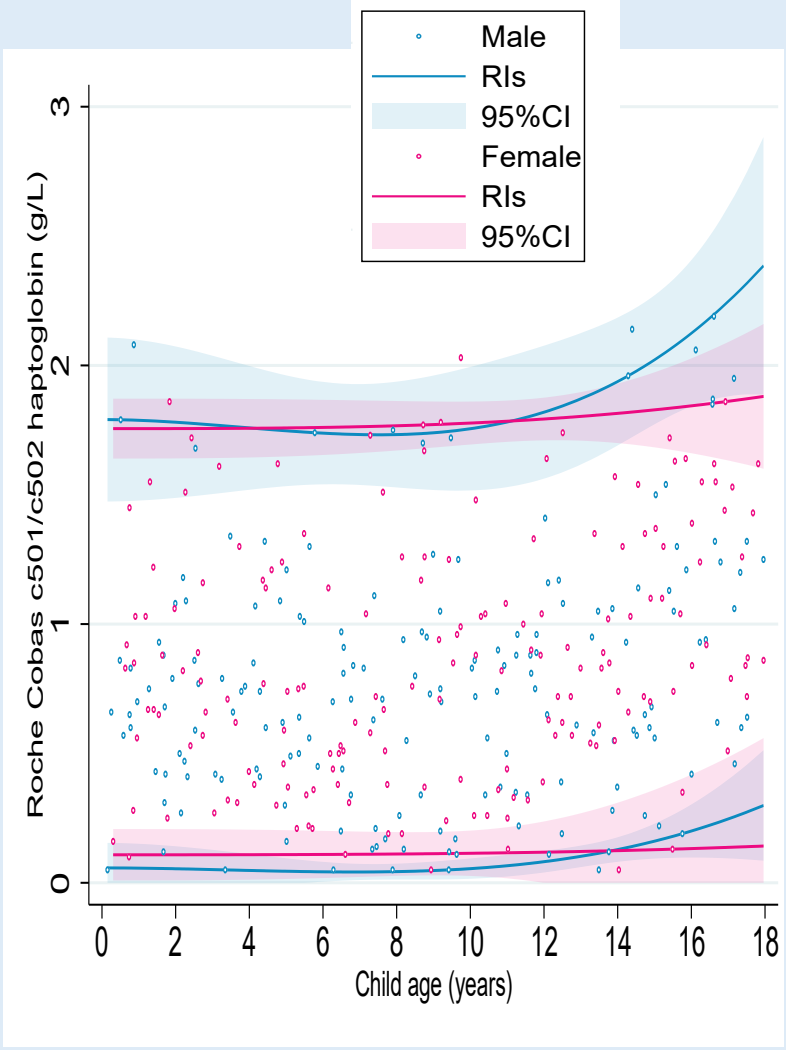
Analyzer comparison

	RCH		CBB		Matched		RCH	CBB	Difference		CV	
FBC Analyte	n	n_0	n	n_0	n	rho	Range	Range	M	(95%CI)	Observed (Median)	Westgard
White cell count	876	2	904	4	472	0.98	2.91,17.60	2.80,18.20	-0.35	(-0.39,-0.30)	4.21	?
Hemoglobin	783	6	851	9	425	0.98	103.00,173.00	102.00,174.00	-0.47	(-0.73,-0.21)	0.79	?
Neutrophil	871	7	902	6	470	0.93	0.38,8.27	0.60,9.00	-0.16	(-0.21,-0.11)	4.19	?
Hematocrit	873	5	899	9	469	0.95	0.29,0.50	0.29,0.50	0.00	(0.00,0.00)	1.90	2.70
Lymphocyte	869	9	897	11	464	0.92	0.50,9.72	0.10,9.30	0.06	(0.01,0.12)	4.26	10.20
Red cell count	870	8	893	15	466	0.93	3.84,5.87	3.77,5.90	0.08	(0.07,0.09)	1.95	?
Monocytes	866	10	902	6	465	0.57	0.07,1.32	0.20,1.70	-0.18	(-0.20,-0.17)	29.50	17.80
Mean cell volume	782	7	842	18	424	0.91	65.30,92.40	65.90,92.60	-0.84	(-0.99,-0.69)	1.36	?
Eosinophil	848	12	885	23	454	0.93	0.01,1.03	0.00,1.10	-0.02	(-0.02,-0.01)	12.78	21.00
Mean cell haemoglobin	779	10	844	16	425	0.88	21.70,31.20	21.80,32.20	-0.56	(-0.62,-0.50)	2.17	?
Mean cell haemoglobin concentration	786	3	856	4	428	0.53	302.00,373.00	315.00,370.00	-3.25	(-4.00,-2.50)	1.75	?
Red cell distribution width	780	9	840	20	421	0.78	10.90,16.60	11.60,16.60	-0.46	(-0.49,-0.42)	3.78	3.50
Platelets	788	1	855	4	427	0.89	136.00,588.00	122.00,531.00	19.63	(17.03,22.22)	8.20	9.10
Mean platelet volume	877	1	898	9	470	0.54	6.30,11.80	6.20,11.30	0.27	(0.20,0.35)	5.87	?

