9TH ANNUAL
Resident Research Fair



2024

Kingston Health Sciences Centre
Centre des sciences de la santé de Kingston

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Research-at-a-Glance

In this catalogue each division has provided a summary of their research projects which reflects previous, present and future resear. Contact Research Leads within each division to learn how to engage!

Available research projects can be divided into 5 overall catergories:

1. *Clinical Case Studies*
2. *Basic Research*
3. *Literature Outcomes Research*
4. *Clinical Trials Research*
5. *Educational Research*

Message from the Program Director



Dr. Stephen Gauthier

Program Director, Core Internal Medicine Program

The Queen's Internal Medicine (QIM) Training Program aims to train exceptional clinicians who are prepared to respond to the needs of their patients, communities, and society. A key step in achieving this goal is for residents to engage in meaningful and impactful scholarship that advances the science and practice of healthcare.

Within the Department of Medicine, QIM residents are surrounded by passionate and innovative faculty equipped to support and mentor them through the research process. The connections formed through resident research projects form the basis of valued mentorship relationships and research collaborations that last well beyond residency training at Queen's

> ***"By bringing together faculty and residents with similar research interests, the Resident Research Fair serves as a catalyst for productive and meaningful research."***

I would like to thank the Department of Medicine, Translational Institute for Medicine, and our amazing faculty members for supporting residents' research endeavors. I would also like to recognize the hard work, dedication and important role QIM residents play in advancing healthcare through scholarship. The future of Queen's Internal Medicine resident research is bright!

Allergy & Immunology



Dr. Anne Ellis
Division Chair
Research Lead

Summary

- *Analysis of Nasosorption and Sponge Sampling Methods for Nasal Fluid Cytokine Profiling in UpperAirway Disease*
- Reproducibility of the Specialized Particulate Control Environmental Exposure Unit (SPaC-EEU) as a Novel Controlled Cat Dander Exposure Room
- *Serum biomarkers and bacterial carriage in allergen-induced allergic rhinitis models*

Please Note: *The Division of Allergy & Immunology, led by Dr. Anne Ellis, focuses on a dual-themed research program which contains elements of both basic science research and important translational and clinical research. We welcome a collaborative effort to develop a project based on your specific area of interest! In the past, Residents have been able to take advantage of our extensive research participant database, historical study data, and ongoing weekly and monthly clinics, to conduct chart reviews, survey studies, nasal allergen challenges, pilot studies, and other projects based on their goals.*

Poster #643

American Academy of Allergy Asthma & Immunology ANNUAL MEETING WASHINGTON, DC · FEBRUARY 23-26, 2024

Comparative Analysis of Nasosorption and Sponge Sampling Methods for Nasal Fluid Cytokine Profiling in Upper Airway Disease

Abigail Davis, MSc (Candidate)[1,2], **Aliya Guttman**[3], **Lubnaa Hossenbaccus,** PhD (Candidate)[1,2] **Sophia Linton,** PhD (Candidate)[1,2], **Anne K. Ellis,** MD, MSc, FRCPC, FAAAAI[1,2,3]

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Abstract

Rationale: Nasal fluid can be utilized for assessing biological processes of allergic conditions impacting the upper respiratory tract. NASOSORPTION™FX•i (Mucosal Diagnostics) and Merocel® nasal sponges have both been utilized for collecting nasal fluid. To our knowledge, there are no studies directly comparing the two methods.

Methods: Five healthy volunteers were recruited from the Kingston, Ontario region. NASOSORPTION™FX•i was placed against the interior turbinate of one nostril for one minute. Next, a Merocel® sponge was inserted in the middle meatus region of the opposite nostril for 5 minutes. Both samples were processed according to previously published protocols. Measurements of EGF, G-CSF, IL-1rα, IL-6, IL-8, IL-10, IL-12p70, IL-13, IP-10, MCP-1, MIP-1β, and VEGF-A were performed using the MILLIPLEX® Human Cytokine/Chemokine/Growth Factor Panel A Magnetic Bead Panel.

Results: Using the Wilcoxon matched-pairs signed rank test to investigate sponge versus NASOSORPTIONTM^{FX}•i across all cytokines, the observed concentration of cytokines collected with sponge was significantly higher ($p<0.0001$). There were no significant differences ($p>0.05$) found between sponge and NASOSORPTION™FX•i cytokine concentrations when assessing each cytokine individually. Anecdotally, participants preferred the NASOSORPTION™FX•i sampling procedure to the sponges.

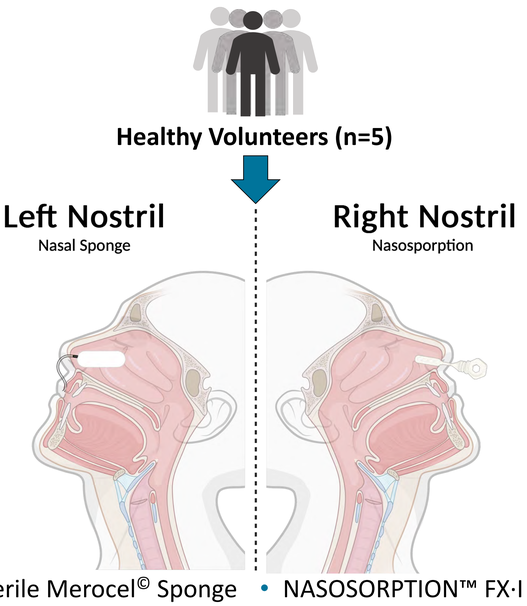
Conclusion: Overall, sponges exhibited higher concentrations of cytokines in nasal fluid than NASOSORPTION™FX•i. When selecting a sampling method, factors such as participant compliance, operator training, desired sample volumes, and serial sampling are also important to consider. Additionally, the region of sampling may influence the secretions and cytokine profiles. Differences between sampling regions should be investigated in future studies.

Background

- The collection of biological samples from the nasal cavity has been critical to study infectious and inflammatory conditions that impact the upper airway (1).
- Several previously published studies have utilized Merocel® sponge (2) and NASOSORPTION™FX•I (3,4) to collect nasal fluid for the investigation of cytokine concentrations in the nose.

Rationale: To our knowledge, there are no studies directly comparing Merocel® sponge and NASOSORPTION™FX•i.

Methods



- Sterile Merocel© Sponge (Medtronic)
- 3.5cm x 0.6cm x 1.2cm
- Middle meatus
- Five minute incubation
- NASOSORPTION™ FX·I
- 0.7cm
- Inferior turbinate
- One minute incubation

Created with Biorender.com

Methods

Merocel® Sponge



- Placed into a sterile elution tube containing 998 uL DPBS with 0.5% (w/v) BSA and 2 uL protease inhibitor
- Sit on ice for 1 hour



Centrifuge at 15,000 g at 4 °C for 15 minutes



Frozen (-80 °C) 2 weeks*

NASOSORPTION™FX•i



- Placed into a sterile elution tube containing 499 uL DPBS with 0.5 % (w/v) BSA and 1 uL protease inhibitor
- Sit on ice for 1 hour



Centrifuge at 3,000 g at 4 °C for 9 minutes



Fresh

Assay:
MILLIPLEX® Human Cytokine/Chemokine /Growth Factor Panel A Magnetic Bead Panel

Instrument:
Bio-Plex 200



Analytes:
EGF, G-CSF, IL-1rα, IL-6, IL-8, IL-10, IL-12p70, IL-13, IP-10, MCP-1, MIP-1β, VEGF-A

*Fresh sponge samples were run, but bead count was < 30, and therefore data is not usable. There was not enough room on the plate to run nasosorption samples frozen.

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Results- Concentration by Sample

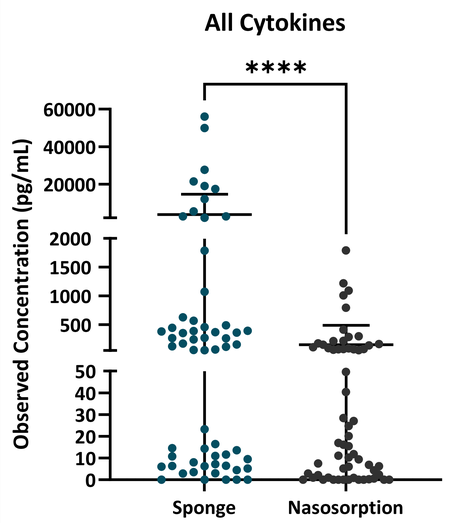


Figure 2. Cytokine concentrations from Merocel© Sponge samples were significantly higher ($p < 0.0001$) than NASOSORPTION™FX•i when grouping all cytokines together (EGF, G-CSF, IL 1rα, IL-6, IL-8, IL-10, IL-12p70, IL-13, IP-10, MCP-1, MIP-1β, VEGF-A) using Wilcoxon matched-pairs signed rank test.

Results- Concentration By Cytokine

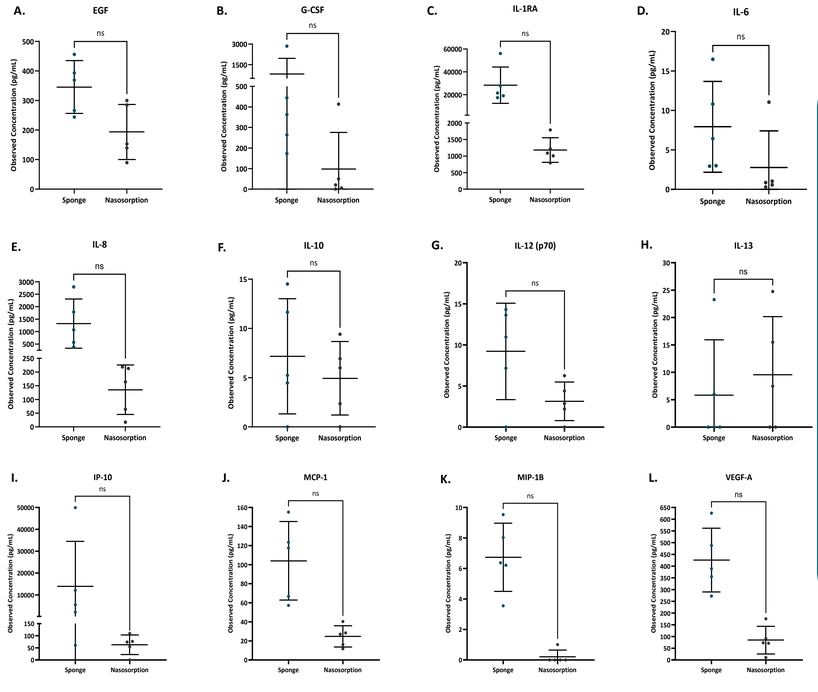


Figure 1. No significant differences were found ($p > 0.05$) between sponge and NASOSORPTION™ FX•i cytokine concentrations when assessing each cytokine individually (A-L) using Wilcoxon matched-pairs signed rank test.

Conclusion

Both Merocel® Sponge and NASOSORPTION™FX•I are suitable nasal fluid collection methods.

- **Method selection should involve a balanced consideration of:**
  - **Anticipated concentrations of analytes**
    - Higher concentrations were detected in Merocel® Sponge than NASOSORPTION™FX•I for most cytokines
  - **Required sample volume**
    - Merocel® Sponge: ~ 800 – 1000 uL
    - NASOSORPTION™FX•I: ~ 300 – 500 uL
  - **Access to trained personnel**
    - Placement of the sponge to the middle meatus requires administration by qualified medical personnel
    - NASOSORPTION™FX•I is placed on the inferior turbinate, which does not require a medically qualified individual
  - **Participant compliance and required collection timepoints**
    - Anecdotally, NASOSORPTION™FX•I was the preferred sample method by participants
    - NASOSORPTION™FX•I may be preferred in protocols with serial sample collection of nasal fluids
- **Cytokine profiles may vary by region of collection in the nose (5).**

References

1. Massey CJ, Diaz Del Valle F, Abuzeid WM, et al. Sample collection for laboratory-based study of the nasal airway and sinuses: a research compendium. Int Forum Allergy Rhinol. 2020;10(3):303-313. doi:10.1002/alr.22510
2. Wu J, Chandra RK, Li P, Hull BP, Turner JH. Olfactory and middle meatal cytokine levels correlate with olfactory function in chronic rhinosinusitis. *Laryngoscope*. 2018;128(9):E304-E310. doi:10.1002/lary.27112
3. Jochems SP, Piddock K, Rylance J, et al. Novel Analysis of Immune Cells from Nasal Microbiopsy Demonstrates Reliable, Reproducible Data for Immune Populations, and Superior Cytokine Detection Compared to Nasal Wash. *PLoS One*. 2017;12(1):e0169805. Published 2017 Jan 20. doi:10.1371/journal.pone.0169805
4. Thwaites RS, Ito K, Chingono JMS, et al. Nasosorption as a Minimally Invasive Sampling Procedure: Mucosal Viral Load and Inflammation in Primary RSV Bronchiolitis. *J Infect Dis*. 2017;215(8):1240-1244. doi:10.1093/infdis/jix150
5. Gokani SA, Espehana A, Pratas AC, et al. Systematic Review of Protein Biomarkers in Adult Patients With Chronic Rhinosinusitis. American Journal of Rhinology & Allergy. 2023;37(6):705-729. doi:10.1177/19458924231190568

Kingston Allergy Research

Kingston Health Sciences Centre
Centre des sciences de la santé de Kingston

Queen's University

Nasal Cytokine Responses Following Ragweed Nasal Allergen Challenge using Nasal Sponges

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BACKGROUND

Allergic rhinitis (AR) is an inflammatory condition that affects the nasal mucosa.

- 15% of Canadian adults are reported to be sensitized to ragweed pollen[1].

The Nasal Allergen Challenge (NAC) is an optimized and validated model of AR developed by the **Allergic Rhinitis Clinical Investigator Collaborative (AR-CIC)**[2].

- Controlled and direct delivery of an individualized concentration of allergen extract into the nasal cavity.

Following NAC, individuals with and without AR exhibit different nasal cytokine responses[3,4].

METHODS

Screening — NAC Visit

Baseline — 6-hours — 24-hours — 48-hours

During a **screening visit**, incremental concentrations of ragweed allergen were administered until each participant achieved a qualifying symptom score. For the subsequent **NAC visit** (21d-28d later), participants were challenged with a single allergen dose cumulative to the amount administered at the screening visit.



Nasal sponges were collected **at 5 different time points**: screening, baseline-NAC, 6-hours after NAC, 24-hours after NAC, and 48-hours after NAC.



The following analytes were measured using **Luminex® xMAP® Technology** and the **Bioplex 200 Analyzer**: IL-1β, IL-4, IL-5, IL-6, IL-10, IL-13, IFN-γ, MIP-1β, MCP-1, RANTES, TNF-α.

Poster #6

Results

SCREENING: Allergic ⟷ Non-Allergic

For the following cytokines: IL-1ß, IL-4, IL-5, IL-6, IL-10, IL-13, IFN-γ, MIP-1ß, MCP-1, RANTES, TNF-α

P > 0.05 (Allergic ⟷ Non-Allergic)
P > 0.05 (Allergic ↕ Non-Allergic)
P > 0.05 (Non-Allergic ↕ Non-Allergic)
P > 0.05 (Allergic ⟷ Non-Allergic)

BASELINE-NAC: Allergic ⟷ Non-Allergic

Figure 1. Schematic of pre-exposure cytokine concentration differences between allergic and non-allergic participants. At the screening visit and Baseline-NAC visit, allergic and control participants had similar concentrations of each analyte (Mann-Whitney test, *P* > *0.05*). No significant differences were found for allergic and control participants when comparing the analyte concentrations between the screening visit and the baseline NAC, respectively (Wilcoxon test, *P* > *0.05*).

6 HOURS AFTER NAC

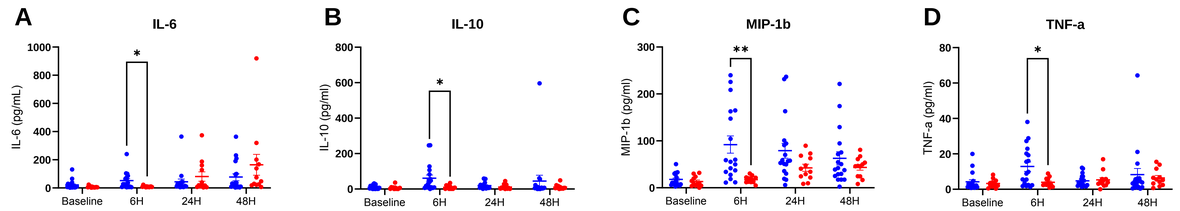
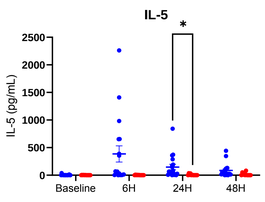


Figure 2. Clinically relevant cytokines are upregulated in the nasal fluid of allergic participants 6 hours after NAC compared to healthy controls. Cytokine concentrations for IL-6 (A), IL-10 (B), MIP-1β (C), and TNF-α (D) were plotted for allergic (blue) and non-allergic (red) participants at Baseline-NAC, 6-hours after NAC, 24-hours after NAC, and 48-hours after NAC. At 6 hours after the NAC, IL-6, IL-10, MIP-1β, and TNF-α were significantly elevated in allergic participants compared to non-allergic participants (2-way ANOVA, Sidak's multiple comparison test, *P* ≤ *0.05*).

24 HOURS AFTER NAC



* P ≤ 0.05; ** P ≤ 0.01; H = hours

Figure 3. Important immunomodulating cytokine, IL-5, is elevated in only allergic participants after challenge. Nasal fluid cytokine concentrations for IL-5 were plotted for allergic (blue) and non-allergic (red) participants at 4 different timepoints. At 24 hours after NAC, the concentration of IL-5 was significantly higher in allergic participants compared the healthy controls (2-way ANOVA, Sidak's multiple comparison test, *P* ≤ *0.05*).

Following an NAC to ragweed, allergic participants exhibit an altered cytokine response in their nasal fluid for up to 24 hours compared to healthy controls.

DISCUSSION

We detected the **majority of the eleven cytokine targets** in nasal secretions, and their changes after NAC.

- IFN-γ and IL-1β concentrations fell below the detection limit in many samples.

Following NAC, an **upregulation of inflammatory** (IL-5, MIP-1β, TNF-α) and **anti-inflammatory** (IL-6, IL-10) cytokines was observed in allergic participants only.

- Consistent with the late phase AR response.
- The 48-hour time point is not a necessary addition to the AR-CIC NAC protocol.

The results of this study are generally in **agreement with previously reported studies**[3,4].

Sponges, as a collection method, provided **greater cytokine recovery** compared to previous studies using Synthetic Absorbent Matrices (SAMs)[4].

- Individual cytokine concentrations, however, were consistent with SAMs.

Future investigations should assess potential correlations between **nasal and serum cytokines responses** following NAC.

- Local nasal eosinophilia and IL-5 correlations should also be assessed.

REFERENCES

1. Chan-Yeung M, Anthonisen NR, Becklake MR, et al. Geographical variations in the prevalence of atopic sensitization in six study sites across Canada. Allergy. 2010;65:1404–13.
2. Ellis, A.K., Soliman, M., Steacy, L. et al. The Allergic Rhinitis – Clinical Investigator Collaborative (AR-CIC): nasal allergen challenge protocol optimization for studying AR pathophysiology and evaluating novel therapies. All Asth Clin Immun 11, 16 (2015). https://doi.org/10.1186/s13223-015-0082-0
3. Scadding GW, Calderon MA, Bellido V, et al. Optimisation of grass pollen nasal allergen challenge for assessment of clinical and immunological outcomes. J Immunol Methods. 2012;384(1–2):25–32. doi: 10.1016/j.jim.2012.06.013.
4. Soliman M, Thiele J, Boulet L-P, et al. Mapping local inflammatory cytokine secretion following a cumulative allergen dose using the Allergic Rhinitis Clinical Investigator Collaborative Nasal Allergen Challenge model. In: Barcelona, Spain; 2015.

Reproducibility of the Specialized Particulate Control Environmental Exposure Unit (SPaC-EEU) as a Novel Controlled Cat Dander Exposure Room

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[1] *Department of Medicine, Queen's University*
[2] *Kingston Allergy Research*

Introduction

Allergic rhinitis (AR) is an inflammatory disease that affects the mucosa of the nose.[1]

20% *of the world's population is affected by cat allergies, the second most common type of perennial AR.[2]*

Felis domesticus allergen 1 (Fel d 1) is the most common allergen that causes cat allergies in humans.[2]

The SPaC-EEU (formerly the House Dust Mite-EEU) is a micro-controlled room within the established EEU in Kingston, Canada, used to study perennial AR.[3,4,5]

Accurate and reproducible clinical models of prolonged cat allergen exposure are limited. We sought to assess the capacity of our SPaC-EEU to accurately and reproducibly distribute cat allergen.

References

[1] Keith PK, Desrosiers M, Laister T, Schellenberg RR, Waserman S (2012) The burden of allergic rhinitis (AR) in Canada: perspectives of physicians and patients. Allergy, Asthma Clin Immunol. https://doi.org/10.1186/1710-1492-8-7
[2]Satyaraj E, Wedner HJ, Bousquet J. Keep the cat, change the care pathway: A transformational approach to managing Fel d 1, the major cat allergen. *Allergy*. 2019;74(Suppl 107):5-17. doi:10.1111/all.14013
[3] Walker TJ, Steacy LM, Ellis AK (2017) Preliminary Proof of House Dust Mite Distribution Capability in the Environmental Exposure Unit. J Allergy Clin Immunol 139:AB119
[4] Hossenbaccus L, Linton S, Thiele J, et al. Clinical validation of controlled exposure to house dust mite in the environmental exposure unit (EEU). *Allergy Asthma Clin Immunol*. 2021;17:34. doi:10.1186/s13223-021-00536-3
[5] Hossenbaccus L, Linton S, Thiele J, et al. Biologic Responses to House Dust Mite Exposure in the Environmental Exposure Unit. *Front Allergy*. 2022;2:807208. doi:10.3389/falgy.2021.807208

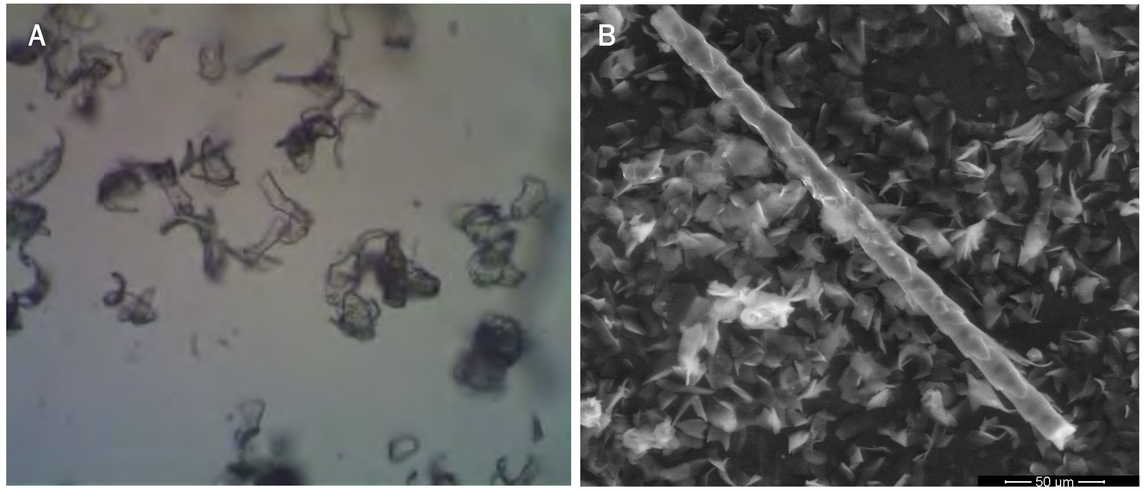


Figure 1. Microscopy images of cat dander product. The cat dander product distributed in the SPaC-EEU was visualized using light microscopy (A) and scanning electron microscopy (B; 526x magnification). It consisted of particles of various sizes, including cat hair, hence the Fel d 1 allergen is not visibly identifiable. As a result, a Fel d 1-specific ELISA was used to accurately quantify the concentration of allergen distributed in the SPaC-EEU from sampling cassettes.