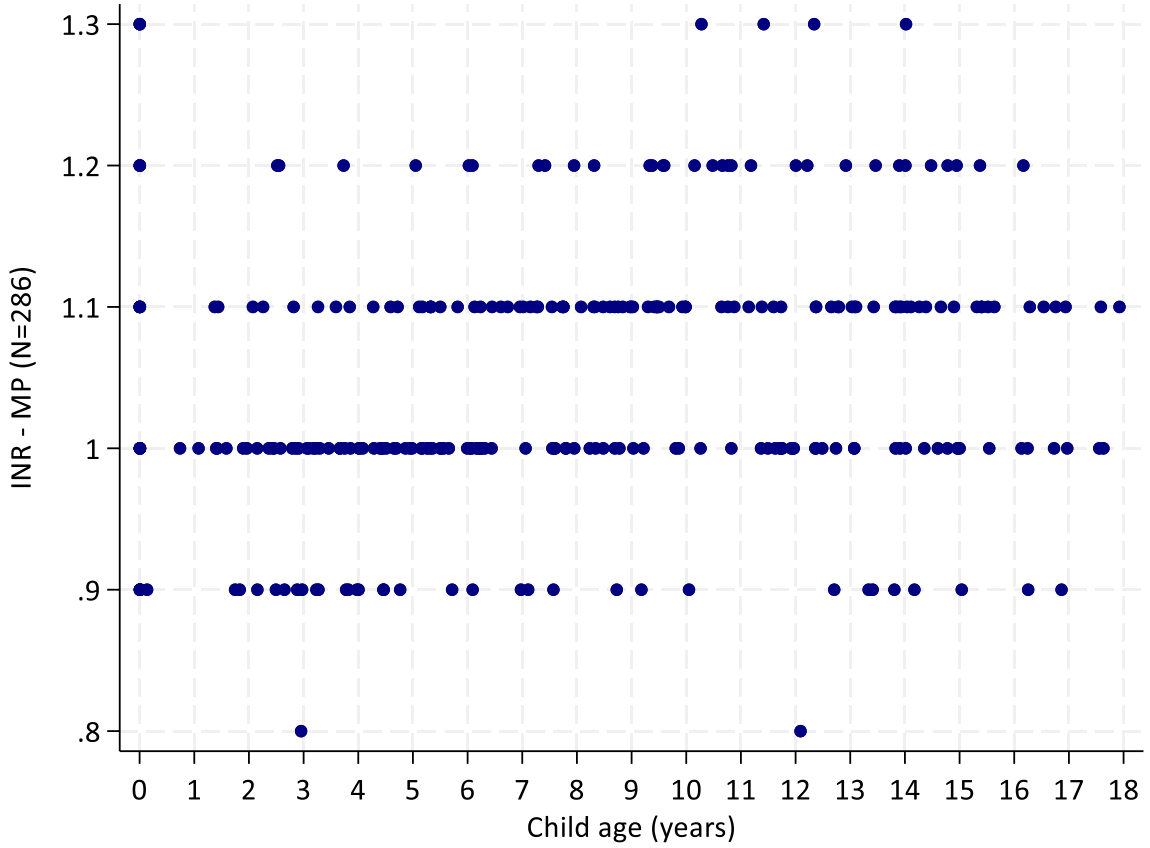
Haptoglobin on 3 different analysers

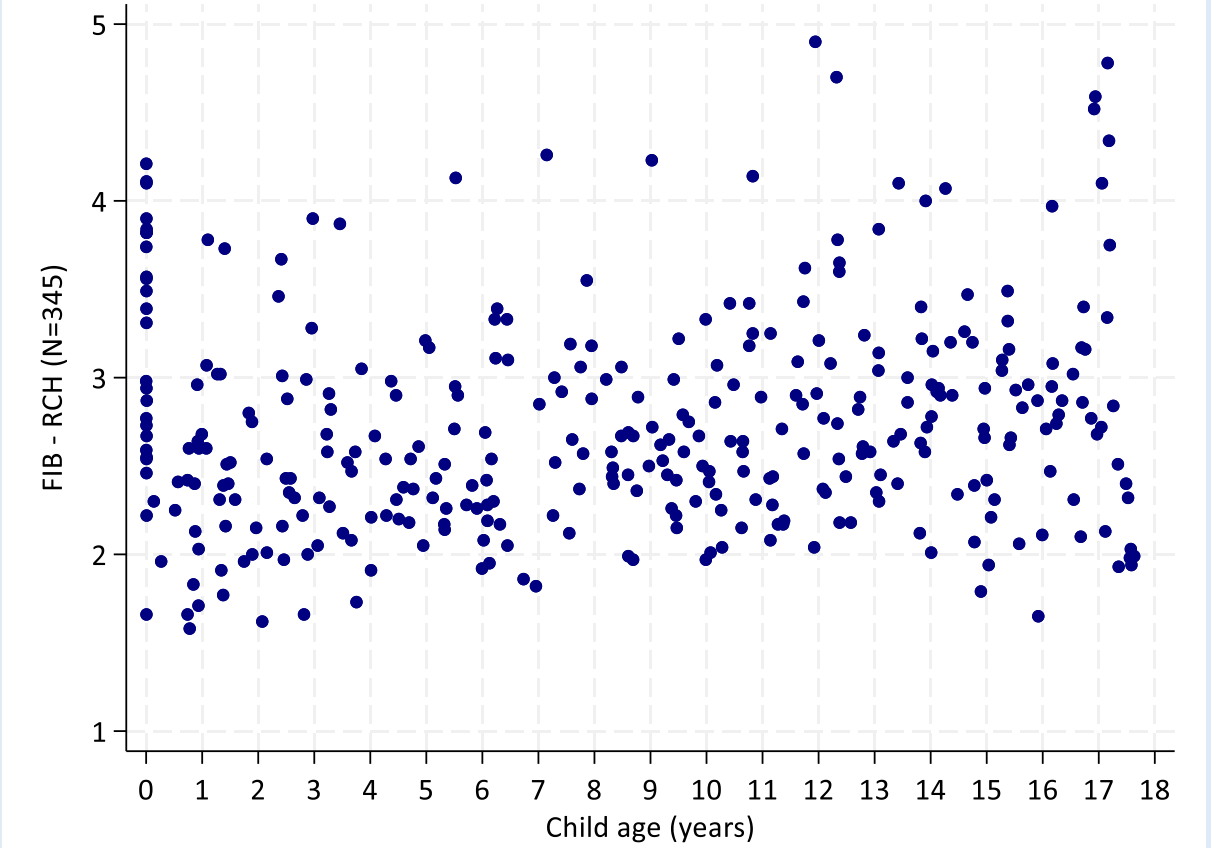




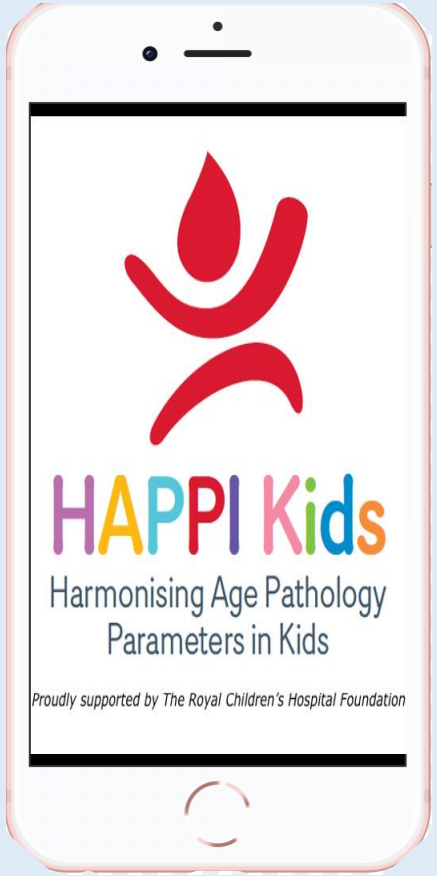


MORE DATA …


INR - MP (N=286)
1.3
1.2
1.1
1
.9
.8
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
Child age (years)


FIB - RCH (N=345)
5
4
3
2
1
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
Child age (years)

TBC projects



App under development

Reference values for full blood count in healthy Children.

Jad El Maamari[1,4], Meredith Wiggins[2,3] Vasiliki Karlaftis[4], Chantal Attard[4], Stephen Hearps[4], Janine Campbell[6], Sharon Yong[6], Janet Burgess[6], Paul Monagle[2,4,5] and Vera Ignjatovic[4,5], on behalf of the HAPPI Kids study team*

Reference values for full blood count in full term, healthy Australian neonates.

Jad El Maamari[1,4#], Meredith Wiggins[2,3#], Vasiliki Karlaftis[4], Chantal Attard[4], Stephen Hearps[4], Janine Campbell[6], Sharon Yong[6], Janet Burgess[6], Paul Monagle[2,4,5] and Vera Ignjatovic[4,5], on behalf of the HAPPI Kids study team*

Reference Intervals for Haptoglobin in Neonates and Children 30 Days to 18 years old

Jad El Maamari[1,2], Vasiliki Karlaftis[2], Chiara Braida[2], Joel Smith[4], Susan Matthews[4,6], Chantal Attard[2], Stephen Hearps[2], Janet Burgess[4], Paul Monagle[2,3,4,5] and Vera Ignjatovic[2,3], on behalf of the HAPPI Kids study team*

Reference Values for coagulation analytes across 5 different analyzers in neonates and children 30 days to 18 years of age.

Jad El Maamari[1,2], Vasiliki Karlaftis[2], Chiara Braida[2], Joel Smith[4], Susan Matthews[4,6], Chantal Attard[2], Stephen Hearps[2], Janet Burgess[4], Paul Monagle[2,3,4,5] and Vera Ignjatovic[2,3], on behalf of the HAPPI Kids study team*

THANK YOU

The Team

Paul Monagle – Principal Investigator
Vicky Karlaftis – Study Coordinator
Vera Ignjatovic – Scientific Advisor
Jad El Maamari- Researcher/clinician
Janet Burgess – Pathology Advisor
Monsurul Hoq – PhD Student/Statistician
Stephen Hearps - Statistician
Pathology Collectors – Chauvy Burgess, Kathryn Bowers, Jody Hand

Funding

The Royal Children's Hospital Foundation (Core Funding)

RCH1000

Ortho Diagnostics (Supplementary Funding)
Roche Diagnostics (Reagents)

Anaesthetic Departments

- The Royal Children's Hospital
- Western Health – Sunshine
- Northern Health

Post Natal Wards

- The Royal Women's Hospital
- Northern Health
- Western Health – Sunshine

Laboratories

- The Royal Children's Hospital Laboratory Services
- Melbourne Pathology
- Dorevitch Pathology
- Australian Clinical Laboratories
- Monash Pathology
- The Royal Melbourne Hospital Laboratory

THE UNIVERSITY OF BRITISH COLUMBIA

Department of Pediatrics
Faculty of Medicine

BC Children's Hospital Research Institute

Celebrate Research Day 2024

Dr. Elad Machtey

POCUS for Pediatric neck Lymphadenopathy

An Online Educational Tool

April 12, 2024

Dr Elad Machtey

Preseptor: Dr Melissa Skaugset

land acknowledgment

"I acknowledge that I am speaking to you from the traditional and unceded territory of the Coast Salish Peoples, including the Musqueam, Tsleil-Waututh, and Squamish Nations of Vancouver. Let us acknowledge the Indigenous lands we stand on and respect the enduring care and cultural heritage of Indigenous peoples that enrich our nation."

Presenter Disclosure

Presenter: Elad Machtey

Relationships with commercial interests:

I have nothing to disclose.

Introduction:

- Bedside diagnostic tool
- Dynamic Assessment
- Guidance for Procedures
- Reduce LOS
- Radiation-free
- $

POCUS Remote/Online Learning

Effective as in person teaching

Requires minimal setup

Easily reproducible

“Anytime, Anywhere Access”

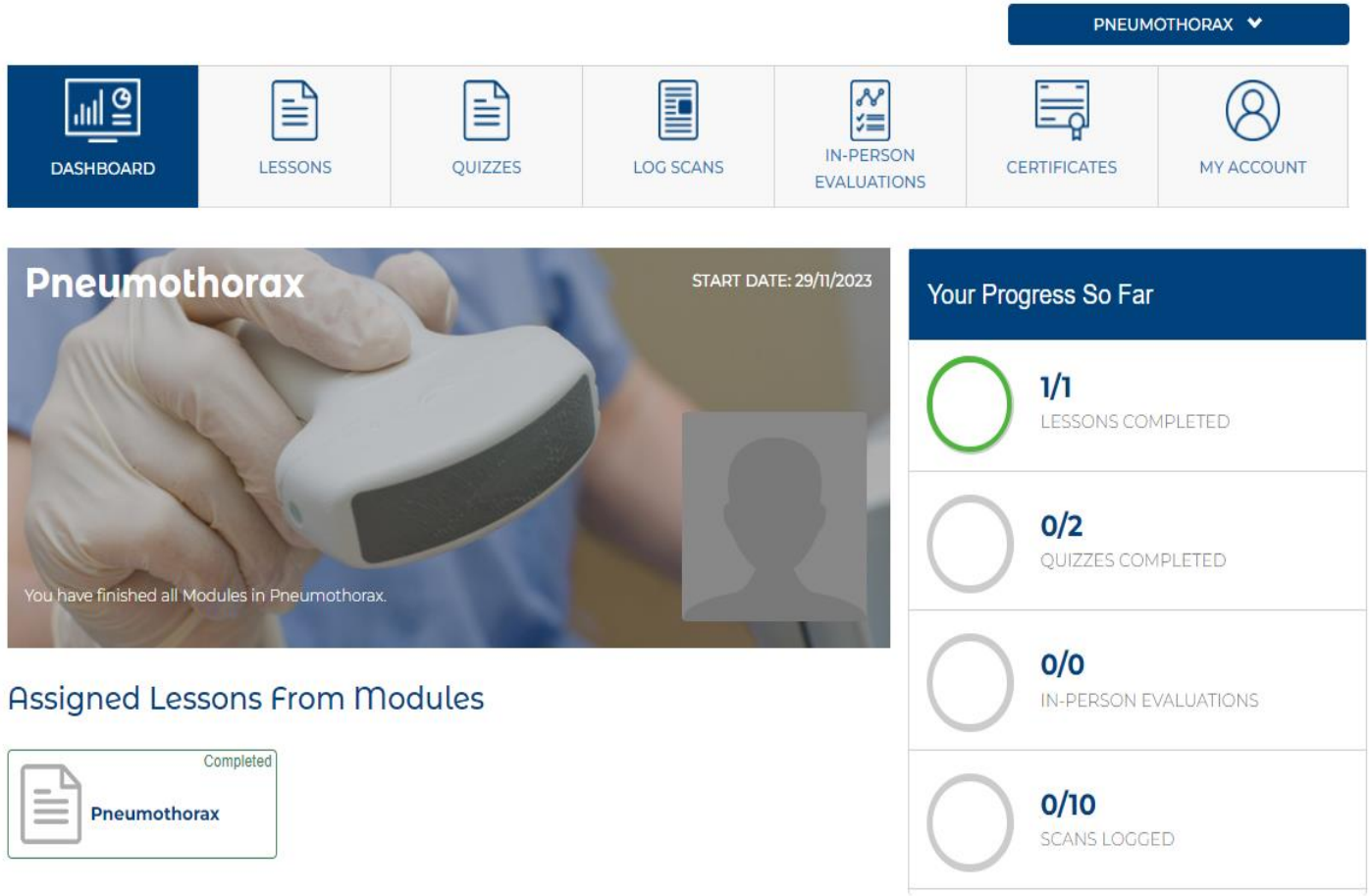
Knowledge retention

Cost-Effectiveness

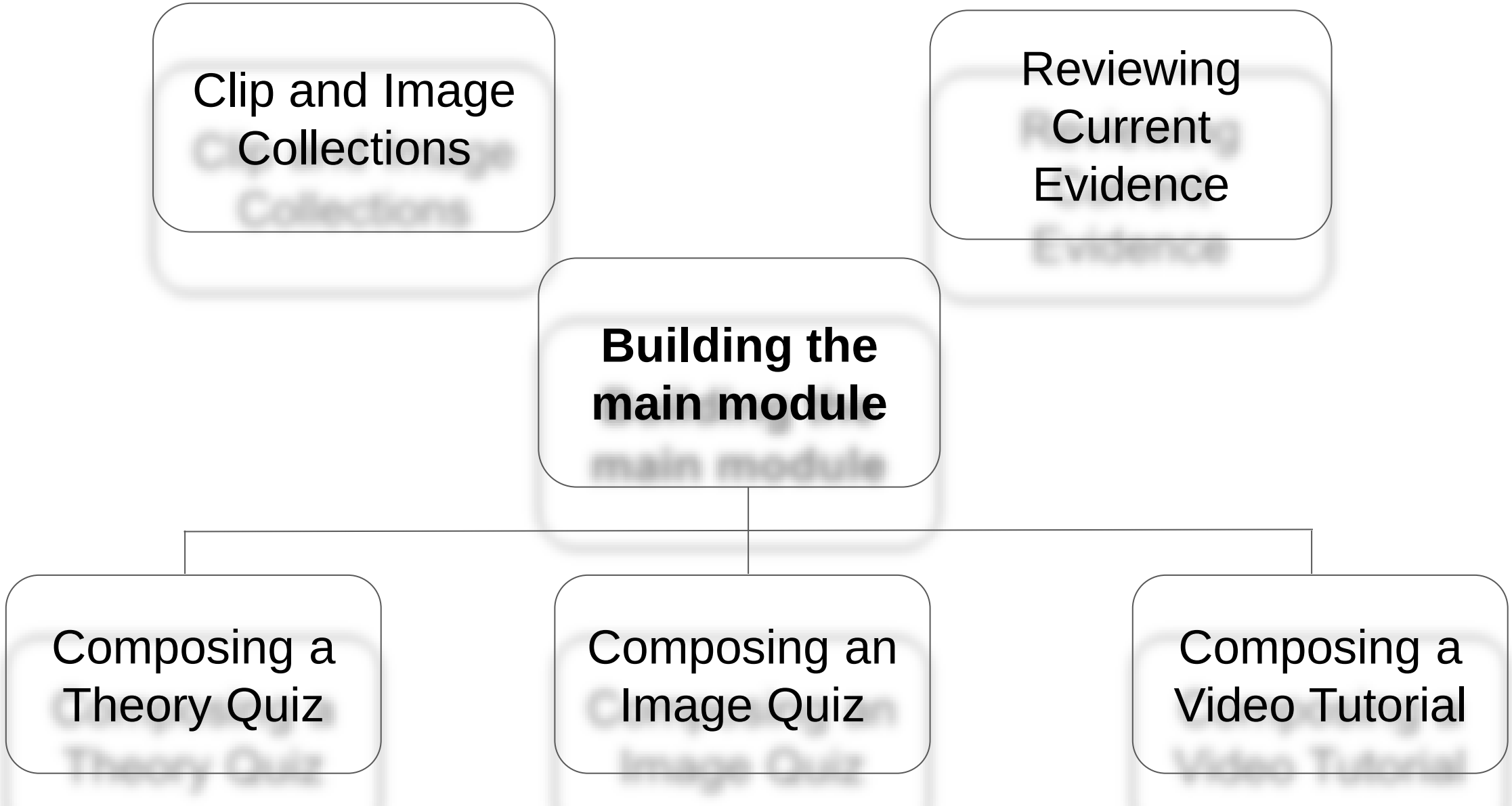
Objectives

To develop a comprehensive remote learning course for healthcare providers aimed at improving their ability to assess children presenting with neck lymphadenopathy.

Objectives


PNEUMOTHORAX
DASHBOARD
LESSONS
QUIZZES
LOG SCANS
IN-PERSON EVALUATIONS
CERTIFICATES
MY ACCOUNT
Pneumothorax
START DATE: 29/11/2023
You have finished all Modules in Pneumothorax.
Assigned Lessons From Modules
Completed
Pneumothorax
Your Progress So Far
1/1
LESSONS COMPLETED
0/2
QUIZZES COMPLETED
0/0
IN-PERSON EVALUATIONS
0/10
SCANS LOGGED

Methods/Technique



Results

Clip and Image Collections

37 POCUS Studies

355 videos clip
63 images.

18 Reactive Nodes
5 Suppurative lymphadenitis
4 Parotitis
2 Abscesses
1 Submental Mass
1 Odontogenic cyst
1 Thyroglossal Duct Cyst
5 Unclear\Normal Findings

Reviewing Current Evidence

7 Relevance Studies

4 Evaluation and management of neck swelling in children and imaging findings.
3 Pediatric POCUS for Lymph nodes and neck Swelling.