Across **5** independent test runs, the SPaC-EEU showed **consistent Fel d 1 concentrations** and **total particle counts**.

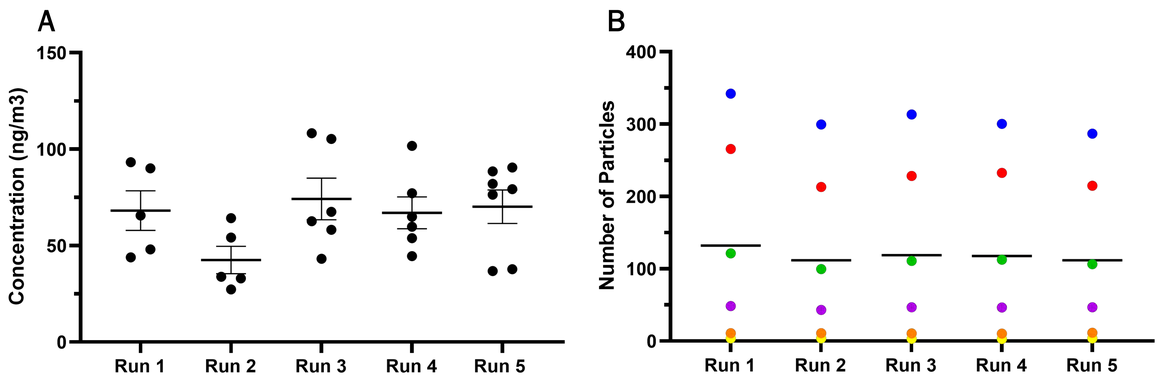


Figure 2. No significant differences were observed in Fel d 1 concentration (ng/m^3) and total particle counts across repeated trials in the SPaC-EEU. Five independent runs showed statistically similar concentrations of Fel d 1 (A; p=0.1735) and particle counts (B; p=0.9871). The average Fel d 1 concentrations ranged between 42.48 to 74.15 ng/m3, while mean particle counts ranged from 111.5 to 132.0 particles, with 2.5 µm particles being the most prevalent (C). ● 2.5 um ● 5.0 um ● 10.0 um ● 15.0 um ● 20.0 um ● 25.0 um

Methods

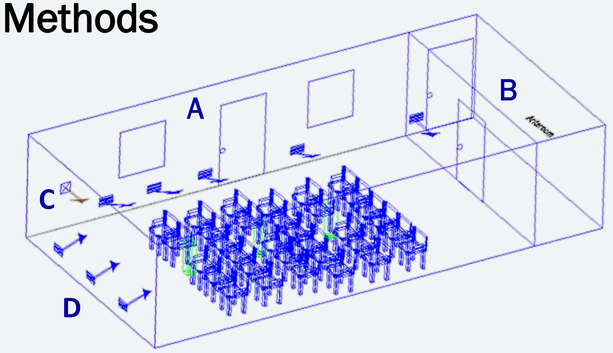
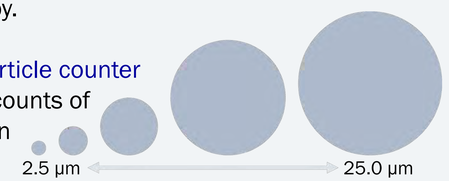


Figure 3. Rendering of the SPaC-EEU. The SPaC-EEU consists of a central room (A), which can seat up to 30 participants, and an anteroom (B), to buffer the effects of exiting. The influx of allergen is regulated through the feeder (C) located near the front. Floor-level airflow registers (D) are distributed throughout the room to disperse the allergen. Sampler locations are identified in green.

Cat dander (Greer®, USA) was distributed in the SPaC-EEU over 2-hour exposure periods and visualized using light and scanning electron microscopy.

A laser particle counter reported counts of particles in real-time.





Sampling cassettes (Zefon International, USA) were used to sample the distributed air.

Fel d 1 concentrations were assessed using a Fel d 1-specific enzyme-linked immunosorbent assay (Indoor Biotechnologies, USA).



Summary & Future Directions

The SPaC-EEU is a reproducible and reliable model of cat dander exposure.

Following this successful technical validation, next steps involve performing a clinical validation of the facility with human participants.



Poster #327

MICR 499
Guttman
042

Effects of Fel d 1 Exposure in the SPaC-EEU on Cytokine Levels in Cat-Allergic and Non-Allergic Individuals

Aliya Guttman[1,2], Lubnaa Hossenbaccus[2,3], Dr. Anne K. Ellis[1,2,3]

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Background

> 400 million people worldwide suffer from allergic rhinitis (AR).[1]

7-25% of the global population has cat allergen-induced AR.[2]

Fel d 1 → the major cat allergen

- Ubiquitous in homes and public spaces, regardless of cat presence.[2]
  - **Pervasive impact on Fel d 1-allergic individuals**
- Current management strategies for Fel d 1-induced AR are limited to avoidance-based management and nonspecific pharmacotherapy.[2,3,4]

- The Specialized Particulate Control Environmental Exposure Unit (SPaC-EEU) is an allergen exposure chamber located at Kingston General Hospital.
  - Previously validated for use with house dust mite, birch, and grass pollen, and since has had extensive use.[5-9]
  - **Important tool for analyzing biological outcomes of allergen exposure**

Serum cytokine levels in response to Fel d 1 exposure in an EEU have been studied before, but not extensively.[10,11]

Objectives

1. To assess the serum cytokine levels in cat-allergic individuals compared to non-allergic controls upon exposure to Fel d 1 in the SPaC-EEU
2. To compare the levels of serum cytokines at each timepoint.
3. Explore relationships between individual cytokines in response to allergen exposure

Methodology

Screening of participants for study qualification
Screening sampling

↓

Study Visit

1. **Baseline sampling**
2. 3-hour long Fel d 1 exposure in the SPaC-EEU
3. **3-hour timepoint sampling**
4. **6-hour timepoint sampling**
5. Follow-up visit (24 hours post exposure): **follow-up sampling**

↓

Serum Cytokine Analysis

Assays: MILLIPLEX® Human Cytokine/Chemokine/Growth Factor Panel A Magnetic Bead Panel, MILLIPLEX® Human Cytokine/Chemokine/Growth Factor Panel B Magnetic Bead Panel

Analytes: IL-4, IL-5, IL-10, IL-13, IL-17E/IL-25, MCP-1, MIP-1ß, eotaxin (Panel A); IL-33 (Panel B)

Instrument: Bio-Plex 200 (with Luminex xMAP technology)

Results

Participant Cytokine Levels: Screening versus Baseline Timepoints

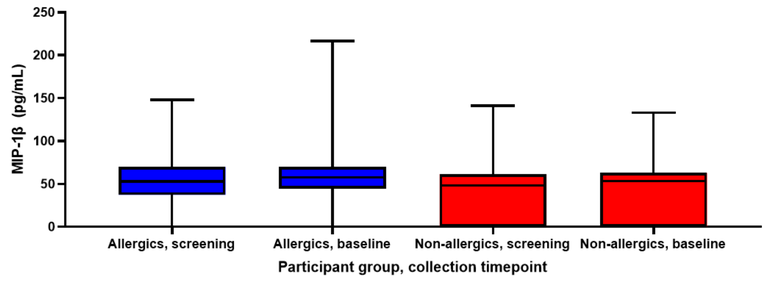


Figure 1. No significance was observed between screening and baseline MIP-1ß concentrations in both Fel d 1-allergic participants and non-allergic controls. A Kruskal-Wallis test was used to determine significance ($p < 0.05$) between screening and baseline cytokine levels. $p < 0.4698$.

Participant Cytokine Levels: Exposure Timepoints

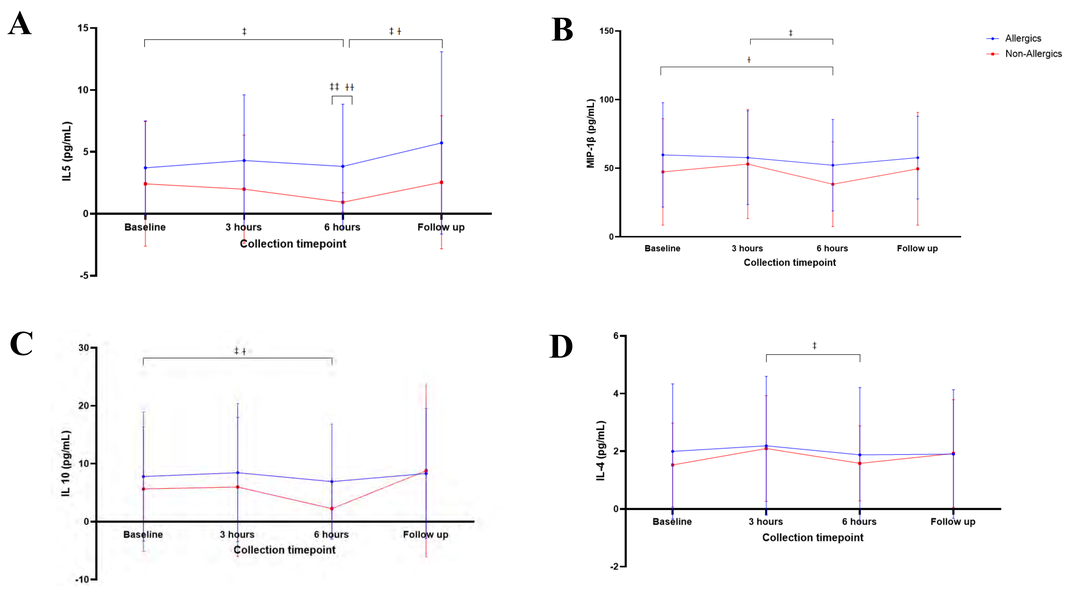


Figure 2. Cytokine concentrations were significant between Fel d 1-allergic versus non-allergic controls, and between baseline, 3 hour-, 6 hour-, and follow-up serum collection timepoints. (A) IL-5, (B) MIP-1ß, (C) IL-10, and (D) IL-4. Mixed-effects analyses with Tukey's multiple comparisons tests were performed to determine significance between the means of the allergic and non-allergic participant cytokine levels over time. Significance in allergics was represented by ǂ , and significance in non-allergics was represented by ‡. ǂ /‡ = $p < 0.05$. ǂǂ / ‡ ‡ = $p < 0.01$.

Correlations between Related Cytokines

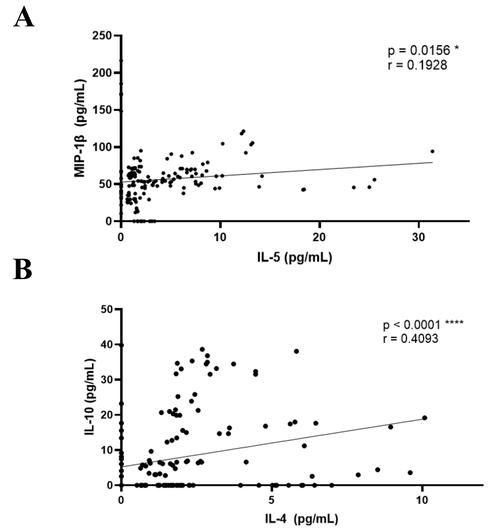


Figure 3. A significant positive correlation was observed between (A) IL-5 and MIP-1ß concentrations ($p < 0.05$) and between (B) IL-4 and IL-10 concentrations at all timepoints. Correlation analyses were completed on the cytokine pairs. The line of best fit was created with a simple linear regression. (A) Slope of the line of best fit = 0.8402. (B) Slope of the line of best fit = 1.355. * = $p < 0.05$, **** = $p < 0.0001$.

Conclusions

- Cytokine levels were not significantly different in screening compared to baseline collection timepoints, suggesting no significant day-to-day changes in their levels.
- Cytokine concentrations in both allergic and non-allergic participants changed significantly over various timepoints during and after Fel d 1 exposure
- Significant correlations between physiologically related cytokines were present.

Changes in cytokine concentrations may be interrelated and dependent on allergic status and time post allergen exposure for Fel d 1-induced AR.

Acknowledgements

I would like to extend my sincerest gratitude for the support of my supervisor, Dr. Anne K. Ellis throughout this project. I would also like to thank Lubnaa Hossenbaccus for sharing her expertise and knowledge with me.

References

Cardiology



Dr. Damien Redfearn
Division Chair



Dr. Wael Abuzeid
Research Lead

Summary

- *Combining intraplaque neovascularization with risk stratification by carotid stress ECHO*
- *Improving management and outcomes for patients requiring admission for heart failure*
- *Expanding point-of-care ultrasound training to remote health care providers*
- *Gender-based differences in POCUS use in the emergency department*
- *Assess successful transcatheter mitral valve repair*
- *Creation of a structural heart disease database by examine the effects of intertribal block as predictive for atrial fibrillation patients*
- *Improving TAVI workflow and reducing waitlist time for TAVI*
- *Heart Failure & Chronic obstructive pulmonary disease Integrated Care Pathways*

Division of Cardiology

Resident Research Fair

Introduction

- Research ideas and projects available across various subspecialties in Cardiology
  - Cardiovascular Imaging (CINQ)
  - Cardiovascular Institute for Research at Queens (CIRQ)
    - Interventional Cardiology
    - Interventional Electrophysiology
    - Heart failure

Introduction

- Reviews
- Retrospective studies
- Quality Improvement
- Administrative health database studies
- Clinical trials

Division of Cardiology
Current Opportunities for Residents

The Cardiovascular Imaging Network (CINQ) is a centre for cardiovascular research, clinical practice, and medical training in advanced cardiac and vascular ultrasound imaging techniques. We offer opportunities for residents to explore research projects in a dynamic and busy research environment. Here are current ongoing research programs at our centre and opportunities to join our team.

www.CINQLab.com

Director of CINQ: Dr. Amer Johri
amerschedule@gmail.com

CINQ Research Manager: Marie-France Hétu, PhD
cinq.research@gmail.com

CIRCE

Combining Intraplaque Neovascularization with Risk Stratification by Carotid Stress Echo (The CIRCE Study)

Stress echo (SE) is one of the most accessible tests used to select patients for angiography, but suffers from moderate sensitivity and specificity for cardiovascular (CV) outcomes. Plaques can be assessed by intraplaque neovascularization (IPN), which occurs in response to hypoxia or inflammation within the lesion. IPN occurs when vessels grow from the vasa vasorum into the lesion, resulting in a fragile and leaky network at risk of rupture and hemorrhage. This is a prospective, parallel, 6-centre study assessing IPN+ SE in 1500 consecutive outpatients referred for SE. Patients will be recruited from KGH , the Kingston Heart Clinic, Dalhousie, Calgary, Toronto, and RUMC (Chicago).

Project opportunity: Working with CINQ, there are opportunities to be involved in patient recruitment in the echo lab and carotid ultrasound image analysis.

PRIME-POCUS

Primary Prevention through Risk prediction Improvement of Major Cardiovascular Events Using POCUS.

The proposed project introduces a novel protocol enabling primary care providers to perform carotid ultrasound using handheld devices for point-of-care-ultrasound (POCUS). This study aims to assess the feasibility of integrating this protocol into primary care clinic workflow to detect subclinical atherosclerosis in statin naïve asymptomatic patients. We will evaluate whether POCUS influences physician care strategies particularly in decision-making regarding medications and testing. Additionally, we will investigate changes in patient behaviour following POCUS, focusing on adherence to physician recommendations regarding lifestyle modifications, smoking cessation, and medication compliance after visualizing their plaque.



Project opportunity: Working with CINQ, there are opportunities to be involved in healthcare provider and patient recruitment with the Queen's family health team.

POCUS Journal

POCUS Journal is a resource for the latest information and case studies on point of care ultrasound, written by physicians, researchers, and educators.

Project opportunity: Get involved in running and managing the journal, become an integral part of the reviewing committee, or manage the social media account.

POCUS Journal

ARCTICA Modules (https://arcticapocus.com)



We have a dedicated e-learning platform that we host POCUS teaching and training modules. We are looking to add new modules. If you are interested in creating a teaching module, please reach out to us!

Interventional Cardiology – Structural Heart

Research lead: Wael Abuzeid

1. Determinants of successful Transcatheter Mitral Valve repair: This is a research topic utilizing administrative health databases in Ontario to examine the effect of several clinical variables on patients undergoing transcatheter mitral valve repair

Project opportunity: Involvement in data and statistical analysis and presentation of findings in abstract/oral and manuscript forms

2. Structural heart disease database: This will involve setting up a database of all patients undergoing structural interventions and allowing us to study outcomes and factors affecting success locally.

Project opportunity: examining the effect of interatrial block (ECG finding) as predictive for Atrial fibrillation patients

Interventional Cardiology – Structural Heart

Research lead: Wael Abuzeid

3. The role of Machine learning in prediction of Structural heart disease outcomes

Project opportunity: Involvement in data and statistical analysis and presentation of findings in abstract/oral and manuscript forms

4. The role of serum biomarkers including BNP in prediction of Structural heart disease outcomes – Systematic Review and metanalysis

Project opportunity: Involvement in data collection, data analysis, writing reviews and editorials

Interventional Cardiology – Coronary

Research lead: Wael Abuzeid

1. Systematic review on the variability of definition of high risk PCI and CHIP patients

Project opportunity: Involvement in data collection, data analysis, writing reviews and editorials

2. Systematic review on the effect of gender on outcomes in patients presenting with SCAD.

Project opportunity: data collection, data analysis, writing reviews and editorials

Interventional Cardiology – Coronary

Research lead: Wael Abuzeid

3. Vanguard and pilot registry on contemporary incidence LV thrombus in STEMI patients and treatment strategy (dual vs triple therapy for anticoagulation)

Project opportunity: Involvement in data collection, data analysis, presentation

4. A comparison of efficacy of LV ventriculography and echocardiography in patients post inferior myocardial Infarction

Project opportunity: data collection, data analysis, presentation

Interventional Cardiology – Abstracts accepted for presentation at AHA November 2024

Association of renal function with mortality and heart failure hospitalization rates after Transcatheter Mitral Valve Edge to Edge Repair

Wael Abuzeid, Ethan Sacoransky, Andrew Czarnecki, Danny Ke, Carolyn Teng, Prasham Dave, Mark Osten, Brigita Zile, Xuesong Wang, Mony Shuvy, Warren Cantor, Shamir R. Mehta, Neil Fam, Husam Abdel-Qadir

Background

- Transcatheter edge to edge repair (TEER) is an established treatment for patients with symptomatic severe functional MR on optimal medical therapy or severe symptomatic primary MR and high surgical risk. Renal dysfunction is associated with adverse outcomes but the threshold at which risks rise are uncertain.

Methods

- This was a population-based retrospective cohort study using linked administrative datasets of patients who underwent TEER in Ontario, Canada, between 2011 and 2023. The key exposure was eGFR, which was modeled using restricted cubic splines. Outcomes were 1-year mortality, cardiovascular mortality (CV) and heart failure hospitalization (HF). Cause-specific hazards regression was used to model the association between eGFR and outcomes, utilizing eGFR 30ml/min/1.73m2 as the reference value.

Association of renal function with mortality and heart failure hospitalization rates after Transcatheter Mitral Valve Edge to Edge Repair

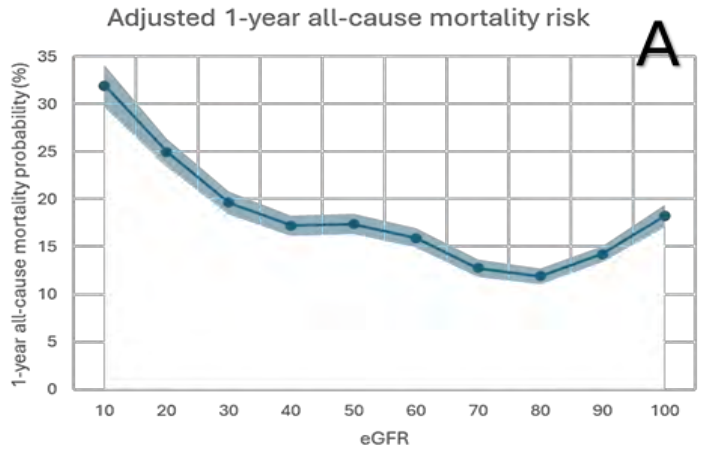
Wael Abuzeid, Ethan Sacoransky, Andrew Czarnecki, Danny Ke, Carolyn Teng, Prasham Dave, Mark Osten, Brigita Zile, Xuesong Wang, Mony Shuvy, Warren Cantor, Shamir R. Mehta, Neil Fam, Husam Abdel-Qadir

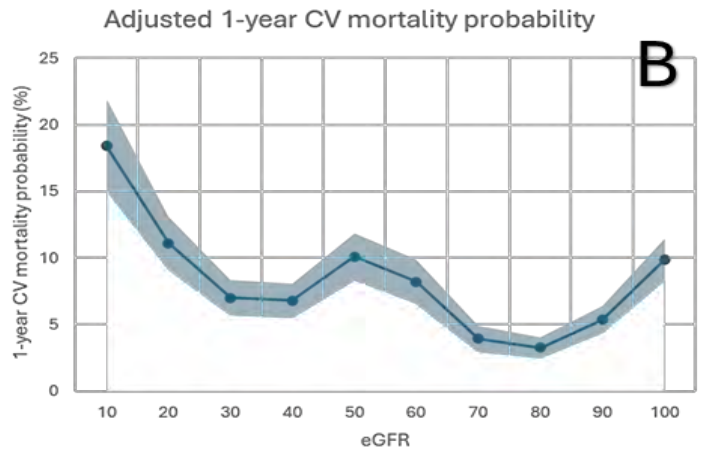
Results

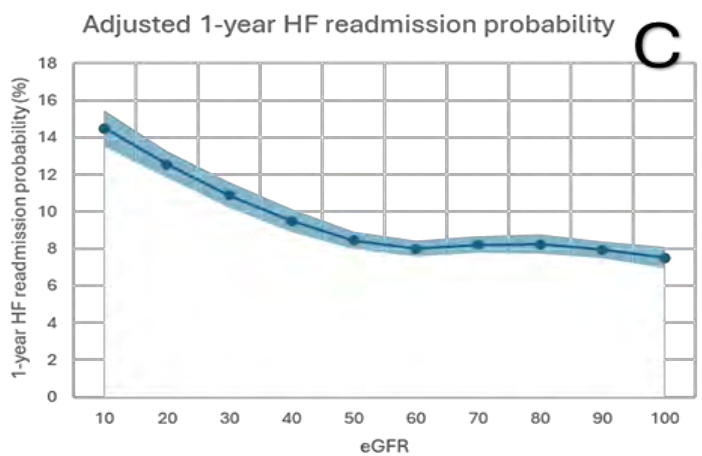
- We studied 2076 patients, of whom 294 (14.2%) had eGFR <30ml/min/1.73m2 and 841 (40.5%) had eGFR 30-60ml/min/1.73m2. The incidence at one year was 16.8% for all-cause mortality, 3.9% for cardiovascular mortality, and 14.2% for HF hospitalizations. The Figure illustrates that the predicted incidence of adverse outcomes increases with lower eGFR, with subtle differences in patterns of change in risk at lower eGFR levels such that all-cause mortality and cardiovascular begin to rise rapidly at eGFR values ≤30ml/min/1.73m2, while HF hospitalization increases linearly at eGFR ≤50ml/min/1.73m2.

Conclusions

- There was a progressive increase in all-cause, CV mortality and HFR hospitalization after TEER for patients with lower eGFR, particularly those with values <30 ml/min/1.73m2. These data can inform patient selection for TEER.


Adjusted 1-year all-cause mortality risk
A
1-year all-cause mortality probability (%)
0
5
10
15
20
25
30
35
10
20
30
40
50
60
70
80
90
100
eGFR


Adjusted 1-year CV mortality probability
B
1-year CV mortality probability (%)
0
5
10
15
20
25
10
20
30
40
50
60
70
80
90
100
eGFR


Adjusted 1-year HF readmission probability
C
1-year HF readmission probability (%)
0
2
4
6
8
10
12
14
16
18
10
20
30
40
50
60
70
80
90
100
eGFR

Machine Learning Predicts Successful Transcatheter Mitral Valve Edge to Edge Repair: A Systematic Review and Meta-Analysis

Ethan Sacoransky[1], Danny Yu Jia Ke[1], Wael Abuzeid[1,2]

Introduction: Transcatheter Mitral Valve Edge to Edge Repair (TEER) is an established percutaneous treatment for patients with severe symptomatic Mitral Regurgitation (MR). The current AHA/ACC guidelines recommend TEER for inoperable patients with severe primary MR or patients with symptomatic severe secondary MR despite medical therapy. Machine learning (ML) has emerged as a tool for TEER risk stratification due to the paucity of established risk scores. To address the lack of consensus on its efficacy, we conducted a systematic review and meta-analysis of studies that utilized ML to predict the success of TEER.

Methods: Electronic databases, including Embase, MEDLINE, and the Cochrane Library, were searched from inception through April 2024. We included studies that used TEER and employed at least one ML model to predict the success of TEER. The Area Under the Receiver Operating Characteristic Curve (AUC) was used to measure the accuracy of ML risk stratification algorithms.

Machine Learning Predicts Successful Transcatheter Mitral Valve Edge to Edge Repair: A Systematic Review and Meta-Analysis

Ethan Sacoransky[1], Danny Yu Jia Ke[1], Wael Abuzeid[1,2]

Results: 102 publications were screened, with seven eventually included in this analysis. Two studies employed clustering techniques, two utilized extreme gradient boosting, and three used multiple ML algorithms to predict outcomes. Of the four studies that compared the accuracy of ML with traditional Cox regression, all four demonstrated higher accuracy with ML, and this difference was statistically significant in three of the four studies. The mean AUC of the aggregated ML data was 0.737 [95% CI: 0.717, 0.758], compared to 0.627 [95% CI: 0.600, 0.653] for the pooled traditional methods.

Conclusions: To our knowledge, we conducted the first systematic review and meta-analysis of ML methods for prediction of TEER success. ML outperformed established risk scores, demonstrating promising potential. Future ML models, trained on larger patient datasets, may further improve predictive accuracy in this patient population.

Elevated Pre-Procedural Serum Natriuretic Peptide Levels Are Associated with All-Cause Mortality in Patients Undergoing Transcatheter Edge-to-Edge Mitral Valve Repair: A Systematic Review and Meta-Analysis

Edward Cui, Annie Hung, Grace Ko, Holly Cheung, Andrew Day, Patrick Norman, Wael Abuzeid

Background: Transcatheter edge-to-edge mitral valve repair (TEER) is an established procedure in patients with severe mitral regurgitation (MR) and elevated surgical risk on optimal medical therapy. However, there remains considerable mortality in this patient population. Some studies have shown that serum brain natriuretic peptide (BNP) and N-terminal pro b-type natriuretic peptide (NT-proBNP) predict all-cause mortality after TEER, whereas other studies have shown mortality to be independent of these markers. To address this gap in knowledge, we sought to examine the existing literature to determine whether there is an association between pre-procedural serum natriuretic peptides and mortality after TEER.

Methods: Databases including MEDLINE, Embase, and Cochrane Library were searched from inception through September 2023 for studies assessing pre-procedural serum natriuretic peptide levels and mortality among patients undergoing TEER. Pooled hazard ratios (HR) and standardized mean differences (SMD) were calculated using a random-effects model estimated by restricted maximum likelihood with the Hartung-Knapp modification.

Elevated Pre-Procedural Serum Natriuretic Peptide Levels Are Associated with All-Cause Mortality in Patients Undergoing Transcatheter Edge-to-Edge Mitral Valve Repair: A Systematic Review and Meta-Analysis

Edward Cui, Annie Hung, Grace Ko, Holly Cheung, Andrew Day, Patrick Norman, Wael Abuzeid

Results: A total of 30 studies comprising 10259 patients undergoing TEER met inclusion criteria. 25 studies measured NT-proBNP and 5 studies measured BNP. Elevated pre-procedural NT-proBNP (>5000 or >10000 pg/mL) was associated with increased all-cause mortality in both adjusted (HR = 2.94; 95% CI = 1.75 - 4.95; I^2 = 46.8%) and unadjusted (HR = 5.16; 95% CI = 1.85 - 14.40; I^2 = 0.0%) analyses (Figures 1 and 2). Pre-procedural BNP and NT-proBNP were also significantly lower among survivors at 12 months compared to non-survivors (SMD = 0.82; 95% CI = 0.37 - 1.27; I^2 = 78.3%) (Figure 3). This association was demonstrated in patients with primary or secondary MR.

Conclusions: Pre-procedural BNP and NT-proBNP levels are significant predictors of all-cause mortality in patients undergoing TEER for primary or secondary MR. This supports the inclusion of BNP or NT-proBNP in pre-procedural assessments to help inform patient discussions and guide post-procedural follow-up and monitoring.

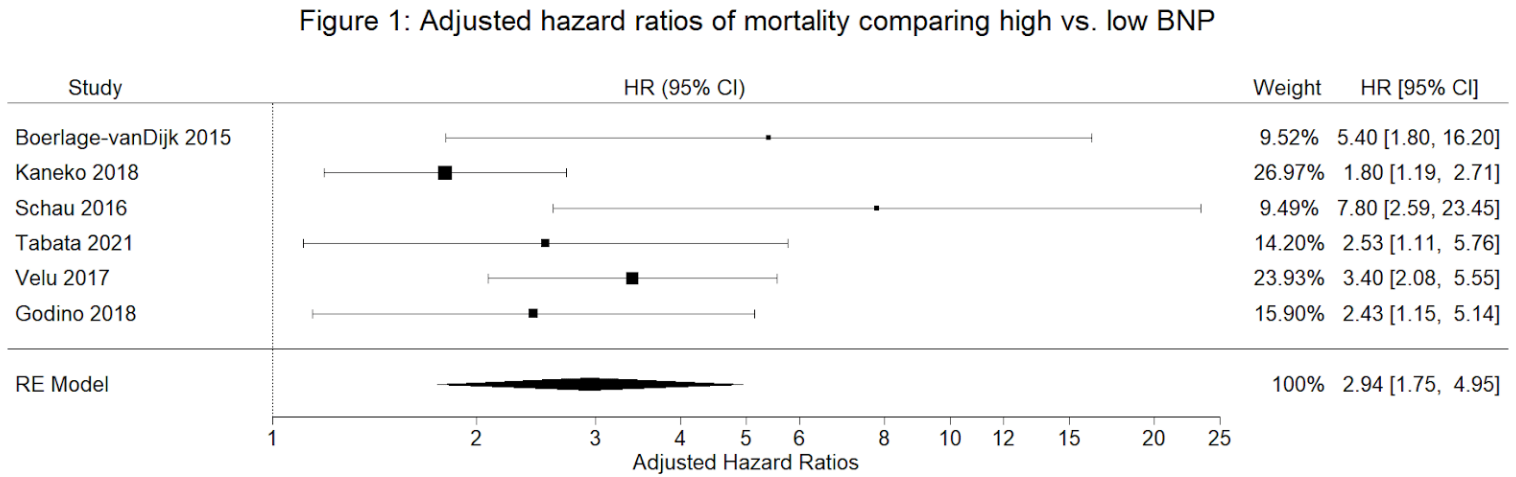


Figure 1: Adjusted hazard ratios of all-cause mortality comparing high and low pre-procedural NT-proBNP

Interventional Cardiology – Clinical Trials

- Participation in multiple RCT Clinical trials on a national and international scale and opportunity to be involved in patient recruitment

Interventional Cardiology – QI

- Improving TAVI workflow and reducing waitlist time for TAVI
- Increasing number of radial coronary angiography cases performed

Heart Failure

- Research lead: Aws Almufleh

1. ACCELERATE-HF: Prospective clinical study examining the effectiveness HF decision aids and POCUS in reducing readmission rates for HF patients
2. Systematic review on “Gender-based differences in POCUS use in the emergency department”.

Projects opportunity: Patient recruitment, data collection, data analysis, writing reviews and editorials

Heart Failure II

- Research lead: Aws Almufleh

3. Systematic review “Do outcomes differ in heart failure managed by primary care physicians vs specialists?”
4. Improving heart failure outcomes via implementing a heart failure management pathway for primary care physicians in Kingston; a quality improvement project

Projects opportunity:

For the systematic review: Screening studies, data extraction, writing reviews, metanalysis. and editorials

For the QI project: Designing HF management pathway for primary care, reviewing health metrics.

Heart Failure III

- Research lead: Aws Almufleh

5. Cardiac Amyloid Project “Local registry of patients suspected or diagnosed with cardiac amyloidosis?”
6. HF Discharge Project “Local registry of HF clinic patients; aimed at investigating barriers to successful discharge from HF clinic”
7. Predictors and outcomes of HF diagnosed in the community compared with acute care settings (ICES)

Projects opportunity:

Data collection, data analysis, literature review, and writing manuscript

Heart Failure (and Echo) IV

- Research lead: Aws Almufleh

8. Case-based Simulation of HF Diagnosis and Management; the Heart Success App.
9. Building a point-of-care risk communication tool to improve perioperative risk estimation and mitigation for heart failure patients undergoing non-cardiac surgery
10. The Canadian Echocardiography Competency Evaluation and Optimization Project

Projects opportunity:

Data collection, patient recruitment, data analysis, literature review, and manuscript writing

Outcomes in Heart Failure Patient Management by Primary Care Providers Compared With Cardiologists; A Systematic Review and Meta-Analysis

Tereza Florica, Alex Van, Drew McLean



Outcomes in Heart Failure Patient Management by Primary Care Providers Compared with Cardiologists; a Systematic Review and Meta-Analysis

Tereza Florica, Alex Van, Drew McLean, Amanda Ross-White, Morgan Slater, and Aws Almufleh

Heart failure (HF) is a global pandemic, associated with substantial resource utilization and healthcare costs. While the incidence of HF is stable, prevalence is increasing due to advances in medical therapy and improved life expectancy. Specialists do not have the capacity to manage all heart failure patients and thus most healthcare systems depend on primary care practitioners. HF outcomes for patients solely followed by primary care practitioners have not been well studied. We herein aim to evaluate differences in outcomes in patients with HF managed by cardiologists compared with primary care practitioners.

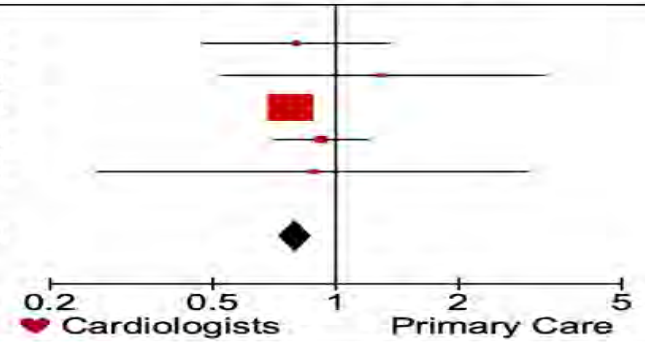
We conducted a systematic review of studies (observational and experimental) of adults receiving outpatient HF care by cardiologists compared with primary care providers. Outcomes included all-cause deaths, HF/cardiovascular disease deaths, HF hospitalization, readmissions rates, emergency department visits, and rates of HF medication use. We searched Embase, Cochrane Central Register, PubMed, and Web of Science for studies published 1946 to April 2023.

2024 Canadian Cardiovascular Congress
October 24-27, 2024
Vancouver, BC

All Cause Deaths

Study or Subgroup	log[RR]	SE	Weight	Risk ratio IV, Random, 95% CI
Ansari 2003	-0.223144	0.271053	2.5%	0.80 [0.47 , 1.36]
Diller 1999	0.262364	0.466718	0.8%	1.30 [0.52 , 3.24]
Indridason 2003	-0.256183	0.04609	86.5%	0.77 [0.71 , 0.85]
Lee 2010	-0.083382	0.137502	9.7%	0.92 [0.70 , 1.20]
Sakakibara 1999	-0.127833	0.622205	0.5%	0.88 [0.26 , 2.98]
Total (95% CI)			**100.0%**	**0.79 [0.73 , 0.86]**

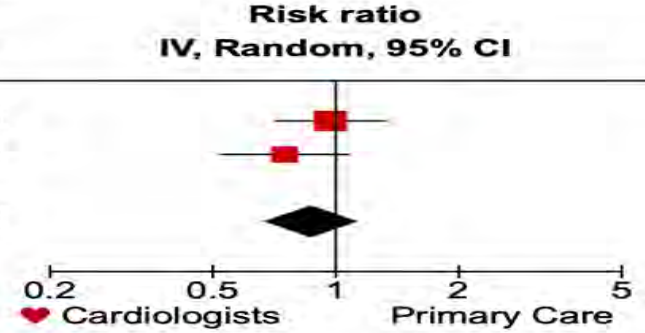
Heterogeneity: Tau² = 0.00; Chi² = 2.59, df = 4 (P = 0.63); I² = 0%
Test for overall effect: Z = 5.45 (P < 0.00001)
Test for subgroup differences: Not applicable



Heart Failure Re-Admissions

Study or Subgroup	log[RR]	SE	Weight	Risk ratio IV, Random, 95% CI
Ansari 2003	-0.030459	0.160123	56.9%	0.97 [0.71 , 1.33]
Diller 1999	-0.287682	0.186454	43.1%	0.75 [0.52 , 1.08]
Total (95% CI)			**100.0%**	**0.87 [0.68 , 1.11]**

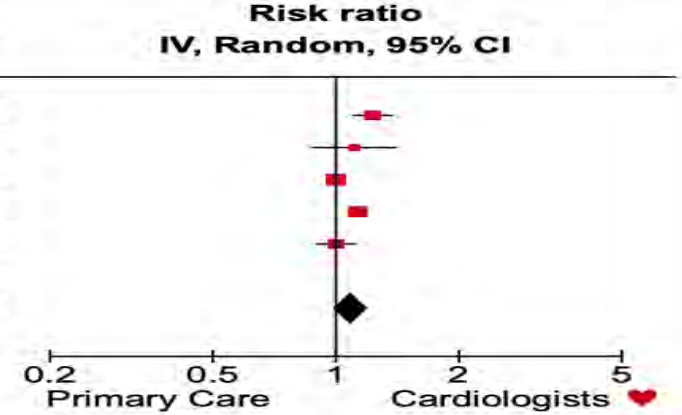
Heterogeneity: Tau² = 0.00; Chi² = 1.10, df = 1 (P = 0.30); I² = 9%
Test for overall effect: Z = 1.11 (P = 0.27)
Test for subgroup differences: Not applicable



Angiotensin Converting Enzyme Inhibitor / Angiotensin Receptor Blocker Prescription

Study or Subgroup	log[RR]	SE	Weight	Risk ratio IV, Random, 95% CI
Ansari 2003	0.207014	0.058326	19.1%	1.23 [1.10 , 1.38]
Diller 1999	0.10436	0.123179	9.0%	1.11 [0.87 , 1.41]
Jankowska 2014	0	0.010206	27.8%	1.00 [0.98 , 1.02]
Lee 2010	0.122218	0.029251	25.2%	1.13 [1.07 , 1.20]
Tebbe 2014	0	0.058639	19.0%	1.00 [0.89 , 1.12]
Total (95% CI)			**100.0%**	**1.08 [0.99 , 1.18]**

Heterogeneity: Tau² = 0.01; Chi² = 26.89, df = 4 (P < 0.0001); I² = 85%
Test for overall effect: Z = 1.78 (P = 0.08)
Test for subgroup differences: Not applicable



Cardiac Amyloid Project

Conor Sheridan, Faisal Oglah, Hasan Al-Hasani, Jim Sun

2024 Canadian Cardiovascular Congress
October 24-27, 2024
Vancouver, BC



Background: Cardiac Amyloidosis is an underdiagnosed cause of heart failure with preserved ejection fraction, and some patients wait up to 7 years and see 2 or more cardiologists before diagnosis and treatment initiation. Transthoracic echocardiography (TTE) is the imaging modality of choice for patient screening; yet it must be followed by pyrophosphate (PYP) scan or endomyocardial biopsy to confirm the diagnosis. Unfortunately, our centre and many others struggle with substantial delays in the suspicion, diagnosis and treatment initiation.

Aim: Map the cardiac amyloidosis journey through the KHSC system to identify points of delay, and assess the impact of implementing educational & quality interventions to reduce diagnoses time and improve patient outcomes.

Methods: Collect information on 1) performance indicators to reflect efficiency of amyloid detection, diagnosis and management, 2) process measures (# of educational events) to ensure implementation of quality interventions & 3) balancing measures – resource utilization and accuracy of amyloid suspicion.

Key findings: 34/70 patients had a positive PYP scan. Pre-educational & quality intervention, an average of 2.4 PYP scans/month (48% negative) were completed. After the intervention, PYP scans increased to 3.8 per month (57% negative). Pre-intervention, patients underwent an average of 1.9 (SD=1.9) ECHOs within 5 years of the suggestive TTE, which decreased to 1.5 (SD=1.4) post-intervention ($p=0.6$). TTE-to-PYP time decreased from 7.9 (SD=7.5) to 1.6 (SD=1.8) months ($p<.001$).

Sep 2024
Atlanta, Georgia,
United States

HFSA 2024
ANNUAL SCIENTIFIC MEETING
WHERE HEART FAILURE TEAMS GATHER

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HF Discharge Project –

Ansh Patel & Dhruv Srikanth

Control/Tracking Number: 2024-A-1187-HFSA
Activity: Abstract
Current Date/Time: 3/16/2024 8:07:53 AM

Barriers Of Successful Implementation Of Discharge Criteria At A Tertiary Heart Function Clinic

Author Block: Ansh Patel, Dhruv Srikanth, Rebecca Wood, Drew McLean, Kelly McNabb, Sam Gouett, Wendy Earle, Dianne Kirkpatrick, Hoshiar Abdollah, Josh Durbin, Aws Almufleh. Kingston Health Sciences Centre, Kingston, ON, Canada

Abstract:
Introduction: Most multidisciplinary heart function clinics cannot absorb the high volume of referrals they receive. The effectiveness of discharge protocols to offload stable patients from HF clinics has been poorly studied. We aimed to examine the predictors and barriers of implementing discharge criteria at a tertiary HF clinic.
Methods: We reviewed patients with >=3 visits to our heart function Clinic between Aug 1st and Feb 29th, 2024. We extracted patient-related and provider-related characteristics at initial and most recent clinic visits. The clinic's established discharge algorithm (Figure 1), was used to categorize patients as eligible or ineligible for discharge. The primary outcome was rate of successful discharge (defined as actual discharge of patients deemed suitable for discharge according to the protocol).
Results: Of 144 patients reviewed (mean age 71+/- 13 yrs, 65% men, and 8% HFpEF), 60 patients (41.7%) were deemed suitable for discharge, however, only 25/60 (41.7%) were actually discharged.Failure to discharge was associated with atrial fibrillation (AF) (20.8% of patients with AF were discharged vs 55.6%; p-value 0.009), having a HF hospitalization within 12 months (28.6% vs 53.1%; p-value 0.054), and those with improved EF to less than 50% (33.3% vs 64.7%; p-value 0.027). For provider-specific characteristics, there was a trend towards an association between having a cardiologist (discharge rate 100% among patients with a cardiologist vs 38.6%; p-value 0.067); whereas having a primary care provider did not correlate with discharge success (p-value >0.05). As for heart function providers' characteristics, low clinical experience (defined as <5 years in practice) was associated with a low rate of successful discharge (10.5% vs 52.6%; p-value 0.002).Thematic analysis revealed the desire to re-repeat the echocardiogram to confirm consistent improvement in ejection fraction (14/34, 41.7%), and to follow-up on non-heart failure consultants' opinions (arrhythmia, surgery, structural heart team; 9/34. 26.5%), to be the most common reasons for failure to discharge.



Tier I
Very stable patients

No LV thrombus or specific cardiomyopathy (sarcoid, HCM, amyloid)

No recent HF exacerbations

No ED visits for HF/ arrhythmia, ICD shocks in past year

No ACS in past 6 months or diuretic escalation in past 3 months.

Minimal functional impairments

No moderate or severe: valvular dysfunction, dilated ascending aorta, pulmonary hypertension

- EF >40%
- BNP <500
- PASP <50mmHg
- NYHA I-II

Suitable for safe discharge

On maximally tolerated medical therapy







Tier II
Stable HF patients with residual cardiac disease

No specific cardiomyopathy (sarcoid, HCM, amyloid)

No recent exacerbations

No HF ED/hospitalizations in past 6 months or diuretic escalation in past 3.