3 Text Books

1 Head and Neck Sonography
1 Pediatric Sonography
1 Pediatric POCUS

Building the module Intro and technique

1. Introduction:
   - Clarification of the indications for utilizing US.
   - Examination of evidence supporting bedside US for lymph node assessment.
   - Translation of findings into actionable insights for patient care.
   - Indication of POCUS

2. Technique and Scanning Methods:
   - Covering aspects such Equipment needed, as probe selection, optimal settings.
   - Technique- patient Positioning, probe placement, “Pro TIPS”, Image acquisition, and interpretation techniques.

Technique

1. Place patient comfortably supine
2. Position neck to best expose the swelling*
3. Apply lots of gel for comfort if the area is tender (7)
4. Consider providing analgesia
5. Using the linear transducer, scan the area of interest on the longitudinal plane
6. Scan the area of interest on the transverse plane
7. Assess the size, shape, echogenicity, borders, and vascularity of the nodes
8. Apply color doppler to describe flow to the area
9. Document and describe characteristics of the mass

**This will usually require turning the head to the contralateral side and in extension. This might be achieved by placing the patient in a semi recumbent position or in the parents lap which might offer some holding as well.*

Figure 1. Probe position

Pro TIPS

Direction of the mass may not be in the traditional anatomic planes, you might need to slide, sweep, rock, fan and adjust your depth in order to characterize the mass and define its relation to the surrounding area including where it lies in relation to glands, other soft tissue, vessels, or muscles.

Building the module- Illustration

Characteristics

Margins

- Are the margins smooth?
- Is there any definable capsule?

Shape

- Describe the mass in three dimensions: Ovoid? Round? Irregular?

Echogenicity/internal structure

- Homogeneous?
- Heterogenous?
- Lobulated?
- Is there a central hilum?
- Ducts?
- Calcifications?

Surrounding tissue

- Tissue edema or echogenic fat?
- Is the mass embedded in a structure such as a muscle?
- Posterior acoustic enhancement?
- Gas or fluid in the tissue?

Vascularity

- Is there flow?
- Vascularity radiating from a hilum?
- Peripheral vascularity?

What am I looking at?

Lymph nodes:

Lymph nodes are solitary ovoid structures composed of lymphoid tissue and are distributed along the lymphatic vessels.

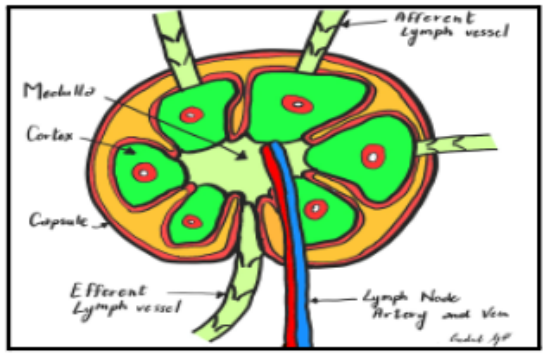


Figure 2. Lymph node- illustration

Each node is divided internally into cortex and medulla, and encased by a capsule. Artery and vein enter and exit the lymph node at the hilum.

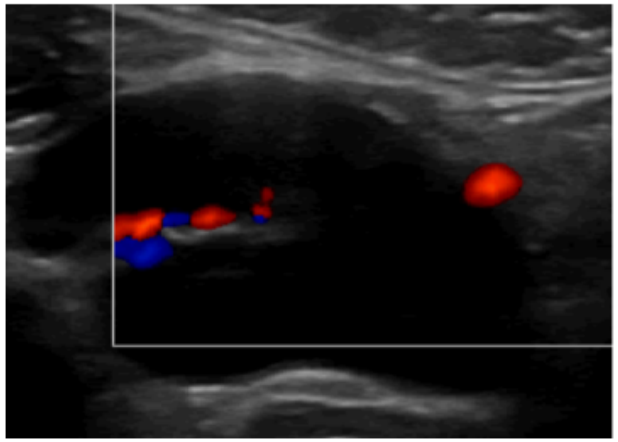


Figure 3. Normal Lymph node

Normal lymph node:

Size: Lymph Nodes in the head and neck, excepting the submandibular region, nodes larger than 10 mm (1 cm) in the short axis are considered abnormal. In the submandibular region, a short axis of up to 15 mm can be considered normal. (8)

Shape: normal Lymph Nodes are ovoid, or "kidney shaped ". In the submandibular region a normal node can appear round rather than ovoid.

Echogenicity: Normal lymph nodes have a distinct appearance of cortex and medulla. The outer cortex is hypoechoic due to lymphoid follicles, while the central medulla is hyperechoic due to a dense network of lymphatic cords and a central sharp linear hyperechoic fatty hilum containing blood vessels.

Surrounding tissue: in a normal or reactive lymph node, usually the surrounding tissue doesn't demonstrate anatomical or echogenic change.

Vascularity: in a normal node, the central hilum is vascular on color Doppler.

Building the module- Specific conditions

Suppurative Lymphadenitis

Suppurative Lymphadenitis is caused by an infection of one or more nodes. The most common pathogens are Staphylococcus aureus and group A Streptococcus. This might occur following reactive lymphadenopathy. Infections that occur after dental or oral surgeries are typically polymicrobial, predominantly anaerobic.(9)

Imaging:

Size: Typically enlarged node or confluence of nodes. Usually 1-4 cm range

Shape: Ovoid to round

Echogenicity: Heterogenous with areas of increased echogenicity.

Internal structure: The node appears hypoechoic with irregular wall thickness. The central hilar stripe is not visible. Internal echoes are present, indicating the presence of purulent material and debris.

Surrounding tissue : There is thickening observed in the surrounding tissues and subcutaneous layers. Additionally, there is often posterior acoustic enhancement.

Vascularity: Central avascularity, often with Increased vascularity to the nodal periphery and to the inflamed soft tissues surrounding.

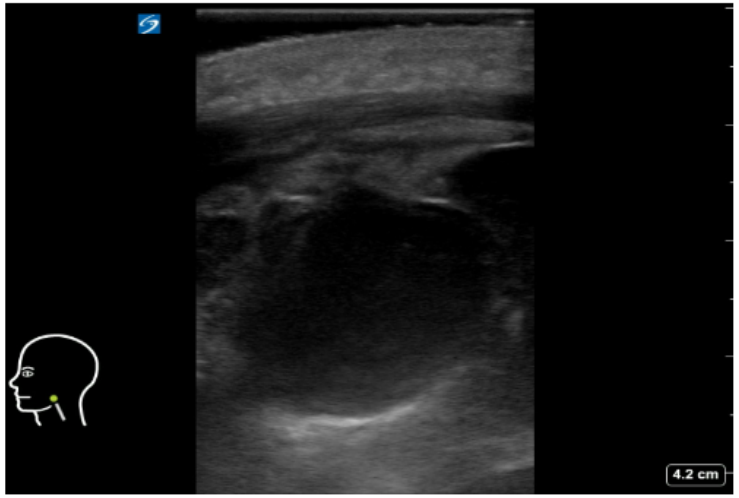


Figure 7: Suppurative Lymph node in longitudinal plane. Enlarged round cervical node. Hypoechoic central hilum, with debris peripherally. Note the thickening of the surrounding tissue.

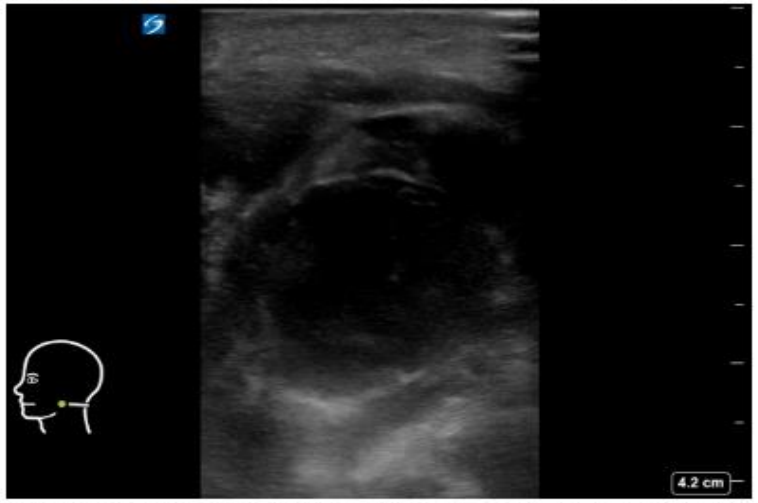


Figure 8: Corresponding Suppurative Lymph node on the transverse plane. Note that the shape of this node is round on both planes.