Non-severe functional impairments

EF >30%*, BNP <1000, NYHA I-III

*In rare cases very stable and optimally treated patients with EF 20-30% may be transferred to community cardiology

Suitable for safe discharge

On maximally tolerated medical therapy

Abbreviations
LV - Left ventricle
HCM - Hypertrophic cardiomyopathy
HF - Heart failure
ED - Emergency department
EF - Ejection fraction
BNP - Brain natriuretic peptide
PASP - Pulmonary artery systolic pressure
ICD - Implantable cardioverter-defibrillator
ACS - Acute coronary syndrome

Criteria for safe discharge from the Heart Function Clinic

- **Tier I: For patients with recovered ejection fraction** and no residual heart disease --> to follow with primary care providers
- **Tier II: For patients with improved ejection fraction** and some residual heart disease --> to follow with community cardiologists

Predictors and Outcomes of **Heart Failure Diagnosis in the Community compared to Acute Care Settings**: Insights from Linked Administrative Health Databases

Van, A., McLean, D., Willms, H., Wei, X., Stewart, K., Simpson, C., Green, M., & Almufleh, A.

Background:

Heart failure (HF) diagnosis is associated with worse outcomes when made in acute care settings (emergency department (ED) or during hospital admissions) compared to ambulatory care settings (the community), but little is known about this in Canada which has a comprehensive primary care system. We aim to evaluate the rate, predictors, and outcomes of HF diagnosis when made in acute care settings compared to the community in Ontario.

Methods:

This is a retrospective cohort study utilizing administrative databases of HF in Ontario, Canada from 2010 to 2022. We estimated HF diagnosis rates in each setting, patient/provider characteristics, and clinical outcomes.

Results:

597,025 patients had new HF diagnosis; 37% were in acute care settings (Table 1). Patients without a primary care provider (PCP), those with lower income, and with multiple comorbidities were more likely to be diagnosed in acute care settings ($p<0.0001$). Those diagnosed in acute care settings had an increased risk of all-cause mortality, hospital admissions for HF, and ED visits for HF (rate ratios: 1.82 [1.80, 1.83]; 2.80 [2.75, 2.85]); 2.68 [2.61, 2.75], respectively; adjusted for age, sex, and comorbidities).

Conclusion:

Over a third of HF diagnoses in Ontario occur in acute care settin
patients of lower socioeconomic status and those without a PCP.
increased mortality and admissions. The findings highlight the im
diagnosis and management of HF.

Submitted for ACC Young Investigator Award

Alex Van



HF & COPD Integrated Care Pathways

Pis: Mike Fitzpatrick & Aws Almufleh

Hasan Al-Hasani
Mehak khangura

Longitudinal research course

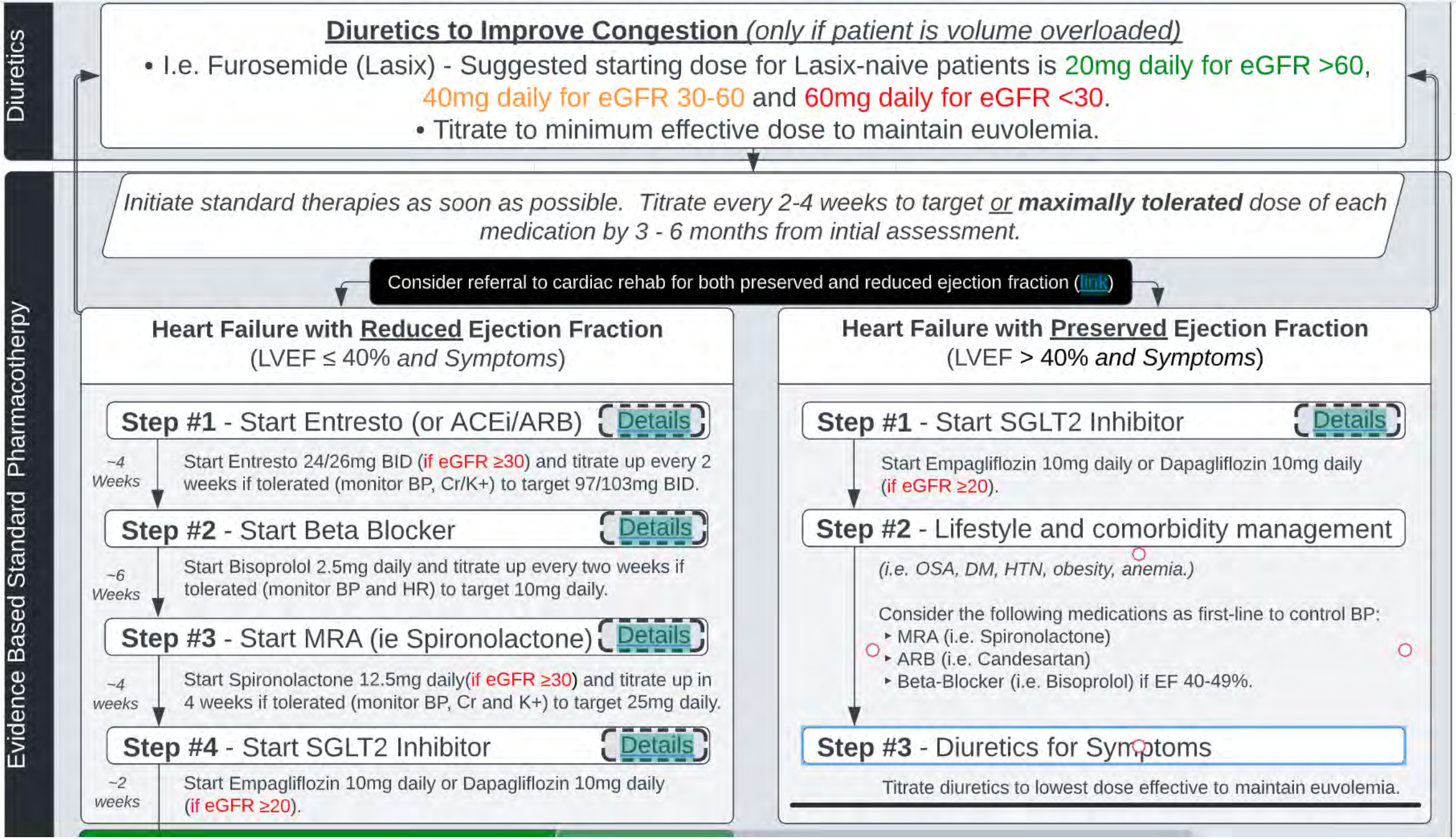
Background:

Integrated care pathways were launched in 2023 to improve management for COPD and HF, funded by Ontario Health, and launched in collaboration between KHSC and Ontario Health Team of Frontenac, Lennox and Addington FLA OHT

Project includes inpatient arm (aimed at reducing readmissions and return to ED), and outpatient arm (aimed at empowering PCPs to manage HF and COPD)

Data collection included 2019-2024 HF admissions, and March-July 2024 ED visits.

Primarily focused on quality improvement, this work resulted in important institutional changes including hiring virtual care HF nurse practitioner, HF physician assistant, COPD nurse navigator, and launching the lunch/learn PCP educational sessions.


Diuretics
Diuretics to Improve Congestion (only if patient is volume overloaded)
• I.e. Furosemide (Lasix) - Suggested starting dose for Lasix-naive patients is 20mg daily for eGFR >60, 40mg daily for eGFR 30-60 and 60mg daily for eGFR <30.
• Titrate to minimum effective dose to maintain euvolemia.
Evidence Based Standard Pharmacotherpy
Initiate standard therapies as soon as possible. Titrate every 2-4 weeks to target or maximally tolerated dose of each medication by 3 - 6 months from intial assessment.
Consider referral to cardiac rehab for both preserved and reduced ejection fraction (link)
Heart Failure with Reduced Ejection Fraction
(LVEF ≤ 40% and Symptoms)
Step #1 - Start Entresto (or ACEi/ARB) Details
~4 Weeks
Start Entresto 24/26mg BID (if eGFR ≥30) and titrate up every 2 weeks if tolerated (monitor BP, Cr/K+) to target 97/103mg BID.
Step #2 - Start Beta Blocker Details
~6 Weeks
Start Bisoprolol 2.5mg daily and titrate up every two weeks if tolerated (monitor BP and HR) to target 10mg daily.
Step #3 - Start MRA (ie Spironolactone) Details
~4 weeks
Start Spironolactone 12.5mg daily(if eGFR ≥30) and titrate up in 4 weeks if tolerated (monitor BP, Cr and K+) to target 25mg daily.
Step #4 - Start SGLT2 Inhibitor Details
~2 weeks
Start Empagliflozin 10mg daily or Dapagliflozin 10mg daily (if eGFR ≥20).
Heart Failure with Preserved Ejection Fraction
(LVEF > 40% and Symptoms)
Step #1 - Start SGLT2 Inhibitor Details
Start Empagliflozin 10mg daily or Dapagliflozin 10mg daily (if eGFR ≥20).
Step #2 - Lifestyle and comorbidity management
(i.e. OSA, DM, HTN, obesity, anemia.)
Consider the following medications as first-line to control BP:
▸ MRA (i.e. Spironolactone)
▸ ARB (i.e. Candesartan)
▸ Beta-Blocker (i.e. Bisoprolol) if EF 40-49%.
Step #3 - Diuretics for Symptoms
Titrate diuretics to lowest dose effective to maintain euvolemia.

Gender-based differences in POCUS use in the Emergency Department – Mohammed Wali (Ahmer) PGY-5 GIM & Ash Subbiah (BSc)



Background:

Are women as likely to receive POCUS in the emergency department when presenting

with cardiac symptoms?

Barries: lack of privacy (hallway beds), provider implicit bias (women can't have heart disease)

Aim:

Review all previous studies of POCUS in the emergency department and compare women representation

with reported prevalence of disease in the general public

Progress: Abstract screening completed.

Fulltext review underway

ACCELERATE-HF – Robyn Jackson, Bryce Alexander. (Cardio fellows)

Background: Guideline-directed medical therapy (GDMT) optimization and effective de-congestion can improve outcomes in heart failure (HF) patients, yet their implementation is suboptimal.

Aim: Use an HF decision aid and point-of-care ultrasound (POCUS) at admission to improve GDMT and reduce admissions.

Methods: Prospective, single center resident-led quality improvement initiative. Compared resident performed POCUS & HF decision aid use (QI arm) with routine hospital care in admitted HF patients. Examined 30-day hospital readmission, 30-day mortality and GDMT use, and adverse outcome occurrence.

Key findings: At discharge, the QI arm had higher use of renin-angiotensin system inhibitors (65% vs controls 43.1%, p=.033). Adverse effect occurrence and 30-day outcomes were not significantly different between groups. More people in the QI arm with unknown ejection fraction had an echo in the hospital, but this was not significant (5/7 (71%) vs controls 2/6 (33%), p=.286).

Achievements:

Project team: Aws Almufleh (PI), Robyn Jackson, Bryce Alexander, Laura Scott, Taylor Nikel, Shahad Sheerah, Arjun Sharma, Laura Scott, Drew McLean, Sheung Wing Sherwin Wong, Rebecca Wood.

Submitted for ACC Young Investigator Award





Case-based Simulation of HF Diagnosis and Management; the Heart Success App

Aws Almufleh MBBS, MPH

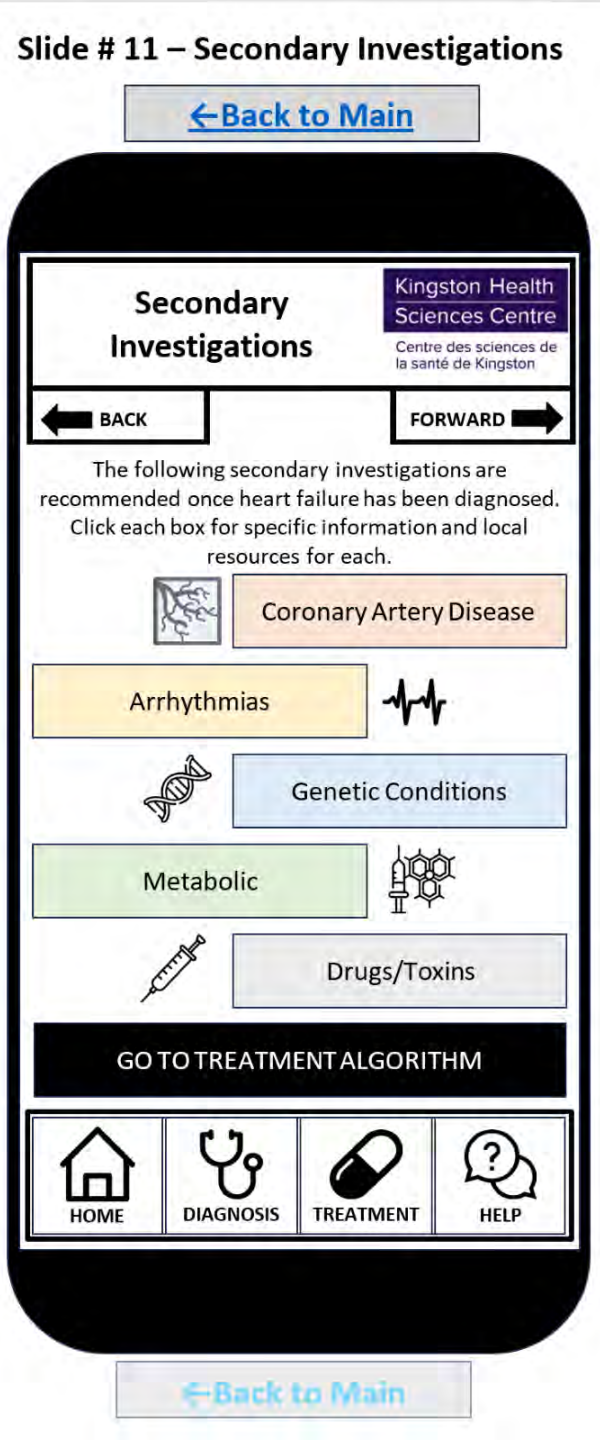
Bryce Alexander BSc, MD



Queen's University

Kingston Health Sciences Centre

Centre des sciences de la santé de Kingston



Canadian Institutes of Health Research | Instituts de recherche en santé du Canada

PROTECTED WHEN COMPLETED

Appl. #	520145

Complete Summary

HF Perioperative Risk Score

Aws Almufleh

PROJECT IMPACT

The Problem: Even though patients with heart failure (HF) are **at the greatest risk of surgical complications** after surgery, there is no available perioperative risk score to provide accurate risk estimation and mitigation in this patient population.

The Solution: We will directly **address this gap by developing and validating an HF-specific perioperative risk score** which will be packaged into a user-informed risk communication tool for patients and clinicians to facilitate discussion and risk mitigation heading for surgery.

Title: Building a point-of-care risk communication tool to improve perioperative risk estimation and mitigation for heart failure patients undergoing non-cardiac surgery

The Canadian Echocardiography Competency Evaluation and Optimization Project

Dr. Parvathy Nair and Dr. Aws Almufleh

AIM

Develop and deliver an echocardiography assessment tool to test competence in independent echocardiography performance and interpretation



Canadian Journal of Cardiology 39 (2023) 693–696

Training/Practice
Training in Cardiovascular Medicine and Research

Evaluating Independent Echocardiography Interpretation Skills: A Novel Assessment Tool

Aws Almufleh, MBBS, MPH, FASE, FRCPC,[a] Dominique Kushneriuk, MD, FRCPC,[b] Eric Yu, MD, MEd, FRCPC, FACC,[c] Amer Johri, MD, MSc, FRCPC, FASE,[a] Robin Ducas, BSc, MD, FRCPC,[d] Nicolas Thibodeau-Jarry, MD, MedEd, FRCPC,[e] Sarah Ramer, MD, FRCPC,[f] Sabe De, MD, FRCPC,[g] Sarah Blissett, MD, FRCPC,[g] Clarissa Yu,[h] Arianna Yu,[i] Kenneth Szeto, CRCS,[j] Annabel Chen-Tournoux, MD[k] and Parvathy Nair, MD, FRCPC[b]

CJC Canadian Journal of Cardiology

2023 CCS/CSE Standards for Physician Training and Maintenance of Competence in Adult Echocardiography: Executive Summary

Primary Panel:Parvathy Nair, MD, FRCPC • Annabel Chen-Tournoux, MD • Aws S. Almufleh, MBBS, MPH, FASE, FRCPC • Sarah Blissett, MD, FRCPC • Robin Ducas, BSc, MD, FRCPC • Nowell M. Fine, MD, SM, FRCPC • Amer M. Johri, MD, MSc, FRCPC, FASE • Dominique Kushneriuk, MD, FRCPC • Sarah Ramer, MD, FRCPC • Anthony Sanfilippo, MD, FRCPC • Nicolas Thibodeau-Jarry, MD, MMSc (MedEd), FRCPC • Eric Yu, MD, MEd, FRCPC, FACC • Secondary Panel: David Bewick, MD, FRCPC • Ian G. Burwash, MD, FRCPC • Chi-Ming Chow, MD, FRCPC • Heather Cooley, RDCS, RDMS, MRT • Sabe De, MD, FRCPC • Ghislaine Douflé, MD • Susan M. Fagan, MD, FRCPC (C) • Christine Henri, MD, FRCPC • Davinder S. Jassal, MD, FACC, FCCS, FRCPC (C) • Tom Jelic, MD, FRCPC, DRCPSC, FACEP • Dana Lee, MD, FRCPC • Jonathon Leipsic, MD, FRCPC • Howard Leong-Poi, MD, FRCPC • Warren Luksun, MD, FRCPC • Andrew J. Mulloy, MD, FRCPC • Sharon Mulvagh, MD, FRCPC • Gillian Nesbitt, MD, FRCPC • Steven Promislow, MD, FRCPC • Igal A. Sebag, MD, FRCPC, FASE • Diem T.T. Tran, MD, FRCPC, MSc • Teresa S.M. Tsang, MD, FRCPC, FACC, FASE • Show less

Open Access • Published: June 22, 2023 • DOI: https://doi.org/10.1016/j.cjca.2023.06.418 •

Dermatology



Dr. Yuka Asai
Division Chair
Research Lead

Summary

- *Previous case studies included: treatment side-effects and documenting rare diseases*
- *Scoping Review: Population, delivery and efficacy of patient education in atopic dermatitis*
- *Effect of declining of dermatology education of physicians and trainees*
- *Therapeutic treatments for basal cell carcinoma*
- *Patient education in prevention and risk of skin disease*
- *Clinical case: drug-induced interstitial lung disease associated with dupilumab for the treatment of atopic dermatitis*
-

Clinical case: drug-induced interstitial lung disease associated with dupilumab for the treatment of atopic dermatitis

Bethany Wilken[1], Onofre Moran-Mendoza[2], Marina Pourafkari[3], Yuka Asai[4]

[1] Translational Medicine Graduate Program, Department of Medicine, Queen's University
[2] Division of Respirology and Sleep Medicine, Department of Medicine, Queen's University
[3] Division of Diagnostic Radiology, Department of Medicine, Queen's University
[4] Division of Dermatology, Department of Medicine, Queen's University

BACKGROUND

Dupilumab is an anti-IL4Ra monoclonal antibody approved in the treatment of atopic dermatitis **(AD)** and other diseases and has few reported adverse events. Drug-induced interstitial lung disease **(ILD)**, associated with interstitial inflammation and fibrosis, can be caused by chemotherapeutic agents, antibiotics, and immunosuppressive agents (1). There are no distinct physiologic, radiographic or pathologic patterns of DILD- a diagnosis is made when patients with **ILD** are exposed to a medication and when avoidance of the medication results in improvements (1). We present a patient who developed **ILD** after being treated with **dupilumab** for severe **AD**.

CASE PRESENTATION

A 73-year-old female non-smoker with a longstanding history of AD presented to the dermatology clinic on a short course of oral prednisone to treat a severe AD flare. The patient's previous treatments for AD included topical steroids and methotrexate. The patient declined treatment with cyclosporine. She had asthma and known allergies to Alternaria mold, dust mites and cats.

July 2018
Patient starts dupilumab

October 2020
First complaint of persistent cough

Denied weight loss, fever, chills and night sweats, dry cough

Prescriptions: Rupatadine 10 mg p.o once daily

Blood work:
CBC normal
White blood cell count - 7
Eosinphils - 0.1

April 2021
Allergy clinic

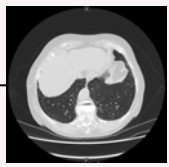
Cough mainly during day, occasional shortness of breath

Prescriptions: Montelukast 10 mg once daily, budesonide/formoterol (Symbicort ®)

Differential diagnosis:
1) Cough variant of uncontrolled asthma
2) Post-nasal drip secondary to rhinitis

Differential diagnosis: Hypersensitivity pneumonitis (HP)

October 2021
ILD clinic- differential diagnosis of hypersensitivity pneumonitis



Mild fibrotic changes in the lower lobe of the right lung and reticulations in the right middle lobe, indicating a pattern of probable usual interstitial pulmonary fibrosis (UIP).

Mild dyspnea, cough that affects daily activities

Bronchoalveolar lavage (BAL) results:

Eosinophils - 1%
Macrophages - 8%
Lymphocytes - 84%
Neutrophils - 10%

Connective tissue disease (CTD) and rhinosinusitis investigations negative.

Differential diagnosis: Foam-related HP

November 2021
Mold discovered in patient's foam pillows

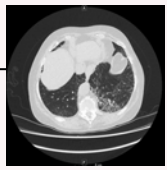
- Mold in foam pillows has been associated with ILD (2).
- Patient switches pillows from foam to polyester
- Incased pillows and mattress with anti-allergic waterproof casings.

Expect resolution of symptoms almost immediately (2).

Radiologic abnormalities can resolve within 6 weeks after removal (2).

Differential diagnosis: Drug induced interstitial lung disease

January 2022
Differential diagnosis of drug induced interstitial lung disease



Worsening interstitial changes with reticulation, mostly in the left lower lobe with some right middle lobe involvement.

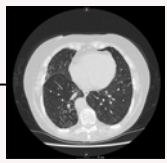
Worsening dyspnea and cough - productive of clear septum (50 mL/day).

March 2022
Patient discontinues dupilumab



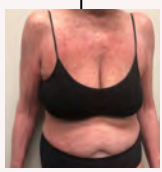
- **BSA - 97%**
- **EASI - 61**

April 2022
Patient erythrodermic



Significant improvements in the ground glass appearance and reticulations in the left lower lobe yet, the right middle lobe had progressive fibrosis.

Decline in pulmonary function



June 2022
Patient started tralokinumab





- **EASI - 0**

September 2022
AD controlled on tralokinumab



Complete resolution of reticulations in the right middle lobe, right lower lobe, and left lower lobe.

Cough controlled, no dyspnea

Pulmonary function returned to normal (and above)

March 2023
Resolution of ILD

References

1. Matsuno O. Drug-induced interstitial lung disease: mechanisms and best diagnostic approaches. Respiratory research 2012;13:1-9.
2. Moran-Mendoza O, Aldhaheri S, Black CJ, Clements-Baker M, Khalil M, Boag A. Mold in Foam Pillows and Mattresses: A Novel Cause of Hypersensitivity Pneumonitis. Chest 2021;160:e259-e63.
3. Bridgewood C, Wittmann M, Macleod T, et al. Th2 IL-4/IL-13 dual blockade with Dupilumab is linked to some Emergent Th17 type Diseases including seronegative arthritis, enthesitis/enthesopathy, but not humoral autoimmune diseases. Journal of investigative Dermatology 2022.
4. Mirza F, Wang A, Ramachandran S, Damsky W, Cohen J. Dupilumab-induced phenotype switch from atopic dermatitis to psoriasis is characterized by de novo interleukin-17A expression: a case report. British Journal of Dermatology 2021;185:432-4.
5. Spagnolo P, Bonniaud P, Rossi G, Sverzellati N, Cottin V. Drug-induced interstitial lung disease. European Respiratory Journal 2022.

SUMMARY

- Definite temporal relationship between dupilumab initiation and the onset of symptoms - no other new medications started within time period.
- Disease progressed despite removal of foam pillows that contained mold - resolution would have been expected sooner if ILD was foam-related.
- No evidence of CTD, infection or malignancy on bronchoscopy, BAL, or blood work.
- Exact causal mechanism is unknown - could be related to the recent reports of a dupilumab-induced shift to Th17 predominant diseases (3-4).
- **Improvement of symptoms, pulmonary function and imaging after discontinuation of dupilumab-** symptoms and radiographic abnormalities of ILD caused by biological agents develop tend to improve over 2-6 months after drug discontinuation (5).

YA reports honoraria and speaker fees from Sanofi, Pfizer, AbbVie, Leo, Sun Pharma, Novartis, Miravo, Eli Lilly, Kyowa Kirin, L'Oreal; research and education grants from Sanofi Canada, AbbVie, Pfizer, Novartis, Canadian Dermatology Foundation, Eczema Society of Canada; and performs clinical trials for Novartis and Leo. BW, OM &MP report no conflicts of interest.

Population, delivery and efficacy of patient education in atopic dermatitis: a scoping review

Bethany Wilken[1], Michele Zaman[2], Yuka Asai[3]

[1]Translational Institute of Medicine, Queen's University [2]School of Medicine, Queen's University [3]Division of Dermatology, Department of Medicine, Queen's University

INTRODUCTION

- **Atopic dermatitis (AD)** is a chronic, relapsing disease that can be difficult to manage.
- **Patient education** has improved the management of many chronic diseases.[1]
- AD treatment guidelines recommend patient education as an adjunct to conventional therapy.[2-5]
- However, there are no guidelines or official recommendations on how to educate AD patients.

RESEARCH QUESTIONS

1. ***What is known from the literature about patient education in AD?***
2. ***Has it improved management of the disease?***
3. ***What can be done to improve patient education for AD?***

METHODS

The protocol was drafted using the Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocols (PRISMA-ScR). Search performed October 2021.

KEYWORDS:
Atopic dermatitis
Eczema
Patient education
Therapeutic education
Health education
Action plan
Questionnaire
Survey
Patient interview

DATABASES:
MEDLINE
Embase
Grey Matters
ClinicalTrials.gov

EXCLUSION:
Occupational & contact dermatoses
Poster/abstracts
Not in english

RESULTS

SCREENING

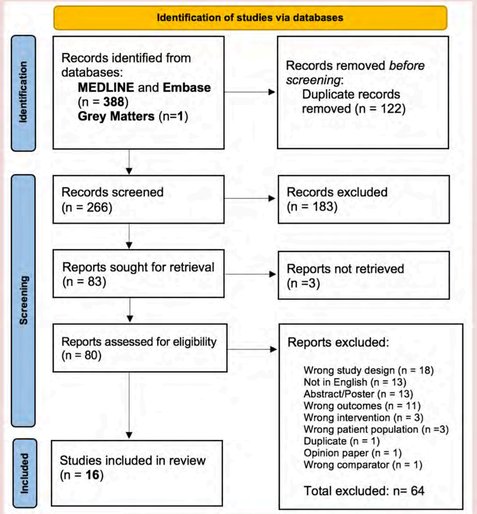


Figure 1. PRISMA flow chart of the screening process. **16** studies were included in the review.

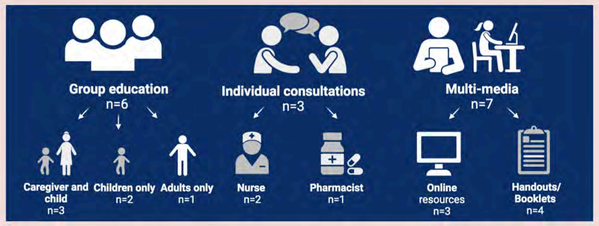
INCLUDED STUDIES

Year	Author	Journal
2021	LeBovidge et al.	Journal of Allergy and Clinical Immunology
2021	Muzzolon et al.	Asia Pacific Allergy
2018	Cheong et al.	Pediatric Dermatology
2018	Liang et al.	Pediatric Dermatology
2018	Brown et al.	Clinical Pediatrics
2017	Heratizadeh et al.	Journal of Allergy and Clinical Immunology
2015	Ryu & Lee	Western Journal of Nursing Research
2015	Rolinck- Werninghaus et al.	Pediatric Allergy and Immunology
2014	Son & Lim	Journal of Advanced Nursing
2013	Shi et al.	JAMA Dermatology
2013	Ohya et al.	Pediatric Dermatology
2012	Bostoen et al.	British Journal of Dermatology
2011	Armstrong et al.	Journal of the American Academy of Dermatology
2007	Guerra-Tapia et al.	Actas Dermo-Sifiliográficas
2002	Chinn et al.	British Journal of Dermatology
2002	Staab et al.	Pediatric Allergy and Immunology

POPULATION



DELIVERY



EFFICACY

Quality of Life	✓✓✓✓XXXXX	N=9
Disease Severity	✓✓✓✓✓✓XXX	N=9
Self-efficacy	✓	N=1
Knowledge	✓✓✓✓✓✓	N=6
Comfort	X	N=1
Family Impact	✓XXX	N=4
Anxiety	✓XX	N=3
Coping behavior	✓	N=1
Steroid anxiety	✓	N=1
Usage of steroid cream	✓	N=1
Confidence	✓✓	N=2
Sleep disturbance	✓	N=1

Figure 2. Outcome measures of included studies (n=16). Significant improvement represented by check mark. No significant improvement represented by X. Number of studies that included the outcome measure represented by n=.. at the end of each row.

RESEARCH GAPS

- Validated tools for measuring the efficacy of patient education in AD, including **knowledge** and **attitude** questionnaires.
- Comparative studies to determine the best method of education.
- Specialized educational efforts for adults with AD.
- Most cost-effective methods of education delivery.
- Longer study follow-up times and follow-up during different seasons.

CONCLUSION

1. ***Various education methods have been used and most are effective in improving outcomes related to AD management.***
2. ***Future studies are needed to provide validated and consistent patient education recommendations for AD.***

REFERENCES

1. Weingarten SR, Henning JM, Badamgarav E, Knight K, Hasselblad V, Gano Jr A, et al. Interventions used in disease management programmes for patients with chronic illnesswhich ones work? Meta-analysis of published reports. BMJ. 2002;325(7370):925.
2. Wollenberg A, Barbarot S, Bieber T, Christen-Zaech S, Deleuran M, Fink-Wagner A, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part II. Journal of the European Academy of Dermatology and Venereology. 2018;32(6):850-78.
3. Sidbury R, Tom WL, Bergman JN, Cooper KD, Silverman RA, Berger TG, et al. Guidelines of care for the management of atopic dermatitis: Section 4. Prevention of disease flares and use of adjunctive therapies and approaches. Journal of the American Academy of Dermatology. 2014;71(6):1218-33.
4. Katoh N, Ohya Y, Ikeda M, Ebihara T, Katayama I, Saeki H, et al. Japanese guidelines for atopic dermatitis 2020. Allergology International. 2020;69(3):356-69.
5. Lynde C, Barber K, Claveau J, Gratton D, Ho V, Krafchik B, et al. Canadian practical guide for the treatment and management of atopic dermatitis. J Cutan Med Surg. 2005;8(Suppl 5):1-9.

Endocrinology & Metabolism



Dr. Robyn Houlden
Division Chair
Research Lead

Summary

- *Previous case studies included: documenting rare diseases and their long term development, potential risk predictors of paraganglioma, diagnostics challenges of comorbidities, affects of seizures on hormone production, and transgender studies*
- *Improving disease management on general and specialized diabetes populations*
- *Investigating autoimmune disease factors in the development of thyroid, pancreatic disorders and cancer*
- *Studying treatments of diabetics post-renal transplant*

Research Projects

- We usually encourage individuals interested in Endocrinology to meet with a division member so we can customize a project for you
- Historically most resident projects have focused on
  - Case reports with literature review
  - Quality improvement projects related to endocrine disease management (typically inpatient or other specialized diabetes populations)

Current research opportunity

Predictors of Thyroglobulin Antibody Development in Thyroid Cancer Patients

Contact Dr. Josh Lakoff (Joshua.Lakoff@kingstonhsc.ca)

- Although current clinical and laboratory guidelines recommend measuring antithyroglobulin autoantibodies (TgAbs) for recurrent and persistent differentiated thyroid cancer (DTC), the long-term clinical significance and predictive factors for positive TgAbs have not been fully elucidated. This retrospective cohort study aims to establish predictive factors that are associated with the development of positive TgAbs.
- The objectives of this proposal include:
  - to determine the long-term significance of positive TgAbs;
  - to understand what patient factors correlate with the development of TgAbs;
  - to improve the management of patients diagnosed with DTC.

- We believe the results of this study will be beneficial to physicians when determining appropriate assessments for patients who test positive for TgAbs with DTC recurrence. This would lead to an improvement in tailored monitoring for patients with DTC.

Factors Associated with Pain from Thyroid Nodule Fine Needle Aspiration Biopsy: A Literature Review

Tao Liu MD FRCPC[1,2], Manisha Tilak MD[2], Sara Awad MBBS FRCPC[1,2], Joshua Lakoff MD FRCPC[1,2]
[1]Department of Medicine, Division of Endocrinology, [2]Queen's University School of Medicine, Queen's University, Kingston, Ontario, Canada

Introduction

- Thyroid nodules have tripled their yearly incidence from 4.9 per 100,000 individuals in 1975 to 14.3 per 100,000 individuals in 2009[1]
  - Thyroid cancer accounts for 5-24% of all thyroid nodules[2,3]
  - Fine needle aspiration biopsy (FNAB) is recommended in suspicious thyroid nodules
- FNAB can be uncomfortable in 25% of patients immediately post-procedure[4,5]
- This is the first literature review aimed to identify factors affecting FNAB related patient pain

Method

- Conducted literature searches on EMBASE, MEDLINE, CINAHL, Cochrane databases
- Identify studies which assessed factors associated with pain following FNAB
- 2244 studies were screened
- 22 studies were identified

Results

Author, Year	Study Type	Patients (M/F)	Pain Scales Used
Patient Related Factors			
Toman, 2016	Cohort study	98 (17/81)	VAS[1]
Leboulleux, 2013	Cohort study	218 (55/163)	VAS
Stangierski, 2012	Cohort study	75 (20/55)	VAS
Procedure Related Factors			
Ay, 2021	RCT[2]	50 (14/36)	VAS
Lee, 2019	RCT	99 (20/79)	NRS[4]
Tanaka, 2019	CCT[3]	200 (unknown)	Original Scale
Kim, 2019	Cohort study	167 (30/137)	VAS
Jeong, 2018	Cohort study	200 (30/170)	VAS
Jung, 2017	RCT	88 (75/13)	NRS
Yuce, 2016	CCT	58 (23/35)	VAS, NRS, VRS[5]
Nasrollah, 2014	Cohort study	61 (unknown)	Original Scale
Carpi, 2013	Cohort study	126 (16/110)	VRS
Lee, 2013	Cohort study	157 (17/140)	NRS
Sibbitt, 2011	Cohort study	110 (unknown)	VAS
Kumarasinghe, 1995	Cohort study	410 thyroid nodules (unknown)	VRS
Analgesia Related Factors			
Cao, 2020	Cohort study	585 (157/428)	Likert pain scale
Liao, 2018	Cohort study	183 (45/138)	VRS
Demirci, 2010	RCT	50 (0/50)	VAS
Kim, 2009	CCT	50 (unknown)	VAS, NRS, VRS
Gursoy, 2009[15]	RCT	138 (25/113)	VAS, NRS, VRS
Gursoy, 2007[17]	RCT	107 (90/17)	VAS, NRS, VRS
Gursoy, 2007[15]	CCT	99 (14/85)	VAS, NRS, VRS

Results

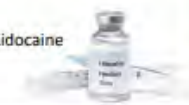
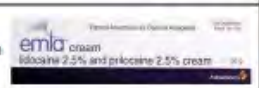
Patient Related Factors

Patient demographics 	•Leboulleux et al. - age <25, female sex and anxiety were associated with increased pain (OR 5 [1.5–6.5], p = 0.009; OR 11.2 [1.5-84], p = 0.02; r2 = 0.20, p = 0.02; respectively)[4]
Nodule depth 	•Toman et al. – deeper nodules correlated with increased pain (r = 0.43, p < 0.001)[6] •Leboulleux et al. - no correlation between % of patients reporting pain and depth (depth > 10 mm: 18%, depth ≤ 10mm: 28% of patients, OR 0.6 [0.3–1.2], p = 0.12)[4]
Nodule calcification 	•Liao et al. – presence of calcification was associated with pain (OR: 3.56, 95% CI: 1.08-11.68, p-value=0.04)[7]

Procedure Related Factors

Needle gauge 	•Lee et al. - no significant differences between 23- vs. 25-gauge (mean NRS 2.1 ± 1.3, 1.6 ± 1.3, p = 0.135)[8] •Jung et al. - no significant difference between 21- vs. 23-gauge (mean NRS 1.8 ± 1.3, 1.4 ± 1.1, p = 0.567)[9]
Core needle biopsy 	•3 of 4 studies did not identify association between type of procedure and pain[10-12] •1 of 4 studies (Nasrollah et al.) - 21-gauge CNB was associated with 39.3% of participants reporting pain compared to 16.4% in the FNAB group (p = 0.008)[13]
Number of FNAB attempts 	•Tanaka et al. - the second FNAB attempt was more painful in 46% of participants compared to the first in 19.5% of participants (p < 0.001)[14] •Leboulleux et al. - increased pain when 2 or 3 nodules were biopsied compared to 1 nodule[4]

Analgesia Related Factors

Subcutaneous (sc) Lidocaine 	•Liao et al. - 8% of patients with lidocaine reported significant pain vs. 20% of patients who did not receive placebo, p = 0.01[7] •Gursoy et al. - reduction in mean VAS, NRS and VRS in patients who received lidocaine[15] •Kim et al. – increase in mean VAS, NRS and VRS in patients who received lidocaine vs. those who did not[16]
EMLA cream 	•Gursoy et al. – reduction in mean VAS, NRS and VRS in patients who received EMLA cream vs. those who did not[17] •Demirci et al. – did not find a difference[18]
Sc lidocaine vs. EMLA cream or topical 4% lidocaine	•Gursoy et al.. – reduction in mean VAS, NRS and VRS in patients who received sc lidocaine compared to EMLA cream[19] •Cao et al. – sc lidocaine reduced number of patients reporting mild pain[20]

Discussion

- Patient related factors
  - Out of 3 studies assessing patient related factors, only Leboulleux et al. found differences in pain based on age, sex and anxiety levels
  - None of the studies found association between nodule size and pain
  - Deeper nodules and presence of calcification was associated with increased level of pain in some studies
- Procedure related factors
  - Needle gauge or type of biopsy procedure (CNB, LNAB or FNAB) did not appear to have a significant effect on pain scale ratings in 6 of 7 studies
  - Higher number of FNAB attempts was associated with more pain
  - Other factors that associated with less pain: non-aspiration technique, parallel technique and safety needles[21-23]
  - Factors that did not associate with pain: expertise of radiologist[24]
- Analgesia related factors
  - Subcutaneous lidocaine appear to have a greater effect on pain level reduction especially in patients at higher risk for pain

Conclusion & Future Research

- Patient, procedure and analgesia related factors were identified which can be optimized to improve patients' pain levels during FNAB of thyroid nodules
- Future research with uniform methodology is needed to minimize confounders and resolve conflicting data

References

1.Davies L, et al. 2014
2.Belfiore A, et al. 1989
3.Lin JD, et al. 2005
4.Leboulleux S, et al. 2013
5.Lo WC, et al. 2014
6.Toman H, et al. 2016
7.Liao LJ, et al. 2018
8.Lee YJ, et al. 2019
9. Jung SJ, et al. 2018
10. Jin Kim H, et al. 2019
11. Jeong EJ, et al. 2018
12. Carpi A, et al. 2013
13.Nasrollah N, et al. 2014
14.Tanaka A, et al. 2019
15.Gursoy A, et al. 2007
16.Kim DW, et al. 2009
17. Gursoy A, et al. 2007
18.Demirci H, et al. 2010
19.Gursoy A, et al. 2009
20.Cao C, et al. 2020
21.Kumarasinghe MP, et al. 1995
22.Yuce I, et al. 2016
23.Sibbitt RR, et al. 2011
24.Lee YJ, et al. 2013

A Rare Case of Sparsely Granulated Corticotroph Pituitary Macroadenoma Presenting with Pituitary Apoplexy Resulting in Remission of Hypercortisolism

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Introduction

- Corticotroph adenomas are divided into densely granulated corticotroph tumors (DGCT), sparsely granulated corticotroph tumors (SGCT) and Crooke's cell tumors[1]
- 7–23% of corticotroph tumors are macroadenomas[2,3]
- SGCT account for estimated 19–29% of corticotroph adenomas[4-6]

Case Presentation

- A 33-year-old male presented to a community hospital with sudden onset thunderclap headache accompanied by bitemporal hemianopsia, diplopia, decreased level of consciousness and hypotension
- 3-year history of ongoing symptoms of hypercortisolism including increased central obesity, supraclavicular fat pad, facial plethora, abdominal purple striae and decreased libido (Figure 1)
- Initial bloodwork revealed profoundly elevated cortisol of 1768 nmol/L, ACTH was not drawn (Table 1 for full pituitary panel)
- MRI demonstrated 1.9 cm x 3.2 cm x 2.4 cm heterogenous mass with local invasion suspicious for pituitary tumor with apoplexy (Figure 2)
- The patient underwent successful urgent transsphenoidal resection (TSS) and decompression of pituitary tumor
- Post-operatively, he developed panhypopituitarism with central adrenal insufficiency, hypothyroidism and hypogonadism requiring ongoing hormone replacement (Table 1)
- Pathology was diagnostic SGCT (Figure 3)

References

1.Lopes et al. Acta Neuropathol. 2017
2.Syro et al. Pituitary. 2015
3.Woo et al. J Clin Endo Metab. 2005
4.Doğanşen et al. Turk Patoloji Derg. 2019
5. Mete et al. Mod Pathol. 2018
6. Rak et al. Front Endocrinol (Lausanne). 2021
7. Witek et al. Eur J Endocrinol. 2016
8. McNicol et al. The Journal of Pathology. 1999

Case Presentation

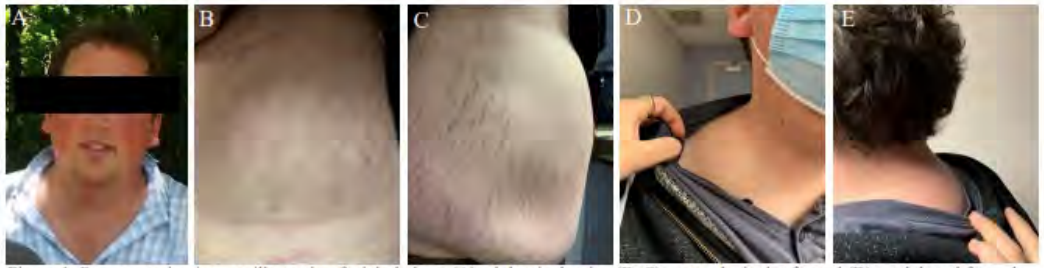


Figure 1. Representative images illustrating facial plethora (A); abdominal striae (B, C); supraclavicular fat pad (D); and dorsal fat pad (E)



Figure 2. Hyperattenuating 2.0 cm x 2.8 cm x 1.5 cm mass (orange arrow) at the sella turcica on unenhanced CT (A); 1.9 cm x 3.2 cm x 2.4 cm heterogeneous mass (red arrow) on T1 (B); and T2-weighted imaging with flattening of the optic chiasm, remodeling/dehiscence of the floor of the sella and extending into the right cavernous sinus with at least partial encasement of the ICA (C)

	Cortisol (65 – 470 nmol/L)	ACTH (0 – 18 pmol/L)	TSH (0.36 – 3.74 mIU/L)	Thyroxine, free (9.8 – 18.8 pmol/L)	LH (1 – 12 U/L)	FSH (1 – 12 U/L)	Testosterone (6 – 34 nmol/L)	Testosterone, free (160 – 699 pmol/L)	IGF-1 (82 – 242 ug/L)	GH (fasting <2 ug/L)	Prolactin (3 – 20 ug/L)
Pre-op	**1768**		0.89	11.7	1	3			179	1.5	<1
POD #2	305	**9**	**0.07**	13	**<1**	**1**	**1**				
POD #16	**<50**	**6.2**	**0.05**	**27**	**1**	**1**	**<0.5**	**<20**	**79**	<0.1	<1

Table 1. Pre-operative, POD #16 and POD #2 pituitary panel. Abnormal results are bolded. Hydrocortisone and levothyroxine were started POD #4.

Case Presentation

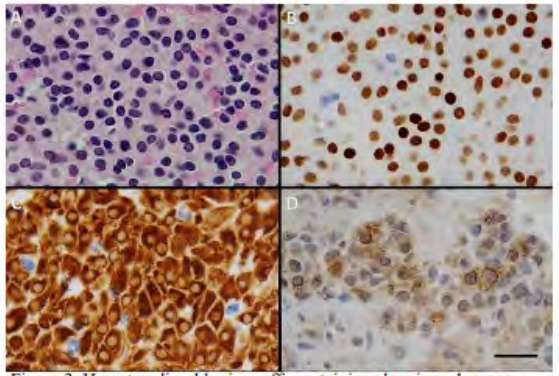


Figure 3. Hematoxylin phloxine saffron staining showing adenoma with solid growth pattern (Figure 3A); immunohistochemical staining showing T-pit reactivity of tumor nuclei (Figure 3B); diffuse cytoplasmic staining for cytokeratin CAM5.2 (Figure 3C); and regional moderately intense granular cytoplasmic staining for ACTH (Figure 3D). Scale bar = 20 µm

Discussion and Conclusion

- SGCT are defined as exhibiting faintly positive PAS alongside weak focal ACTH immunoreactivity and account for an estimated 19-29% of corticotroph adenomas[4-6]
- Multiple studies on corticotroph granulation pattern demonstrated that SGCT were statistically larger, had longer duration of CD prior to diagnosis, were less likely to achieve remission postoperatively, demonstrated increased recovery time of the HPA axis after TSS and had higher proliferative index with Ki-67, which is a marker for cell cycle[4,6,7]
- SGCT represent a subset of corticotroph adenoma with distinct clinical presentation, response to therapy and pathological findings

Pilot Project to Assess Nurse Practitioner Clinic for Adults with Diabetes without Access to Primary Care

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BACKGROUND

- Primary health care providers are responsible for the vast majority of diabetes care throughout a patient's life. However, in Ontario, 8.8% of patients do not have access to a primary care physician.[1]
- This shortage of providers can lead to delays in diabetes management and education and inappropriate usage of urgent care and emergency departments.
- Nurse practitioners have been shown to improve clinical outcomes for patients with type 2 diabetes in primary care and increase the convenience and quality of care while reducing costs.[2,3]
- This project evaluated a nurse practitioner led clinic for adults with diabetes without access to primary care. The weekly clinic was based in a diabetes education centre and received referrals from multiple sources.
- Patients included those identified by a diabetes educator as lacking access to primary care but requiring diabetes management optimization, patients discharged from hospital or the emergency department or urgent care centre and those attending cardiology and renal clinics.