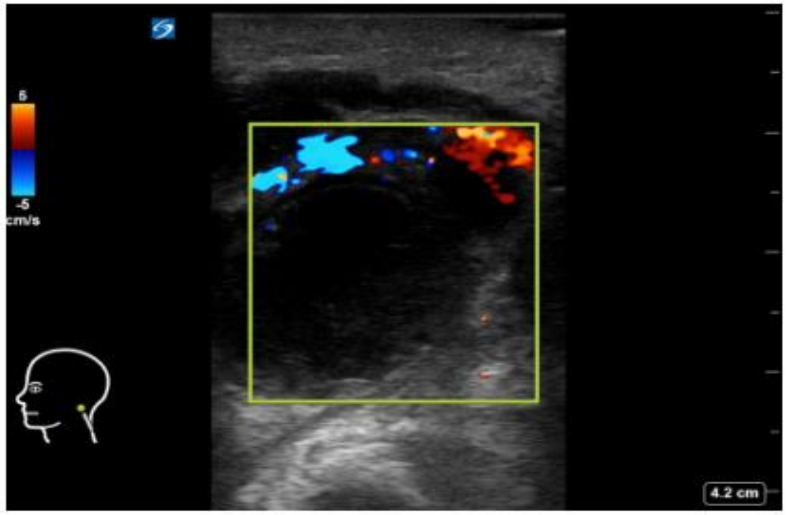


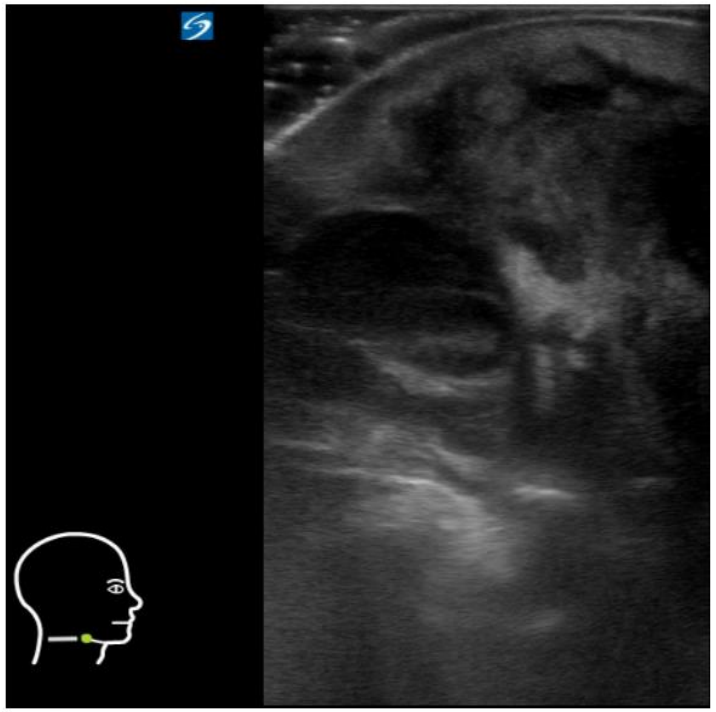
Figure 9: Corresponding image with power Doppler US showing central avascularity with increase of peripheral flow.

Image Quiz

15 MCQ using images depicting various findings and pathologies, each accompanied by correct
answers and detailed explanations.

Image Quiz

15. A 4 year old is seen in the ED with fever with a tender right sided neck swelling. Labs are pending. You perform PoCUS with the following findings:



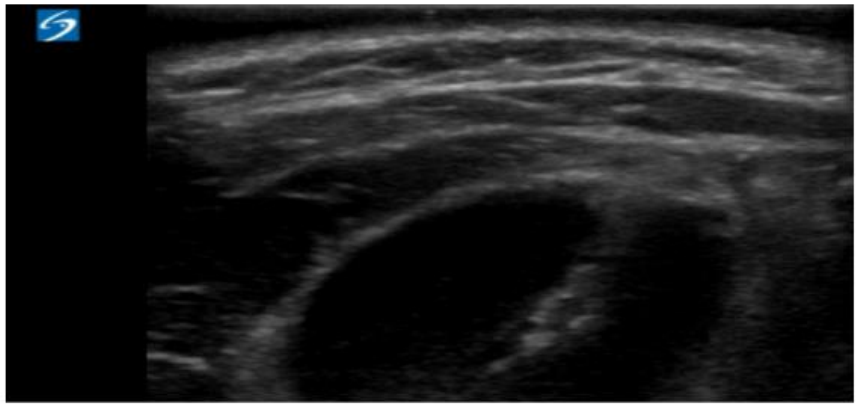
Based on the clinic picture and PoCUS findings, the most probable etiology for his neck swelling is:

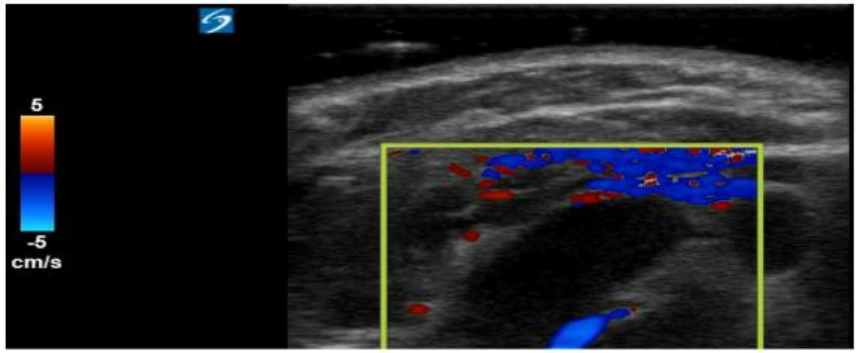
A. **Neck abscess - start antibiotics, considered surgical I & D**
B. Reactive lymph nodes - routine follow up if not resolving
C. Suggestive of lymphoma - refer for urgent further evaluation
D. Suppurative adenitis - start antibiotic treatment

Correct answer: A
Neck Abscess. In this image we can appreciate a large mass with irregular shape and indistinct margins, heterogeneous echogenicity, adjacent hypoechoic lymph nodes with intranodal hyperechoic material consistent with likely purulent debris.

Lymph Node Ultrasound Image Quiz

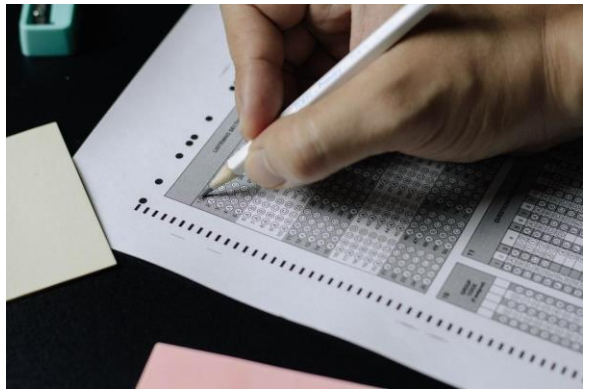
10. You are working as an attending in your department and your resident is reviewing with you his PoCUS scan of a patient with right sided neck swelling. They think this patient has reactive lymph nodes. What feedback will you give?





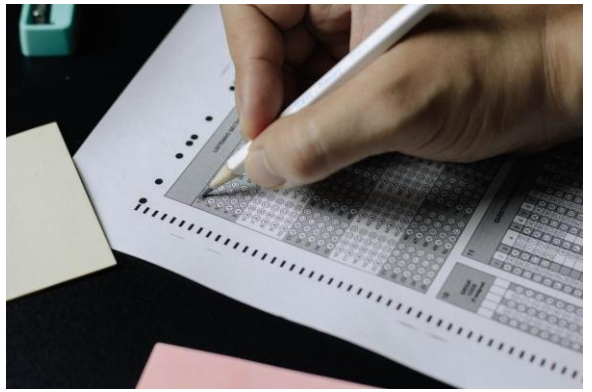
A. You are probably right. There is an enlarged node with normal structure, normal central vascularity, and no edema of the surrounding structure.
B. **You are probably right. There is a node with normal structure, normal central vascularity, and no edema of the surrounding structure. However, in order to be more certain it is important to see the whole structure which could be achieved by increasing the depth and also obtaining a transverse view of the lymph node.**

Theory Quiz



15 multiple-choice questions (MCQs) evaluating the learner's comprehension, accompanied by thorough explanations and referenced answers.

Theory Quiz



1. Use of PoCUS for evaluation of neck swelling in the ED is correlated with:
    - **A. Reduced ED length of stay**
    - B. Increased parental satisfaction
    - C. Reduced use of blood work
    - D. Prolonged ED length of stay

A: Performing PoCUS in the Pediatric Emergency Department was found to reduce length of stay in the emergency department

Claiborne MK, Ng C, Breslin KA, Chamberlain J, Thomas-Mohtat R. The effect of point-of-care ultrasound on length of stay in the emergency department in children with neck swelling. Am J Emerg Med. 2021 Oct;48:295-300. doi: 10.1016/j.ajem.2021.05.009. Epub 2021 May 4. PMID: 34052608.

Friedman N, Tseng F, Savic R, Diallo M, Fathi K, Mclean L, Tessaro MO. Reliability of Neck Mass Point-of-Care Ultrasound by Pediatric Emergency Physicians. J Ultrasound Med. 2019 Nov;38(11):2893-2900. doi: 10.1002/jum.14993. Epub 2019 Apr 1. PMID: 30937939.

2. When assessing lymph node size with PoCUS, you should?
    - A. Obtain short and long axis views
    - B. Obtain only a long axis view
    - C. Obtain short and long axis views, with and without color doppler
    - D. Obtain one view with and without color doppler

C: It is important to assess lesions/masses in 2 orthogonal plans and also use color doppler to assess for vascularity.

Doniger, Stephanie J., ed. *Pediatric Emergency Critical Care and Ultrasound.* Cambridge University Press, 2014.

Anil T. Ahuja (2014). Diagnostic Ultrasound Head and Neck. Elsevier (2014)

Video Tutorial

Implementation

BC Children's Hospital™
Provincial Health Services Authority

How It Works

Choose which topic you want to learn

Read background text and watch instructional video

Pass theory Quiz

Meet with Instructor for hands on scanning

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Summary

- POCUS is a vital tool with diverse applications across the medical field, carrying multiple implications for both patient care and broader health system considerations.
- Online Learning proves to be effective and provides numerous benefits.
- We crafted a Pediatric POCUS training module for both trainees and faculty, featuring a multilayered approach.

References:

Díaz-Gómez JL, Mayo PH, Koenig SJ. Point-of-Care Ultrasonography. N Engl J Med. 2021 Oct 21;385(17):1593-1602. doi: 10.1056/NEJMra1916062. PMID: 34670045.

Lentz, B., Fong, T., Rhyne, R. et al. A systematic review of the cost-effectiveness of ultrasound in emergency care settings. Ultrasound J 13, 16 (2021). https://doi.org/10.1186/s13089-021-00216-8

Kang SY, Yoo J, Park S, Jo IJ, Kim S, Cho H, Lee G, Park JE, Kim T, Lee SU, Hwang SY, Cha WC, Shin TG, Yoon H. Online Learning versus Hands-On Learning of Basic Ocular Ultrasound Skills: A Randomized Controlled Non-Inferiority Trial. Medicina (Kaunas). 2022 Jul 20;58(7):960. doi: 10.3390/medicina58070960. PMID: 35888678; PMCID: PMC9315691.

Wong S, Nihal S, Ke DYJ, Neary E, Wu L, Ocean E, Cenkowski M, Grubic N, Pang SC, Johri AM. Lessons Learned from POCUS Instruction in Undergraduate Medicine During the COVID-19 Pandemic. POCUS J. 2023 Apr 26;8(1):81-87. doi: 10.24908/pocus.v8i1.16410. PMID: 37152346; PMCID: PMC10155734.

Soni NJ, Boyd JS, Mints G, Proud KC, Jensen TP, Liu G, Mathews BK, Schott CK, Kurian L, LoPresti CM, Andrus P, Nathanson R, Smith N, Haro EK, Mader MJ, Pugh J, Restrepo MI, Lucas BP. Comparison of in-person versus tele-ultrasound point-of-care ultrasound training during the COVID-19 pandemic. Ultrasound J. 2021 Sep 6;13(1):39. doi: 10.1186/s13089-021-00242-6. PMID: 34487262; PMCID: PMC8419826.

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Russell FM, Kennedy SK, Rood LK, Nti B, Herbert A, Rutz MA, Palmer M, Ferre RM. Design and implementation of a basic and global point of care ultrasound (POCUS) certification curriculum for emergency medicine faculty. Ultrasound J. 2022 Feb 19;14(1):10. doi: 10.1186/s13089-022-00260-y. PMID: 35182232; PMCID: PMC8858359.

"Developing Multiple Choice Questions for the Royal College Certification Examinations” Royal College of Physicians and Surgeons of Canada

Thank you

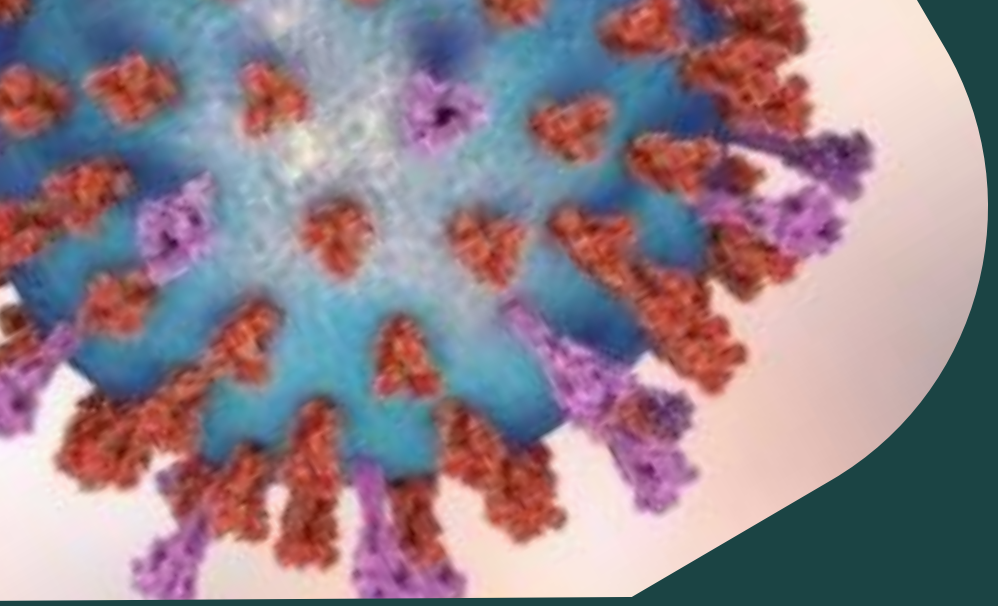
THE UNIVERSITY OF BRITISH COLUMBIA

Department of Pediatrics
Faculty of Medicine

BC Children's Hospital Research Institute

Celebrate Research Day 2024

Dr. Lilian Ping Ling Ngo



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April 12 2024

THE IMPACT OF THE RSV RESURGENCE DURING COVID-19 PANDEMIC ON DISEASE SEVERITY AND THE ROLE OF CO-INFECTION IN INFANTS LESS THAN 6 MONTHS OLD IN BRITISH COLUMBIA, CANADA

Lilian Ngo, Marina Viñeta Paramo, Bahaa Abu-Raya, Frederic Reicherz, Rui Yang Xu, Jocelyn A. Srigley, David M. Goldfarb , Alfonso Solimano , Pascal M. Lavoie