METHODS

Data collection was performed and tabulated from each patient encounter including:

- Demographics (age, gender, type of diabetes, BMI, co-morbidities) and source of referral
- A1C, blood pressure, lipids, adherence with diabetes-related complications screening
- Services provided by the Nurse Practitioner (diagnostics, prescriptions, referrals)
- Depression assessed with the Patient Health Questionniare-9 (PHQ-9)
- Self-efficacy assessed with the Diabetes Empowerment Scale-Short Form
- Diabetes treatment satisfaction assessed with the Diabetes Treatment Satisfaction Questionnaire (DTSQc)

RESULTS

•Data was collected and analyzed from the first 5 months of the clinic. Demographic information was determined from the first visit as shown below.

Patients Referred	35
Average age	54.7 (+/- 13.6)
% Female	48.6
% Male	51.4
Time since diagnosis	11.7 +/- 11.4 years
Average A1C	9.3 +/- 2.13

•The majority of patients had a diagnosis of type 2 diabetes (n=30, 86%). There were also patients with type 1 diabetes n=3, 9%) and Steroid-induced diabetes (n=2, 6%).

•The average number of comorbidities for each patient was 5.1 +/- 2.5. The most common of these are listed below.

Hypertension	15 (43%)
Mental Health	11 (31%)
Stage 3 or higher Chronic Kidney Disease	5 (16%)
Coronary Artery Disease	5 (14%)
Peripheral vascular disease	4 (11%)

•After the initial visit, 77% of patients were recommended to have a follow up appointment with the NP clinic,.

•8 patients were referred to Cardiology and 1 was referred to Nephrology.

DISCUSSION

•Patients seen in the first 5 months of a NP led diabetes clinic had poorly controlled diabetes and multiple comorbidities. **Without access to this clinic, they would have continued to experience delays in intensification of their diabetes medications as well as referrals to specialty services.**

•A large percentage of the patients seen in this clinic had complex mental health issues which likely impacted their glycemic control and other medical conditions. Among these conditions, substance misuse and depression were most common.

•Of the 35 patients referred to clinic, there was only one patient who did not attend the scheduled appointment. This high level of attendance is suggestive of their desire for ongoing assistance in the management of their diabetes.

CONCLUSION

•Integrating a nurse practitioner clinic into a diabetes education centre is an innovative method of providing diabetes care to patients without access to primary care.

•Since data collection, further patients have been referred to the nurse practitioner clinic and those previously seen have returned for follow up visits.

•Ongoing follow-up of these patients will provide insight on the impact on glycemic control, blood pressure, and lipid values as well self-management, patient satisfaction, and types of referrals made for this vulnerable population.

FUNDING SOURCES

- Boehringer Ingelheim
- Queen's University Department of Medicine.

REFERENCES

1. Jaakimainen L, Shah B, Kopp A. Sources of physician care for people with diabetes. Toronto: Institute for Clinical Evaluative Sciences. 2003.
2. Richardson GC, Derouin AL, Vorderstrasse A, et al. Nurse practitioner management of type 2 diabetes Per J 2014;18:e134-e140.
3. Chang K, Davis R, Birt J et al. Nurse practitioner-based diabetes care management. Disease Management and Health Outcomes

KIT Mutation in a Gastric GIST in Patient with Familial Paraganglioma Syndrome Type 4

CASSANDRA HAWCO*, ROBYN HOULDEN

Queen's University

Objective: Familial paraganglioma syndrome type 4 is associated with mutations in the succinate dehydrogenase complex, subunit B gene (SDHB). We report a case of a patient with familial paraganglioma syndrome type 4 with the mutation c.600G>T; p.Trp200Cys who developed a gastric gastrointestinal stromal tumour (GIST) with a KIT mutation.

Methods: Clinical, radiographic and genetic data are presented.

Results: A 40-year-old man with familial paraganglioma syndrome type 4 and recurrent paraganglioma presented with recurrent epigastric pain. He had undergone resection of a paraganglioma superior to the right adrenal gland at age 19 years, resection of two para-aoritc paraganglioma at age 39 years, and resection of a paraganglioma in the interatrial septum at age 40 years. CT scan showed a 3.2 by 3.8 cm gastric body intraluminal polypoid mass. A partial gastrectomy was performed and revealed a GIST with a KIT (CD117) mutation.

Conclusion: This case provides further evidence that mutations in SDHB and KIT are not mutually exclusive with GISTs. It also identifies the need for endoscopic evaluation for GIST in patients with familial paraganglioma syndrome type 4 with unexplained gastrointestinal symptoms.

Resident Clinical Vignette Poster Presentation
Reference # 103

Long-Term Follow-up of One of the First Patients to Receive Human Growth Hormone Therapy

CASSANDRA HAWCO*, ROBYN HOULDEN

Queen's University

A 78-year-old man presented for endocrine followup. He had been one of the first patients to receive GH therapy in 1958. Growth had been normal until age 3 years and then decelerated. At age 17 years, he was 4'3" (129.5 cm) with absent sexual development. Bone age was 7 years. He was referred to Dr. Raben who initiated treatment with thyroid hormone and cortisone for 8 months. Human GH extract from the pituitary glands of deceased donors was then initiated at a dose of 2 mg 3 times a week for 2 years, and 3 mg 3 times a week for 6 months resulting in growth to a final height of 5'6½". Testosterone cyclopentylpropionate in oil 30 mg intramuscularly every 2 weeks was then added with achievement of sexual maturation over 2 years. He remained on testosterone injections until age 40 and then used transdermal testosterone until age 50 years. He received treatment with human chorionic gonadotropin and human menotropins for spermatogenesis restoration under the care of Dr. Raben at age 27 years with successful conception by his wife. At age 78 years, a MRI of the pituitary revealed a tiny amount of pituitary tissue within the floor of a normal-sized sella turcica with absent pituitary infundibulum. A combined pituitary hormone deficiency genetic panel did not reveal any mutations. These features suggest remote pituitary infarction/apoplexy rather than congenital pituitary deficiency. Sixty-two years later the patient remains in good health and is grateful to a pioneer in Endocrinology.

› Can J Diabetes. 2021 Apr;45(3):214-219. doi: 10.1016/j.jcjd.2020.08.100. Epub 2020 Aug 21.

Prevalence and Clinical Characteristics of Adults Presenting With Sodium-Glucose Cotransporter-2 Inhibitor-Associated Diabetic Ketoacidosis at a Canadian Academic Tertiary Care Hospital

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Affiliations + expand

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Abstract

Objectives: In this study, we examined the prevalence and clinical characteristics of sodium-glucose cotransporter-2 inhibitor (SGLT2i)-associated diabetes ketoacidosis (DKA).

Methods: A retrospective chart review of patients admitted for DKA over 4 years. Patients with SGLT2i-associated DKA were invited for pancreatic autoantibody testing. A subset of patients were invited for an interview to identify clinical characteristics suggestive of undiagnosed latent autoimmune diabetes in adults (LADA).

Results: Of 647 DKA admissions, 6.6% were associated with SGLT2i use. Time from SGLT2i initiation and DKA ranged from 2 weeks to 3.25 years; 69.8% had euglycemic DKA. Pancreatic autoantibody testing on 20 patients identified 5 originally diagnosed with type 2 as having LADA. Four were interviewed and had a LADA clinical risk score predictive of this diagnosis.

Conclusions: A larger study is needed to qualify the role of the LADA clinical risk score with confirmatory pancreatic autoantibody testing before SGLT2i initiation to reduce DKA risk.

Efficacy and Safety of SGLT2 Inhibitors in Diabetic Kidney Transplant Patients: Review of the Current Literature

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Introduction

- SGLT2 inhibitors (SGLT2-i) are oral hypoglycemic agents used in type 2 diabetes mellitus (T2DM)
- SGLT2-i:
  - Improve glycemic control
  - Promote weight loss
  - Reduce major adverse cardiovascular (CV) events in patients with T2DM and CV disease[1,2]
  - Reduce albuminuria and the progression of diabetic nephropathy to end-stage renal disease[3,4]
- Studies have excluded renal transplant patients
- The objective of this review was to determine the efficacy and safety of SGLT2-i use in diabetic renal transplant patients

Methods

- A literature review was conducted to identify studies which assessed SGLT2-i use in renal transplant patients with either T2DM or new onset diabetes after transplant (NODAT)
- Outcomes assessed included blood pressure, glycemic control, body weight, kidney graft function, proteinuria and adverse effects

Results

- Nine studies (x4 case series, x3 cohort studies, x1 randomized control trial (RCT), and x1 case report) were reviewed
- 144 diabetic renal transplant recipients (x92 NODAT and x50 T2DM) were included
- Estimated glomerular filtration rate (eGFR) was > 30 mL/min/1.73m^2
- HbA1C was > 6.5%
- Most commonly used SGLT2-i were empagliflozin (n=82), canagliflozin (n=34), dapagliflozin (n=28)

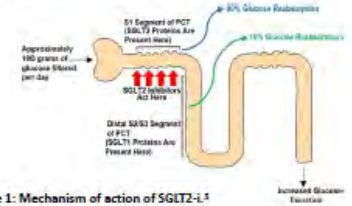


Figure 1: Mechanism of action of SGLT2-i.[5]

Study	Alkindi et al. 2020[6]	Mahling et al. 2019[7]	Shah et al. 2019[8]	Attallah et al. 2019[9]	Halden et al. 2019[10]	Schwaiger et al. 2019[11]	Beshyah et al. 2018[12]	Kwon et al. 2017[13]	Rajasekaran et al. 2017[14]
Type	Retro-spective Case Series	Prospective cohort	Pros-pective cohort	Retro-spective Case Series	Pros-pective RCT (Empa: Placebo)	Prospective cohort	Case report	Pros-pective Case Series	Retrospective Case Series
Center	UAE	Germany	India	UAE	Norway	Austria	UAE	South Korea	Canada
# of patients	8	10	24	8	60	14	1	23	18
Mean Age (yr)	56.8±13.7	66 (56-73)	53.8±9.1	45.9±3.1	63 (21-72)±59 (21-75)	56.5±7.9	58	-	KT: 61.6±12.6, PKT: 49.4±8.9
Gender (M:F)	6:2	8:2	22:1	4:4	17:5, 17:5	7:7	1:0	-	KT: 5:1, PKT: 2:2
Duration	24 months	12 months	6 months	12 months	6 months	12 months	30 months	12 months	22 months
Type of Kidney Transplant	LKD: 8	LKD: 8	-	-	LKD: 9:7	-	LKD: 1	-	-
	DKD: 0	DKD: 2	-	-	DKD: 13:15	-	-	-	KT: 6, PKT: 4
Type of Diabetes	DM II:2	DM II: 6	DM II: 24	DM II: 4	DM II: 0	DM II: 0	DM II: 1	DM I: 3, DM II: 18	DM II: 2
	NODAT: 6	NODAT: 4	NODAT: 5	NODAT: 4	NODAT: 60	NODAT: 14	-	NODAT: 7	NODAT: 8
eGFR	75.75±13.58	57 (45-73) (> 45)	86±10 (> 60)	NR	66 (27-68)±59 (52-72)	54±23.8 (> 30)	93	71±20	KT: 74±18.2, PKT: 60±14
A1c (%)	9.34±1.36	7.3 (6.4-7.8)	8.5±1.5	8.1±0.2	6.9 (6.5-8.2)±6.8 (6.1-7.2)	6.7±0.7	8.8	7.9±1.3	KT:8.6±1.4, PKT:7.4±1.1
SGLT2 Inhibitor / Dose (# patients)	Empa-gliflozin (6) Dapa-gliflozin (2)	Empa-gliflozin	Cana-gliflozin 100mg	Empa-gliflozin	Empa-gliflozin 10mg	Empa-gliflozin 10mg	Dapa-gliflozin 10mg	Dapa-gliflozin 5mg	Canagliflozin 100mg
Outcomes									
Weight	↓↓↓	↓	↓↓↓	↓↓	↓↓↓	↓↓ (Increase in bio-impedance fluid volume)	↓	↓↓	↓↓
BP	↓ SBP/DBP	↓ SBP	↓ SBP/DBP	↓	↓	↓	↓	↓	↓
A1c	↓↓↓	↓↓	↓↓↓	↓↓	↓↓↓	Decreased oral glucose insulin sensitivity	↓	↓↓	↓↓
eGFR	Stable	Stable	Stable	Stable	Stable	↓↓ (transient decrease at 4 wks)	Stable	Stable	Stable
UACR	NR	NR	NR	↓↓	NR	No change	NR	↓	NR
Complications									
	-UTI: 1	-UTI: 2	NR	-UTI: 2	-UTI: 3 -Genital itching: 1 -Genital yeast infection: 1	-UTI: 3	NR	-Cystitis: 2	-Low BS: 1
		-AKI stage 1: 1 -Small lower limb ulcer: 1			-Dizziness: 2 -Facial swelling: 1 -Hematuria: 1	-Balanitis: 1 -Pneumonia: 1 -HyperNa: 1			-Cellulitis: 1

Table 1: Summary of reported studies, outcomes, and adverse effects of SGLT2-i use in diabetic renal transplant patients.

Outcomes & Adverse Effects

- **Blood pressure (BP):** Small or non-significant BP reduction
- **HbA1C:** Modest improvement/reduction in insulin resistance
- **Weight:** Moderate-to-significant weight reduction
- **Renal allograft function:** Remained stable
- **Proteinuria:** Significant reduction of proteinuria (x1 study)[9]
- **Urinary tract infection (UTI):** Most common adverse effect (n=13)
- **Lower limb ulceration:** Small ulcer (x1 event)[7]
- **Euglycemic DKA/Ischemic lower limb amputations:** Not reported

Conclusion & Future Research

- Our literature review suggests:
  - **Beneficial outcomes of SGLT2-i use in diabetic renal recipients**
  - **With *no* significant adverse effects or complications**
- We will conduct a large prospective study to assess the efficacy and safety of SGLT2-i use in diabetic renal transplant patients

References

1. Neal B, Perkovic V, Mahaffey KW, de Zeeuw D, et al. "Canagliflozin and cardiovascular and renal events in type 2 diabetes." N Engl J Med 377 (2017): 633-657.
2. Zinman B, Wanner C, Lachin JM, Fitchett D, et al. "Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes." N Engl J Med 373 (2015): 2117-2128.
3. Heerspink HJL, Stefansson BV, Correa-Rotter R, Chertow GM, et al. "Dapagliflozin in patients with chronic kidney disease." N Engl J Med 383 (2020): 1436-1446.
4. Perkovic V, Jardine MJ, Neal B, Bompoint S, et al. "Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy." N Engl J Med 380 (2019): 2295-2306.
5. Madaan T, Husain I, Akhtar M, Najmi AK. "Exploring novel pharmacotherapeutic applications and repurposing potential of sodium glucose CoTransporter 2 inhibitors." Clin Exp Pharmacol Physiol 45, no 9 (2018): 897-907.
6. AlKindi F, Al-Omary HL, Hussain Q, Al Hakim M, et al. "Outcomes of SGLT2 Inhibitors Use in Diabetic Renal Transplant Patients." Transplant Proc 52 (2020): 175-178.
7. Mahling M, Schork A, Nadalin S, Fritsche A, et al. "Glucose Cotransporter 2 (SGLT2) Inhibition in Kidney Transplant Recipients with Diabetes Mellitus." Kidney Blood Press Res 44 (2019): 984-992.
8. Shah M, Virani Z, Rajput P, Shah B. "Efficacy and Safety of Canagliflozin in Kidney Transplant Patients." Indian J Nephrol 29, no 4 (2019): 278-28.
9. Attallah N, Yassine L. "Use of Empagliflozin in Recipients of Kidney Transplant: A Report of 8 Cases." Transplant Proc. 51, no 10 (2019): 3275-3280.
10. Halden TAS, Kvitne KE, Midtvedt K, Rajakumar L, et al. "Efficacy and Safety of Empagliflozin in Renal Transplant Recipients with Posttransplant Diabetes Mellitus." Diabetes Care 42, no 6 (2019): 1067-1074.
11. Schwaiger E, Burghart L, Signorini L, Ristl R, et al. "Empagliflozin in posttransplantation diabetes mellitus: A prospective, interventional pilot study on glucose metabolism, fluid volume, and patient safety." Am J Transplant, no 3 (2019): 907-919.
12. Beshyah SA, Beshyah AS, Beshyah WS, Yaghi S. "Use of SGLT2 inhibitors in diabetic renal transplant recipients: a mixed method exploratory exercise." Int J Diabetes Metab 24 (2018): 16-21.
13. Kwon HY, Kong JM. "Sodium/Glucose Cotransporter 2 (SGLT2) Inhibitor for Diabetic Kidney Transplant (KT) Patients." Kidney Week 2017. New Orleans, LA, USA: American Society of Nephrology.
14. Rajasekeran H, Kim SJ, Cardella CJ, Schiff J, et al. "Use of canagliflozin in kidney transplant recipients for the treatment of type 2 diabetes: a case series." Diabetes Care 40 (2017): e75e6.

Rare Case of Androgen-Secreting Ovarian Luteoma and Adrenal Adenoma with Subclinical Cushing's Syndrome in a Post-Menopausal Woman with Virilization: A Diagnostic Challenge

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Introduction

- Post-menopausal virilization can be caused by androgen-secreting tumours either from the adrenals or ovaries.
- Ovarian androgen-secreting tumours are very rare, making up <0.2% of all cases of hyperandrogenism and <1% of ovarian tumors, and should be considered in the differential diagnosis of post-menopausal virilization.
- Subclinical Cushing's syndrome (SCS) is a cause of metabolic syndrome; it is usually due to an adrenal adenoma, however rare cases of CS due to an ovarian etiology have been reported.
- This case aims to illustrate a diagnostic and management challenge of a post-menopausal patient with virilization and metabolic syndrome, with both an ovarian and adrenal tumour.

Case

- A 63-year-old female presented with a 3-year history of increasing dark, coarse hair growth around the face, trunk and extremities, androgenic alopecia, aggression, and voice deepening.
- Past medical history was significant for polycystic ovarian syndrome, obesity, type-2 diabetes and hypertension.
- Physical examination was significant for virilization, clitoromegaly and purple abdominal striae.
- See Table 1 for pre- and post-operative investigations; See Figure 1 for imaging.
- The patient underwent bilateral salpingo-oopherectomy (BSO) and right adrenalectomy concurrently.
- Pathology revealed ovarian stromal luteoma and adrenocortical adenoma.
- Post-operatively, the patient lost 20 pounds, insulin requirements decreased by 10 units, and anti-hypertensive doses decreased by half.

Case Cont'd

	Pre-Op	Post-Op
Testosterone (RR 0.3-1.3nmol/L)	10.7 ↑↑	0.7 **N**
AM cortisol following 1-mg dexamethasone suppression test (DST) (normal <50nmol/L)	63 ↑	<28 **N**
DHEA-S (RR 0.8-4.9umol/L)	2.3 **N**	1.2 **N**
Aldosterone/Renin Ratio (normal <50pmol/ng)	<1 **N**	-
Serum Metanephrines (normal <0.50nmol/L)	0.33 **N**	-
17-OHP	6.0 **N**	-

Table 1: Investigations pre- and post-operatively.

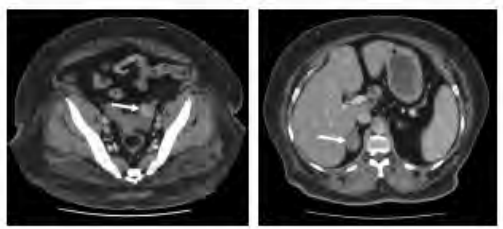


Figure 1: 2.1-cm left ovarian tumour (left, see arrow); 3.2-cm right adrenal tumour (right, see arrow).

Discussion

- A detailed history and physical examination is necessary to assist with the diagnostic evaluation of post-menopausal virilization.
- DHEA-S is useful in hyperandrogenism to distinguish adrenal from non-adrenal source, as it is an adrenal-specific hormone.
- DHEA-S is also useful in SCS as it has comparable sensitivity and greater specificity than 1-mg DST.
- Given normal DHEA-S and degree of elevation in testosterone level, hyperandrogenism in our patient was likely due to ovarian luteoma.
- However, it is possible that DHEA-S was falsely low due to concurrent SCS, therefore making hyperandrogenism from adrenal source possible.
- SCS is most commonly caused by an adrenal adenoma, which was likely the cause in our patient; however given concurrent BSO with adrenalectomy, an ovarian etiology could not be entirely ruled out as a rare cause of SCS.
- Due to two distinctive biochemically active tumours present, a management decision was made to undergo surgical resection of both ovarian and adrenal tumours.

Conclusion

- Post-menopausal virilization can be caused by an adrenal or ovarian source, and it is important to consider ovarian tumours as a rare cause.
- There have been previously reported cases of CS due to an ovarian source, and it is important to consider the rare possibility of SCS from an ectopic ovarian source.
- It is important to recognize challenges in endocrine biochemical testing, in order to make safe surgical management decisions for patients.

Dennedy et al. 2017 J Clin Endocrinol Metab; Markoupoulos 2015 Eur J Endocrinol; Pedowitz et al. 1962 Obstet Gynecol; Young et al. 1987 Int J Gynecol Pathol; Bogdanou et al. 2016 Gynecol Endocrinol; Ebrahimpur et al. 2019 Acta Med Iran; Alpanes et al. 2012 J Clin Endocrinol Metab; Sedhom et al. 2016 J Med Case Rep; Chentli et al. 2016 Eur J Endocrinol; Stoner et al. 1984 Pediatr Res.

Hyperactive Hypothalamic-pituitary-adrenocortical Axis in Patient with Generalized Seizure Disorder

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INTRODUCTION

- Epilepsy is a common neurologic disease affecting 65 million people around the world
- The paraventricular nucleus (PVN) in the hypothalamus regulates CRH secretion and ACTH production through negative feedback on the PVN and limbic structures
- Damage to limbic structures during seizures can alter negative feedback on the HPA axis and cause dysregulation leading to elevated ACTH

CASE

- 60-year-old woman with a history of seizure disorder was referred to Endocrinology Clinic with elevated ACTH and incidental 4mm Rathke cleft cyst
- Investigations revealed an elevated ACTH with normal morning cortisol
- There were no signs or symptoms of cortisol excess or insufficiency on history or physical exam
- Remainder of pituitary hormones were in expected ranges (see table 1)
- Medication history was significant for valproic acid and carbamazepine
- Patient reported longstanding anxiety and increased seizures over the past year despite anti-seizure medication

INVESTIGATIONS

- ACTH Stimulation test revealed a normal response with baseline cortisol 370 nmol/L, 30 minute 598 nmol/L, 60 minute 655 nmol/L
- CT scan was negative for ectopic ACTH syndrome
- Overnight dexamethasone suppression test (1mg) revealed non-supressed AM cortisol 374 nmol/L
- Repeat high dose dexamethasone suppression test (8mg) revealed normal suppression of cortisol (<28 nmol/L)
- CT head to investigate tremor and word finding difficulty was within normal limits
- EEG negative for epileptiform activity but did show delta slowing in the left frontotemporal lobe consistent with a focal abnormality

	May 2020	Nov 2020	March 2021
ACTH	51.1	53.5	46.5
Cortisol	446	383	374
24hr urine cortisol		98 (norm<275)	
TSH	4.07	3.49	
Free T4		10	
LH	19.7	19.4	
FSH	73.7	77.7	
Prolactin	9.3	7.8	

DISCUSSION

- We present a case of 60 year old female with elevated ACTH and no clinical or biochemical evidence of cortisol deficiency or excess
- The elevation could have been secondary to chronic recurrent seizure activity affecting the temporal lobe structures and the PVN leading to dysregulation of the HPA axis
- This dysregulation can explain the chronic elevation in ACTH and failure to supress cortisol with 1mg dexamethasone suppression test

CONCLUSION

- Dysregulation of the HPA axis occurs through chronic changes to the limbic structures in the brain leading to elevation in ACTH and occasionally baseline cortisol levels
- **This case suggests that nocturnal epilepsy can be a cause of hyperactivity of the HPA axis and should be included on the differential diagnosis for otherwise unexplained elevated ACTH level in patient with underlying seizure disorder**

Wulsin et al. 2016 *Physiol. Behav.*, Maquire & Salepkar 2013 *Epilepsy Behav.*, Maquire 2021 *Neurosci. Lett.*, Zhang & Liu 2008 *NeuroSci. Bull.*, Hooper et al. 2018 *Epilepsy Behav.*, Piekut et al. 1996 *Brain Res.*, Gallagher 1987 *YJBM.*

Thyroid Hormone-Based Nutraceuticals: A Rare Cause of Thyrotoxicosis and Thyrotoxic Periodic Paralysis

SHIRLEY SHUSTER*, SARA AWAD, CAITLYN VLASSCHAERT

Queen's University

Background/Objective: Thyrotoxic periodic paralysis (TPP) is a rare disorder characterized by muscle weakness, areflexia, and hypokalemia in the setting of thyrotoxicosis. This case aims to illustrate the use of nutraceuticals as a cause of thyrotoxicosis and TPP.

Methods: Clinical and laboratory data are presented.

Results: A 32-year-old Caucasian male presented to the emergency department with lower limb muscle weakness. Physical examination revealed tremors, diaphoresis, sinus tachycardia (110–120 bpm), and positive lid lag. Thyroid exam was normal and there were no bruits. TSH was < 0.01 mIU/L (reference range (RR) 0.40–4.50), fT4 6 pmol/L (RR 9.0–19), and fT3 15 pmol/L (RR 4.0–6.8). Potassium was 3.1 mmol/L (RR 3.7–5.3) which normalized with supplementation. He was suspected to have Graves' disease (GD) and was discharged home on bisoprolol 2.5 mg and methimazole 10 mg, pending TRAb levels and outpatient follow-up. He re-presented four days later with generalized paralysis, areflexia, and sinus tachycardia (100 bpm). Investigations revealed potassium 1.7 mmol/L, TSH 0.07 mIU/L, fT4 6 pmol/L, and fT3 2.2 pmol/L. Treatment of TPP with intravenous fluids and potassium supplementation resulted in rebound hyperkalemia to 6.1 mmol/L which then normalized, along with resolution of paralysis. Methimazole was also discontinued. Thyroid radioiodine uptake and scan was normal at 23%, however the patient had been ingesting weight loss supplements containing kelp, iodine, licorice, and likely undeclared thyroid hormone or mimics. Following discontinuation of all supplements, bloodwork revealed TSH 3.07 mIU/L, fT4 10pmol/L, fT3 4.4 pmol/L, and potassium 4.2 mmol/L. Symptoms of thyrotoxicosis also resolved.

Conclusion: This case illustrates that ingestion of thyroid hormone-based nutraceuticals should be considered as a cause of thyrotoxicosis and TPP.

Rare Case of Androgen-Secreting Ovarian Luteoma and Adrenal Adenoma with Subclinical Cushing's Syndrome in a Post-Menopausal Woman with Virilization: A Diagnostic Challenge

SHIRLEY SHUSTER*, SARA AWAD

Queen's University

Background/objective: Post-menopausal virilization is caused by excess androgens from the adrenals or ovaries, and ovarian luteoma is a rare cause. Subclinical Cushing's syndrome (SCS) is a cause of metabolic syndrome and virilization, and is usually due to adrenal adenoma; however, rare cases of SCS due to ovarian etiology have been reported. This case aims to illustrate ovarian etiology as a rare cause of post-menopausal virilization and possibly SCS.

Methods: Clinical and laboratory data are presented.

Results: A 63-year-old female presented with a 3-year history of increasing dark, coarse hair growth around the face, trunk and extremities, androgenic alopecia, aggression, and voice deepening. Medical history was significant for obesity, type 2 diabetes and hypertension. Physical examination was significant for virilization, clitoromegaly and purple abdominal striae. Total testosterone was 10.7 nmol/L (RR 0.3–1.3), with bioavailable testosterone 5.74 nmol/L (RR 0.1-0.6), but normal DHEA-S 2.3 umol/L (RR 0.8–4.9). 17-(OH)-progesterone was normal. CT scan revealed a 2.1 cm left ovarian mass and 3.2 cm right adrenal adenoma. Renin, aldosterone and serum metanephrines were normal. However, cortisol failed to suppress to $<$ 50 nmol/L following 1 mg dexamethasone (cortisol 63 nmol/L), concerning for SCS. The patient underwent bilateral salpingo-oopherectomy and right adrenalectomy. Pathology revealed ovarian stromal luteoma and adrenocortical adenoma. One-month post-operatively, testosterone normalized to 0.7 nmol/L and cortisol appropriately suppressed to $<$ 28 nmol/L following dexamethasone suppression. The patient lost 20 pounds, and insulin requirements and anti-hypertensive medication doses decreased.

Conclusion: This case illustrates the importance of considering ovarian luteoma as a rare cause of post-menopausal virilization, and the rare possibility of SCS from an ovarian source.

Diagnosis and Management of Hyperosmolar Hyperglycemic State: A Quality Improvement Study

SHIRLEY SHUSTER*, SARA AWAD, SARAH MOORE

Queen's University

Background/Objective: Hyperosmolar Hyperglycemic State (HHS) is a life-threatening hyperglycemic emergency. Despite high mortality and morbidity, there is a paucity of evidence for HHS management and patients are often treated with diabetic ketoacidosis protocols. This study describes the diagnosis and management of HHS at a teaching hospital.

Methods: A retrospective chart review was conducted of patients 18 years and older from June 1, 2014–June 30, 2019 who were diagnosed with "HHS," "hypernatremia," "hyperglycemia," or "hyperosmolality." Patients diagnosed with and/or who met the Diabetes Canada Clinical Practice Guidelines HHS diagnostic criteria were included.

Results: Forty-nine charts met the inclusion criteria. These included 29 (59.2%) males and 20 (40.8%) females, mean age 65 years (+/-15.3). Forty (81.6%) patients were admitted with an average hospital admission of 7.7 (+/-8.8) days, 9 (18.4%) were discharged from the emergency department, and 2 (4.1%) patients died. Twenty-eight patients (57.1%) had pre-existing type 2 diabetes. The average HbA1C was 11.8% (+/- 2.7). Seventeen (34.7%) patients were diagnosed with HHS without obtaining a serum osmolality, 14 (28.6%) were diagnosed despite serum osmolality of $<$ 320 mOsm/kg, and 4 (8.2%) met diagnostic criteria but were not diagnosed with HHS. Intravenous (IV) normal saline, ringer's lactate and a combination of fluid types were used in 34 (69.4%), 3 (6.1%), and 10 (20.4%) patients respectively. The majority of patients received IV (n = 26, 53%) or subcutaneous (n = 20, 40.8%) insulin.

Conclusion: This study demonstrates variability in HHS diagnosis and management. The heterogeneity of local practices suggests that a standardized protocol may enable a more consistent approach to patient care.

Diagnosis and Management of Hyperosmolar Hyperglycemic State: A Quality Improvement Study

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[1]Department of Medicine, [2]Kingston Health Sciences Centre, [3]Division of Endocrinology and Metabolism, Kingston Health Sciences Centre, Queen's University, Kingston, ON

Background

- Hyperosmolar Hyperglycemic State (HHS) is a relatively common life-threatening hyperglycemic emergency. *(French et al. 2019 BMJ)*
- Despite high mortality and morbidity, there is a paucity of evidence for HHS management. *(Scott 2015 BJD; Pasquel et al. 2014 Diabetes Care)*
- Clinical guidelines for HHS management have been variable, and there is lack of published randomized clinical trials guiding HHS management. *(Scott 2015 BJD; Pasquel et al. 2014 Diabetes Care)*
- Most HHS management recommendations are extrapolated from DKA studies, and patients are often treated with diabetic ketoacidosis (DKA) protocols. *(Scott 2015 BJD; Pasquel et al. 2014 Diabetes Care)*
- Our centre utilizes a DKA management protocol order set to manage DKA; however, the DKA order set is also frequently used to manage patients admitted with HHS, although not intended or validated for HHS management.

Objectives

1. To evaluate the clinical characteristics and management strategies used for the treatment of patients presenting with HHS at our tertiary care centre.
2. To identify the outcomes of patients admitted with HHS who are managed using the DKA protocol.
3. To determine whether there is a necessity for the development of a distinctive HHS management protocol at our tertiary centre.

Methods

- The key words "HHS," "hypernatremia," "hyperglycemia," and "hyperosmolality" were used for the search strategy in our database.
- Patients diagnosed with and/or who met the HHS diagnostic criteria as per the Diabetes Canada Clinical Practice Guidelines were included.
- Patients diagnosed with DKA were excluded.

Results

Clinical Characteristics	Mean ± SD (n) or % (n)
Age	64.90 ± 15.30
Gender	
• Male	29 (59.2%)
• Female	20 (40.8%)
Diabetes Type	
• Type-1	2 (4.1%)
• Type-2	28 (57.1%)
• Pre-diabetes	1 (2.0%)
• No prior history	18 (36.7%)
Duration of Diabetes	
• 0-5 years	4 (8.2%)
• >5 years	8 (16.3%)
• New diagnosis	13 (26.5%)
• Unknown or N/A	24 (49%)
Diabetes Medications	
• None	20 (40.8%)
• Oral hypoglycemic medications only	11 (22.4%)
• Insulin only	7 (14.3%)
• Oral hypoglycemic medications and insulin	11 (22.4%)
HbA1C (%)	11.84 ± 2.75
Presenting laboratory investigations	
• pH	7.35 ± 0.07
• Anion gap (mmol/L)	14.16 ± 4.05
• Bicarbonate (mmol/L)	24.64 ± 4.66
• Serum osmolality (mOsm/kg)	333.59 ± 33.04
• Blood glucose (mmol/L)	36.83 ± 11.06
• Beta-hydroxybutyrate (mmol/L)	1.02 ± 1.16
HHS Diagnosis	
• Diagnosis made without obtaining serum osmolality	17 (34.7%)
• Diagnosis made despite serum osmolality <320mOsm/kg	14 (28.6%)
• Diagnosis not made despite diagnostic criteria being met	4 (8.2%)
HHS Management (Fluids)	
• Normal saline	34 (69.4%)
• Ringer's lactate	3 (6.1%)
• Combination of fluid types	10 (20.4%)
• None	2 (4.1%)
HHS Management (Insulin)	
• Intravenous	26 (53%)
• Subcutaneous	20 (40.8%)
• None	3 (6.1%)
Complications	
• Electrolytes disturbances	37 (75.5%)
• Acute kidney injury	34 (69.4%)
• Cardiac arrhythmia +/- ischemia	3 (6.12%)
• None	23 (46.9%)
• Unknown	12 (24.5%)
Disposition Outcomes	
• Hospital admission	35 (71.4%)
• ICU admission	3 (6.12%)
• Discharged from ED	9 (18.4%)
• Died	2 (4.1%)
Length of stay (days)	6.04 ± 8.49

Table 1: Clinical characteristics of patients with HHS.

Conclusion

- This study demonstrates variability in the diagnosis and management of HHS at our centre, and identifies a need to standardize the work-up and management of patients presenting with HHS.

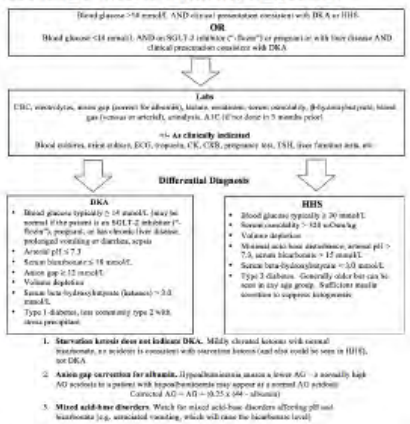
Our Strategy

1. We have edited our centre's current DKA protocol to include HHS-specific management. For example:

For HHS with serum beta-hydroxybutyrate < 1 mmol/L do not start IV insulin as
- Fluid replacement alone will result in a falling blood glucose level
- There is a risk of lowering the osmolality precipitously with IV insulin.
- Insulin treatment before adequate fluid replacement may result in cardiovascular collapse as water moves out of the intravascular space, with a resulting decline in intravascular volume

2. We have edited our centre's current DKA protocol to include guidance on HHS diagnosis. For example:
   - A table with DKA vs. HHS diagnostic criteria
   - Including serum osmolality into pre-checked off investigations on the order set

3. We have created a flowchart to follow for patients presenting to hospital with hyperglycemia:



4. We are planning to deliver an educational session to clinicians, particularly emergency and internal medicine, in order to educate further on this topic and highlight our updated resources.

Lactation Induction in a Transgender Woman Wanting to Breastfeed: Case Report

Rachel Wamboldt [1], Shirley Shuster [1], Bikrampal S Sidhu [2]

Affiliations + expand

PMID: 33513241 DOI: 10.1210/clinem/dgaa976

Abstract

Context: Breastfeeding is known to have many health and wellness benefits to the mother and infant; however, breastfeeding in trans women has been greatly under-researched.

Objective: To review potential methods of lactation induction in trans women wishing to breastfeed and to review the embryological basis for breastfeeding in trans women.

Design: This article summarizes a case of successful lactation in a trans woman, in which milk production was achieved in just over 1 month.

Setting: This patient was followed in an outpatient endocrinology clinic.

Participant: A single trans woman was followed in our endocrinology clinic for a period of 9 months while she took hormone therapy to help with lactation.

Interventions: Readily available lactation induction protocols for nonpuerpural mothers were reviewed and used to guide hormone therapy selection. Daily dose of progesterone was increased from 100 mg to 200 mg daily. The galactogogue domperidone was started at 10 mg 3 times daily and titrated up to effect. She was encouraged to use an electric pump and to increase her frequency of pumping.

Main outcome measure: Lactation induction.

Results: At one month, she had noticed a significant increase in her breast size and fullness. Her milk supply had increased rapidly, and she was producing up to 3 to 5 ounces of milk per day with manual expression alone.

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Exploring resident and faculty perspectives on the impact of transitioning to virtual ambulatory care on clinical exposure, teaching, and assessment during the COVID-19 pandemic

Rebecca Leclair,[1] Jessica S.S. Ho[1], Dr. Heather Braund[1], Jennifer Bunn[1], Dr. Ekaterina Kouzmina[1], Dr. Samantha Bruzzese[1], Dr. Sara Awad[1], Dr. Steve Mann[1], Dr. Ramana Appireddy[1], Dr. Boris Zevin[1]

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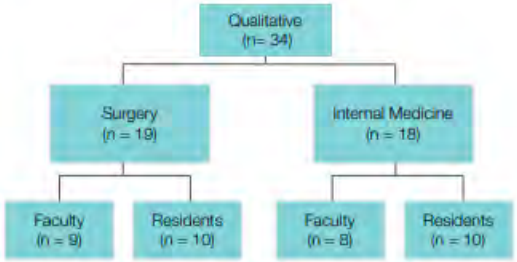
Introduction

- The COVID-19 pandemic has caused a decline of in-person clinical care, and an increase in virtual care.
- This transition may have resulted in diminished opportunities for clinical teaching, learning, and assessment for post-graduate trainees.

RQ: How has the transition from in-person to virtual ambulatory care during the COVID-19 pandemic affected post-graduate trainees' teaching, learning and assessment at Queen's University?

Methods

- Residents (n=20) and faculty (n=17) were recruited from the Departments of Surgery and Medicine at Queen's University (Ontario, Canada)
- Interviews and focus groups, recorded and transcribed verbatim
- Qualitative data were analyzed thematically



Results

Four themes emerged from the data:
1) Teaching/Learning 2) Assessment 3) Logistical Considerations 4) Recommendations



Theme	Sample Quotations
Teaching/Learning	"...I think the impact on the learning is mainly in terms of the volume of people that I am seeing and I am not able to practice my approaches..." (R1)
Assessment	"...there may be fewer opportunities to get meaningful assessments because I think there is a tendency for residents or for junior learners to only feel compelled to trigger assessments when they feel that what they are triggering an assessment for will be evaluated relatively highly." (Surgery FG)
Logistical Considerations	"Doing a phone or virtual clinics in just a typical clinic, they are not set up for that. There are not enough computers or phones. There is not enough space to be able to do that type of work." (F3)
Recommendations	"And those technologies need to be better streamlines, easier to access for patients, less work for the secretary to be able to book the patients and support the patients. We need better virtual technologies where the patients find them easier to use and require less support." (F5)

Conclusion

- Virtual care has imposed many changes to teaching, learning, and assessment
- Residents and faculty faced significant barriers such as lack of space, time, and lack of appropriate EPAs
- Recommendations include faculty development, frameworks for conducting virtual care, and improved infrastructure
- Virtual care is here to stay and medical education needs to adapt to support current and future learners



Demographic and clinical characteristics of type 2 diabetes mellitus patients in Ontario, canada

Robyn L Houlden, **Nilasha Thayalan**, Shane Golden, Scott Shi, Atif Kukaswadia, Arushi Sharma, Kobina Quanshah, Aiden Liu

Study objectives

Investigate the demographic and the clinical characteristics of patients with T2DM in Ontario, Canada with data available from April 1st, 2002, to September 31st, 2017

Compare the demographic and clinical characteristics of T2DM patient populations identified by sensitive and specific cohort definitions to understand their impact on characterizing the disease

Methods – STUDY DESIGN

Selection Period:

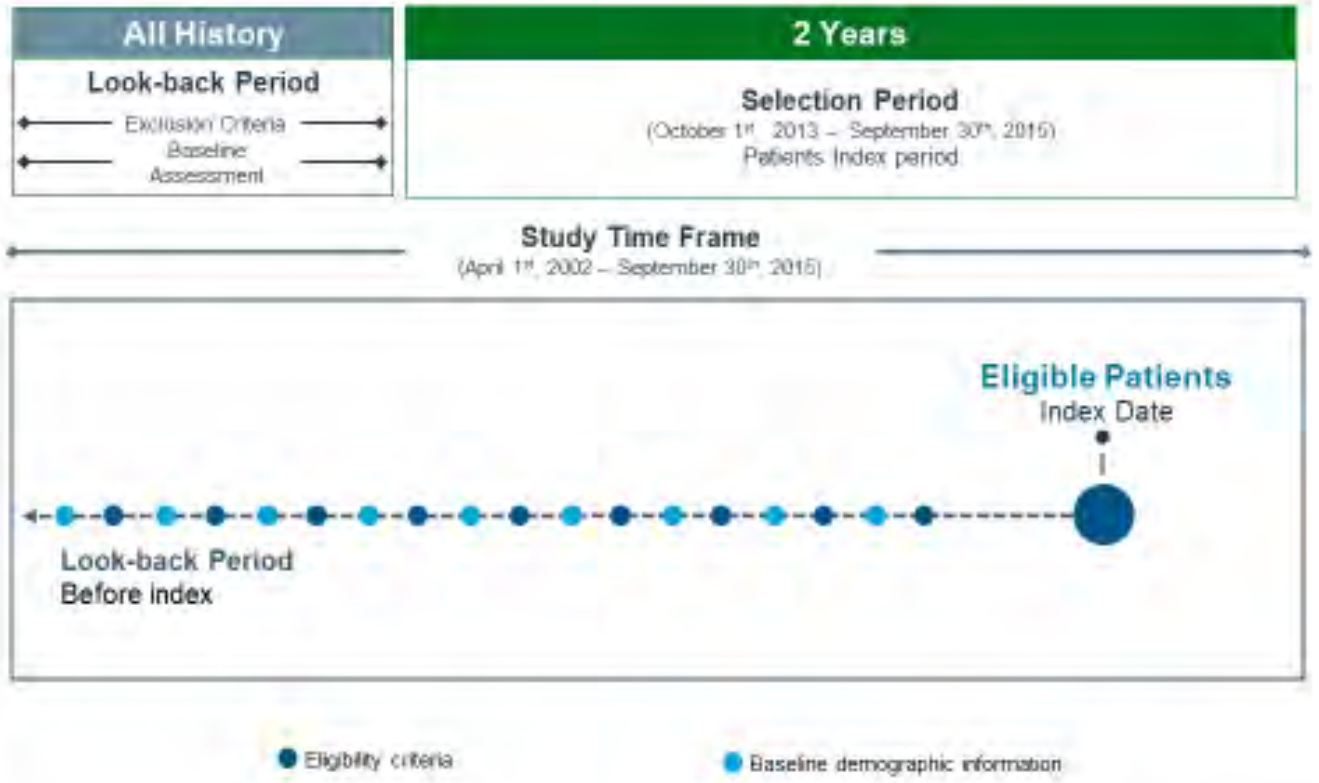
- A 2-year period from Oct 1st, 2013 to Sept 30th, 2015 will be used to select patients that have met the inclusion and exclusion criteria

Index Date:

- Eligible patients will be indexed on their most recent HbA1c in the selection period

Look-back Period:

- Patients' entire histories prior to the index date will be assessed for comorbidities
- In addition, a one-year period prior to index will be evaluated to identify laboratory test values used to determine HbA1c