PRESENTED BY

LILIAN NGO PING LING

NEONATAL CLINICAL FELLOW

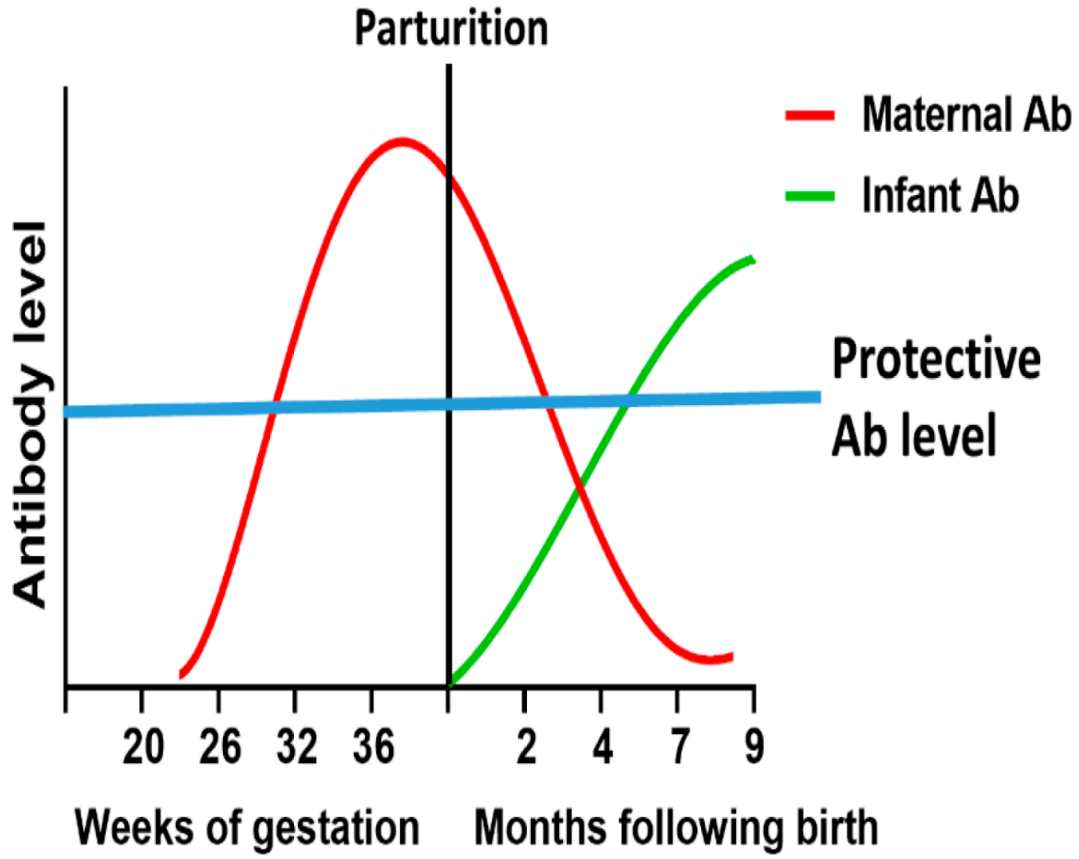
DISCLOSURE

- NONE

BACKGROUND

- The leading cause of lower respiratory tract infections in young children (< 2 years of age, specially < 6 months of age)
- In the absence of RSV exposure, maternal RSV antibodies wane in newborns within 4-6 months
- The lack of RSV circulation during the COVID-19 pandemic has perturbed the seasonality of RSV season
- Role of viral-coinfections remains unclear in the severity of RSV-associated diseases

Reicherz F, J infect Dis (2022)



Crofts, KF et al. 2020

OBJECTIVE

1) Describe the clinical outcomes
2) Explore the role of viral co-infection

…of RSV infections in infants less than 6 months old at BC Children's Hospital

METHODS

Retrospective review of outcomes in infants under 6 months who tested positive for RSV in BC Children's Hospital

September 1st 2017 and May 1st 2023, combining data by year period from Septemb
1st to August 31st each annual period

- Exclude 2020-2021

Hospitalization

- Supplemental oxygen
- ICU admission

Comorbidities

- Prematurity
- Respiratory
- Cardiovascular
- Neurological

Mortality

- RSV related death

TESTING CRITERIA

During the pandemic, since April 2020- Liberal testing with full respiratory panel testing

Latest guideline (Nov 2022)

Extended respiratory NAT panel
COVID, Influenza, RSV, parainfluenza, adenovirus and other viruses and atypical bacterial pathogens

Influenza A/B,RSV, COVID-19

RESULTS

Baseline characteristic

Median age 2M

Average Length of stay 5.1 days

42.5%

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Figure 1

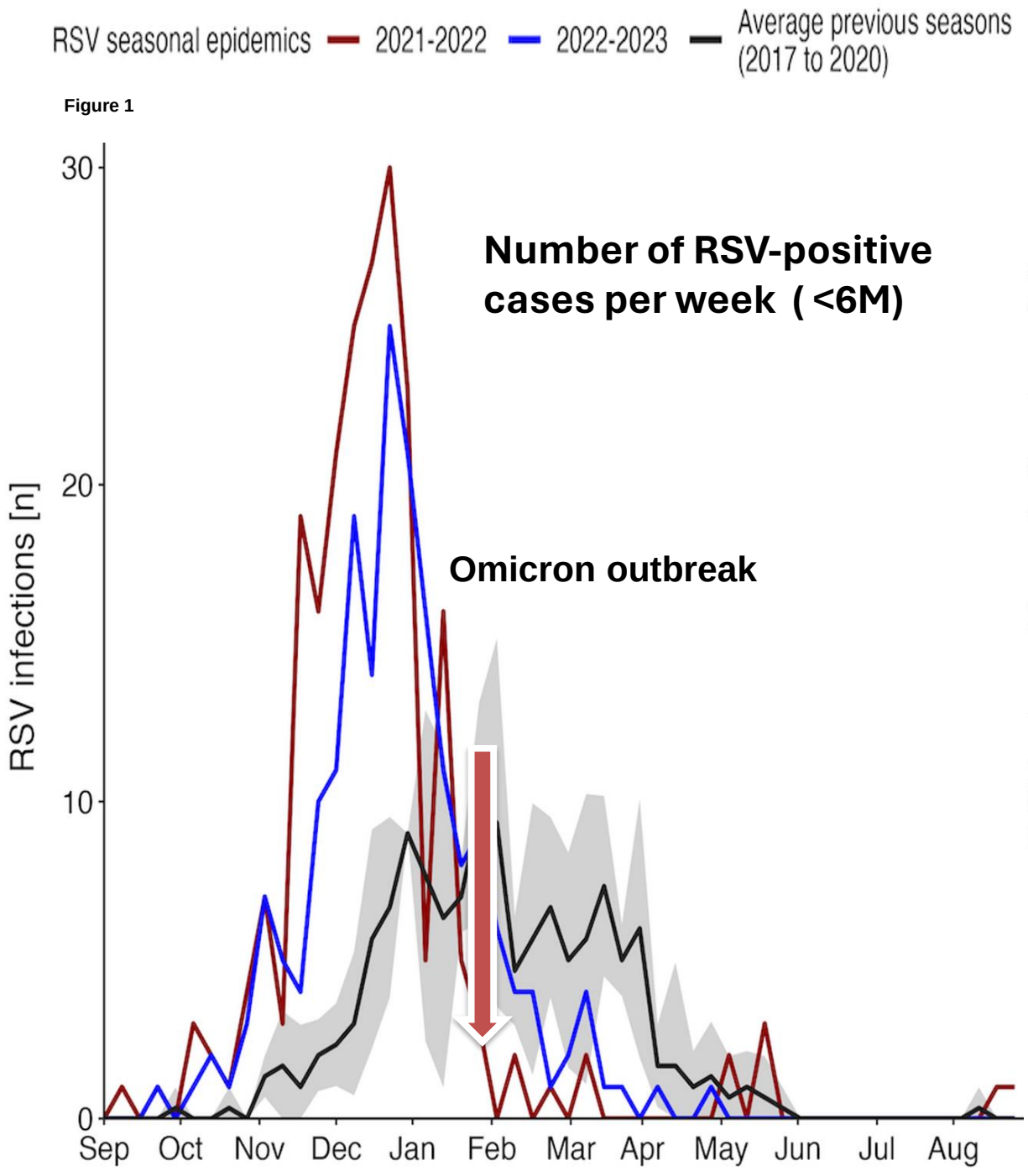
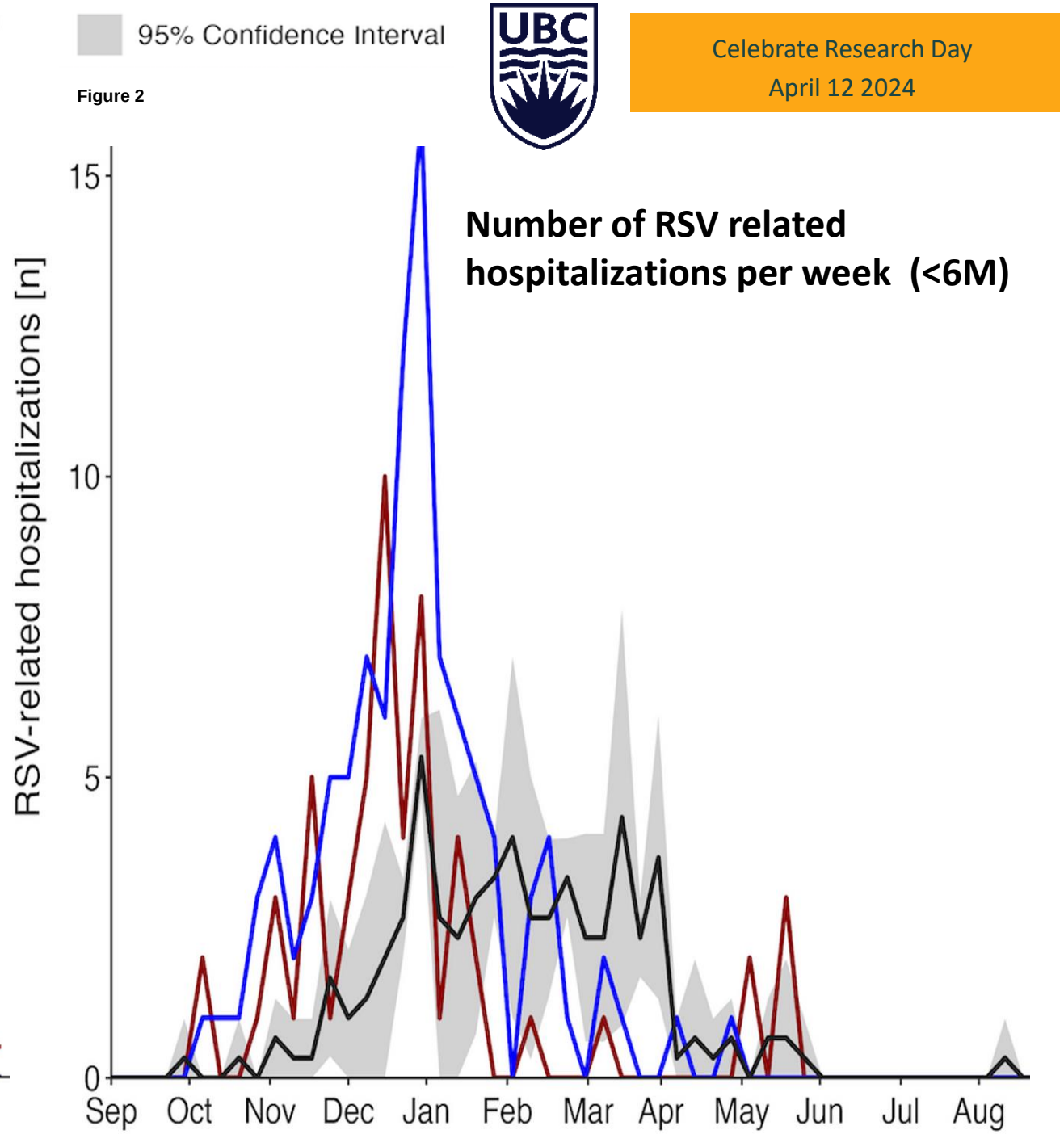


Figure 2



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RESULTS

Table 1: Severity outcome

LIFTING COVID RESTRICTION
2021 SPRING

	2017-18 (N = 159)	2018-19 (N = 136)	2019-20 (N = 104)	2021-22 (N = 241)	2022-23 (N = 224)
Hospitalized, n (%)	**73 (45.9)**	**58 (42.6)**	**52 (50.0)**	**63 (26.1)**	**117 (52.2)**
ICU admission, n (% hospitalized)	**18 (24.7)**	**10 (17.2)**	**13 (25.0)**	**16 (25.4)**	**38 (32.5)**
Supplemental O_2, n (% hospitalized)	**49 (67.1)**	**39 (67.2)**	**39 (75.0)**	**47 (74.6)**	**101 (86.3)**
Mechanical ventilation, n (% hospitalized)	13 (17.8)	1 (1.7)	8 (15.4)	4 (6.3)	12 (10.3)
RSV-related death, n (% hospitalized)	0 (0.0)	2 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)

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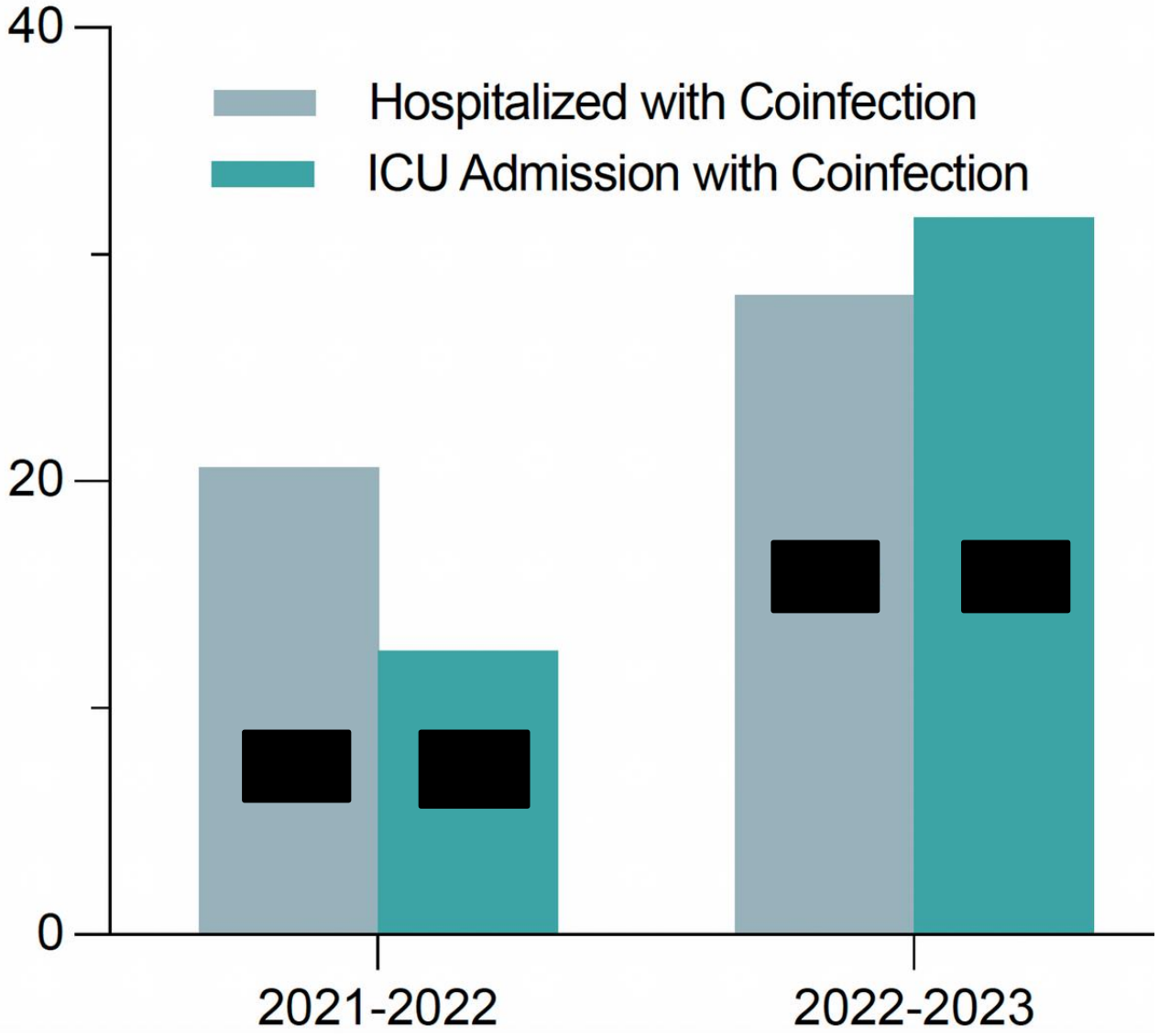
RESULTS

Table 2: Comorbidities

	2017-18 (N = 159)	2018-19 (N = 136)	2019-20 (N =104)	2021-22 (N =241)	2022-23 (N = 224)
Premature <37 weeks GA, n (%)	14(8.8)	12(8.8)	8(7.7)	22(9.1)	16(7.1)
Premature <29 weeks GA, n (%)	0 (0.0)	2 (1.5)	0 (0.0)	2 (0.8)	0 (0.0)
Comorbidity, n (%)	7 (4.4)	9 (6.6)	7 (6.7)	16 (6.6)	10 (4.5)
Cardiovascular, n (%)	1 (0.6)	1 (0.7)	0 (0.0)	8 (3.3)	5 (2.2)
Respiratory, n (%)	2 (1.3)	2 (1.5)	2 (1.9)	2 (0.8)	1 (0.4)

RESULTS

Figure 3 : Viral Coinfection



P value: 0.2667
p-value 0.301, OR: 2.59
95%CI: 0.46-28.19

There is a trend but is statistically insignificant

LIMITATION

- **Differences in testing protocols**
- **Limited sample sizes**
- **Challenges in distinguishing between co-infection and sequential infection**

CONCLUSION

- **BC experienced a surge in RSV cases in 2021-22 followed by an increase in hospitalizations and ICU admissions in 2022-23**

- **The hospitalized cases mainly consisted of term-born infants, who are not eligible for palivizumab prevention in BC**

- **In 2022-23 there was also a notable increase in viral co-infections among ICU-admitted patients, which may have played a role in worsening clinical severity**

FUTURE DIRECTION

- **Maternal RSV vaccination- to prevent RSV infection in this vulnerable population**

REFERENCE

- **Rao, S, Armistead et al (2023). Shifting Epidemiology and Severity of Respiratory Syncytial Virus in Children During the COVID-19 Pandemic. JAMA Pediatrics**
- **Marina VP et al (2023) Respiratory syncytial virus epidemiology and clinical severity before and during the COVID-19 pandemic in British Columbia, Canada: a retrospective observational study**

Q & A ?