Methods – Data source

- The **ICES Data Repository** contains the **ODD**, which uses a validated algorithm to identify individuals with diabetes based on physician service claims and hospitalization records[3]
  - Patients' encrypted OHIP card number was used to link ICES datasets to follow patient through each healthcare touchpoint
- Demographic information were collected from **registered persons database** (RPDB)
- Data on hospital admissions was collected from **discharge abstract database** (DAD) whereas **National Ambulatory Care Reporting System** (NACRS) was used to collect data on emergency department visits
- The **Ontario drug benefit plan database** (ODB) captured data on all prescription claims dispensed
- The **Home care database** collected data on records related to home care
- **Ontario Laboratory Information System Database** was used for collecting laboratory data

Methods – study population

Exclusion criteria:

- A T1DM diagnosis any time during the study period
- Patient was <15 years old at the time when first diagnosed with diabetes
- Patient was <30 years old at their index date
- Gap in Ontario Health Insurance Plan (OHIP) coverage within 1 year before the index date

Cohort definitions:

- Sensitive definition: >2 physician visits (OHIP 250 claims) or >1 drug claim for diabetes OR >1 hospitalization with diabetes within 1 year (Sens: 90.0%, Spec: 97.7%, PPV 82.6%)[3]
- Specific definition: >3 physician visits within 1 year (Sens: 79.9%, Spec: 99.1%, PPV 91.4%)[3]



Methods – analysis

- Descriptive analyses were conducted using number and percent for categorical variables (age groups, sex, income quintiles, rural residence, etc.) and mean and median for continuous variables (age, 1-year average HbA1C, HDL, LDL, etc.)
- Comorbidities were identified using ICD-9-CM and ICD-10-CA diagnoses codes, laboratory values, and OHIP billing codes
  - Prevalence of comorbidities was defined by relevant codes at any time prior to index date

Results

Variable	Value	Specific	Sensitive
Patient Count	N	783,228	1,093,812
Age	Mean ± SD	64.82 ± 12.87	64.05 ± 13.27
	Median (IQR)	65.00 (56.00-74.00)	64.00 (55.00-74.00)
Age Group	30-45	57,032 (7.3%)	96,769 (8.8%)
	46-55	132,714 (16.9%)	196,122 (17.9%)
	56-65	210,427 (26.9%)	290,314 (26.5%)
	66-75	212,508 (27.1%)	282,926 (25.9%)
	76-85	130,304 (16.6%)	171,978 (15.7%)
	86+	40,243 (5.1%)	55,703 (5.1%)
Sex	Female	363,284 (46.4%)	520,404 (47.6%)
	Male	419,944 (53.6%)	573,408 (52.4%)
Income Quintiles	1: Lowest	183,152 (23.4%)	254,818 (23.3%)
	2: Medium-low	174,395 (22.3%)	242,049 (22.1%)
	3: Middle	159,640 (20.4%)	223,432 (20.4%)
	4: Medium-high	140,011 (17.9%)	196,666 (18.0%)
	5: Highest	123,610 (15.8%)	174,672 (16.0%)
	Missing	2,420 (0.3%)	2,175 (0.2%)

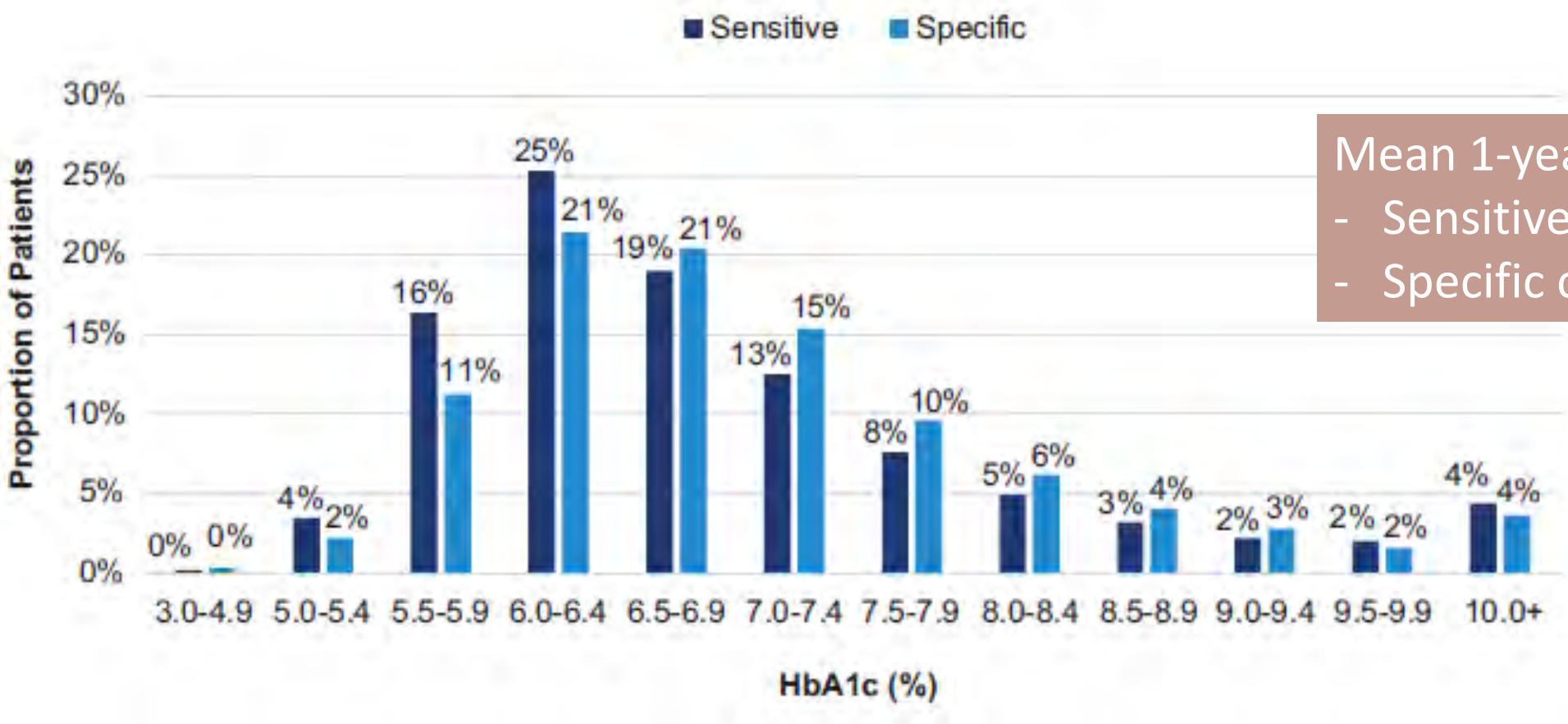
Results

Variable	Value	Specific	Sensitive
Rural Residence	1: 1,500,000+	362,861 (46.3%)	510,321 (46.7%)
	2: 500,000-1,499.999	111,432 (14.2%)	155,372 (14.2%)
	3: 100,000-499,999	166,479 (21.3%)	228,691 (20.9%)
	4: 10,000-99,999	62,156 (7.9%)	85,778 (7.8%)
	5: <10,000: Strong MIZ	40,405 (5.2%)	55,942 (5.1%)
	6: <10,000: Moderate MIZ	26,552 (3.4%)	38,387 (3.5%)
	7: <10,000: Weak/no MIZ	11,789 (1.5%)	17,865 (1.6%)
	9: Missing	1,554 (0.2%)	1,456 (0.1%)
LHIN	01: Erie St. Clair	38,584 (4.9%)	52,900 (4.8%)
	02: South West	54,651 (7.0%)	74,422 (6.8%)
	03: Waterloo Wellington	37,252 (4.8%)	51,054 (4.7%)
	04: Hamilton Niagara Haldimand Brant	81,409 (10.4%)	113,124 (10.3%)
	05: Central West	63,453 (8.1%)	87,261 (8.0%)
	06: Mississauga Halton	67,377 (8.6%)	94,285 (8.6%)
	07: Toronto Central	57,573 (7.4%)	82,664 (7.6%)
	08: Central	110,279 (14.1%)	156,365 (14.3%)
	09: Central East	109,322 (14.0%)	151,960 (13.9%)
	10: South East	30,570 (3.9%)	42,054 (3.8%)
	11: Champlain	62,274 (8.0%)	88,366 (8.1%)
	12: North Simcoe Muskoka	24,074 (3.1%)	33,067 (3.0%)
	13: North East	34,591 (4.4%)	48,448 (4.4%)
	14: North West	11,351 (1.4%)	17,238 (1.6%)
	15: Missing	468 (0.1%)	604 (0.1%)

Results

Variable	Value	Specific	Sensitive
HDL-C	Mean ± SD	1.23 ± 0.36	1.24 ± 0.36
	Median (IQR)	1.17 (0.98-1.42)	1.19 (0.99-1.43)
	0.00-1.00	196,824 (25.1%)	257,221 (23.5%)
	1.01-1.30	260,374 (33.2%)	360,367 (32.9%)
	1.31+	245,154 (31.3%)	355,481 (32.5%)
	Missing	80,876 (10.3%)	120,743 (11.0%)
LDL-C	Mean ± SD	2.05 ± 0.87	2.19 ± 0.92
	Median (IQR)	1.87 (1.42-2.54)	2.01 (1.50-2.76)
	0-<3.5	640,100 (81.7%)	860,576 (78.7%)
	3.5+	50,004 (6.4%)	94,141 (8.6%)
	Missing	93,124 (11.9%)	139,095 (12.7%)
Time from Diagnosis to Index Date	Mean ± SD	8.26 ± 5.89	7.28 ± 6.53
	Median (IQR)	7.00 (3.00-12.00)	6.00 (2.00-11.00)

Results – HbA1c

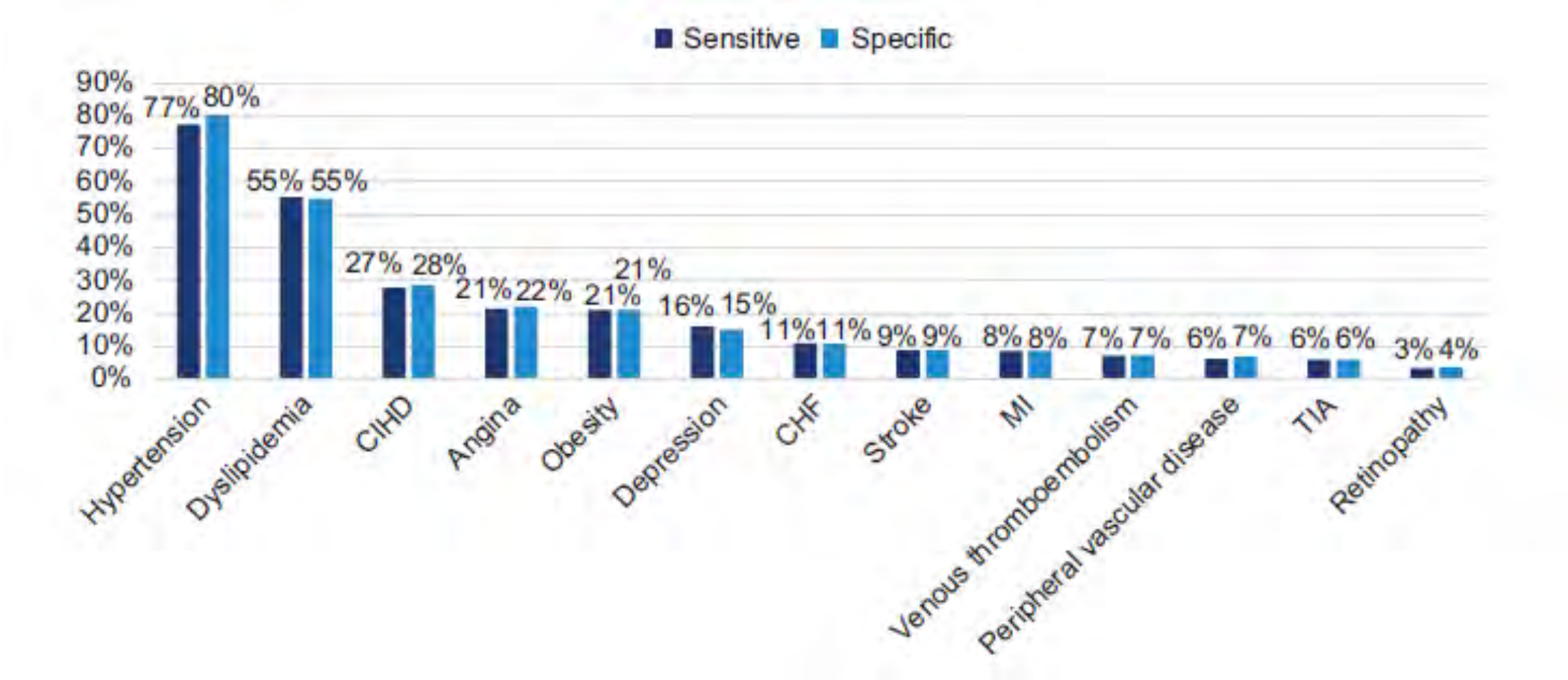


Mean 1-year HbA1c
- Sensitive cohort: 6.9%
- Specific cohort: 7.4%

Discussion - HbA1c

- When using the specific versus sensitive cohort definition, the HbA1c distribution shifted to slightly higher HbA1c values
- Literature suggest patients with high HbA1c are at increased risk of comorbidities[4,5]
- Despite this, the proportion of patients with comorbidities were comparable between the two cohorts
- This suggests that comorbidities experienced by those with T2DM might have been underreported

Results - comorbidities



Discussion - comorbidities

- A high prevalence of cardiovascular disease was identified in our sensitive and specific cohorts
  - Hypertension (77% and 80% respectively)
  - Dyslipidemia (55% and 55% respectively)
  - Chronic ischemic heart disease (27% and 28% respectively)
- Data was collected before widespread use of SGLT-2 inhibitors and GLP-1 receptor agonists for cardiovascular protection in diabetes.

CONCLUSION - SUMMARY

Our study was a large, population-level analysis of patients with T2DM in Ontario, Canada

The results provide a comprehensive look at the demographic and clinical characteristics of patients with T2DM in Ontario

While the sample sizes differed between the populations identified with the sensitive and specific definition, the demographic and clinical characteristics were comparable

Conclusion – NEXT STEPS



The high proportion of patients with comorbidities further illustrate the importance of taking a comprehensive approach to patient management



Future studies should investigate how these comorbid conditions affect the outcomes and management of patients with T2DM

Gastroenterology



Dr. Lawrence Hookey
Division Chair



Dr. Jennifer Flemming
Research Lead

Summary

- *Improving patient-physician interaction in managing disorders of common GI diseasess*
- *Analysis of high rate of liver-related mortality in Hepatitis C cirrhosis in low income neighbourhoods*
- *Recalcitrant Gastroesophageal Reflux Disease (GERD): Evaluating the referral patterns for non-protein pump inhibitors responsive GERD, along with deep patient evaluation*
- *Assessing the relationship between globes sensation and gastric inlet patch, and effectiveness of ablation of the patch*
- *Evaluating the rate of clinically significant upper GI findings in patients with positive stool tests*
- *Improving colonoscopy preparation in patients with diabetes*
- *Cost assessment of endoscopic ultrasound guided biliary drainage compared to percutaneous biliary drainage*
- *Assessment of cognitive load in novice endoscopists using AI*
- *Predictors and outcome of fibrosis in colorectal endoscopic submucsal dissection*
- *Clinical impact of HER2 status on esophageal adenocarcinoma removed with ESD*

Division of Gastroenterology

The division of gastroenterology is involved in a wide variety of research activities. We look forward to mentoring interested residents in research projects. Below are some of the proposed projects that trainees may get involved with:

Motility/Medical Education: Dr. Rodrigues (davidmario.rodrigues@kingstonhsc.ca)

1) **The impact of a scope navigation system on ergonomics and endoscopist hand movement during routine colonoscopy**

Colonoscopy involves inserting a flexible tube into a patient's anus and through the colon and to the cecum. The procedure can be challenging due to sharp angulations and loop formation. These issues can lead to repetitive stress injuries over time. Navigation symptoms can help the gastroenterologist recognize and resolve such issues; however, it is unclear whether the scope navigation system has an appreciable effect on the ergonomics of scope insertion.

This project will utilize hand motion technology and determine if scope navigation positively influences physician hand movement during colonoscope insertion.

2) **How to improve the patient-physician interaction in managing disorders of gut brain interaction: The patient perspective**

Evidence suggests that we need to improve the physician-patient relationship in order to properly care for patients with disorders of gut brain interaction (DGBIs), such as IBS; however, there is no clear guidance from the patient perspective on how to accomplish this.

This study will employ qualitative methodology and examine the patient perspective of the strengths and weaknesses of the patient-physician interaction in the context of DGBIs. We will attempt to establish common themes that will help guide the way we care patients that suffer from these ailments.

Therapeutic endoscopy: Dr. Hookey (lawrence.hookey@kingstonhsc.ca)

1) Understanding bad bowel preps
    - Patient-related factors associated with poor bowel preparation
    - Opportunity to submit a resident PSI grant to perform a clinical trial of oral sodium phosphate to improve preparation in this population

2) The association between CT colonography and incident right-sided colon cancer using ICES data

Higher Rates of Liver-Related Mortality in those with Hepatitis C Cirrhosis Residing in the Most Low-Income and Unstable Neighbourhoods

Nawid Sayed MD[1], Maya Djerboua MSc[2], Jennifer Flemming MD MAS [1-3]

[1]Departments of Medicine and [3]Public Health Sciences, Queen's University; [2]ICES-Queen's, Kingston, Canada

BACKGROUND

- Society has struggled to support marginalized groups typically affected by liver disease.
- Inconsistencies in primary and secondary prevention strategies have disproportionately burdened those who lack appropriate resources to manage their medical conditions.
- A high proportion of individuals with hepatitis C (HCV) cirrhosis come from marginalized socioeconomic backgrounds, however, the impact of their social determinants of health on liver-related outcomes is not well established.

Objective: To evaluate the associations between neighbourhood-level household income, residential instability, and ethnic diversity with liver-related mortality among patients with HCV cirrhosis.

METHODS

- Study Design: Retrospective population-based cohort study using data housed at IC/ES from 2000-2018
- Study cohort: Individuals with HCV cirrhosis between 18-70 years of age identified using validated case definitions incorporating viral serology
- Main exposures: Neighbourhood-level residential instability and ethnic concentration quintiles (derived from the Ontario Marginalization Index – Table 1) and income quintile from postal code of residence.
- Primary outcome: Liver-related mortality
- Statistical approach: The association between the exposures and outcomes were evaluated using 3 separate multivariable competing risk regression models (non-liver death and LT as competing events) to generate sub-hazard ratios with a P <.01 considered statically significant.

Table 1: ON-MARG DIMENSIONS

Residential instability	Proportion of the population living alone	Proportion of the population who are not youth (aged 16+)	Average number of persons per dwelling	Proportion of dwellings that are apartment buildings
	Single/divorced/widowed population	Proportion of dwellings that are not owned	Proportion who moved during the past 5 years	
Ethnic Diversity	Proportion of recent immigrants (arrived in the 5 years prior to census)	Proportion who self-identify as a visible minority		

RESULTS

Table 1: Baseline demographics of study population

Variable	N=22,865
Age (years)	51.6
Sex (M) - n(%)	15,576 (68%)
CHF - n(%)	793 (3%)
Pre-existing hypertension - n(%)	7,136 (31%)
Pre-existing diabetes mellitus - n(%)	6,768 (30%)
MELD-Na score	8.8± 4.2
Rurality (urban) - n(%)	20,552 (90%)
Charlson comorbidity index (mean + SD)	0.3 ± 1.0
History of mood disorder - n(%)	2,894 (13%)
Previous psychiatric admission - n(%)	5,053 (22%)
History of substance abuse - n(%)	5,963 (26%)
Previous suicide attempt or self-harm - n(%)	1,896 (8%)
History of non-HCC malignancy - n(%)	1,286 (6%)
History of HCC - n(%)	1,130 (5%)
History of obesity - n(%)	1,144 (5%)
All-cause mortality - n(%)	8,022 (35%)

Table 2: Multivariate competing risk regression models evaluating association between neighbourhood income quintiles, ethnic diversity, and residential instability with liver-related mortality in Ontario 2000-2018

	Liver-related mortality					
	Unadjusted			*Adjusted		
Exposures	sHR	95% CI	P value	sHR	95% CI	P value
Model 1: Income Quintile						
1 (lowest)	1.19	1.07-1.33	0.002	1.3	1.16-1.46	<.001
2	1.18	1.05-1.32	0.006	1.25	1.11-1.41	<.001
3	1.01	0.90-1.14	0.872	1.06	0.94-1.20	0.362
4	1	0.88-1.14	0.972	1.04	0.91-1.18	0.571
5 (highest)	1	Ref	-	1	Ref	-
Model 2: Residential Instability						
1 (lowest)	1	Ref	-	1	Ref	-
2	1.15	1.02-1.31	0.027	1.17	1.03-1.34	0.02
3	1.12	0.99-1.26	0.083	1.17	1.02-1.33	0.02
4	1.26	1.12-1.41	<.001	1.34	1.19-1.51	<.001
5 (highest)	1.20	1.08-1.34	<.001	1.26	1.12-1.42	<.001
Model 3: Ethnic Diversity						
1 (lowest)	1	Ref	-	1	Ref	-
2	0.89	0.80-0.99	0.033	0.91	0.82-1.02	0.116
3	0.96	0.87-1.07	0.488	0.99	0.88-1.11	0.809
4	0.86	0.78-0.95	0.003	0.85	0.76-0.95	0.004
5 (highest)	0.86	0.78-0.95	0.003	0.84	0.75-0.94	0.002

* All models adjusted for age at cohort entry, sex, co-morbidities, rurality, history of substance abuse, history of self-harm/suicide, and decompensated cirrhosis

RESULTS

A description of the study cohort is outlined in Table 2.

A large proportion of the study population demonstrated some degree of comorbidity, including history of hypertension, diabetes, and previous substance use.

Study population demonstrates a high all-cause mortality rate of 35% at the end of the follow-up period in December 2018

In adjusted analyses, the extremes of income quintile, residential instability, and ethnic diversity were all associated with a higher sub-hazard of liver-related mortality (Table 3).

CONCLUSION

1. In individuals with HCV cirrhosis, residing in neighbourhoods with low household income and residential instability is significantly associated with increased risk of liver-related mortality.
2. Those living in areas of high ethnic diversity had a lower hazard of liver-related death.
3. Poverty is a larger determinant of liver-related deaths than is ethnic diversity.

This information indicates a need to further understand how poverty influences poor and to target efforts around reducing the socioeconomic inequalities faced by individuals with HCV cirrhosis.

Nawid Sayed, nsayed@qmed.ca

General Internal Medicine



Dr. Lauren Marcotte
Division Chair



Dr. Don Thiwanka Wijeratne
Research Lead

Summary

- *Improving patient satisfaction for breast cancer care delivery*
- *Investigation to improve management of diabetes patients with breast cancer*
- *Benefits of virtual medical education for large groups*
- *Remote training of Point-of-Care Tele-Ultrasound for non-experts*
- *Text messaging in cancer support care*
- *Strategies to prevent re-admissions to hospital for COPD*
- *Improve language barriers for safe medicine use in immigrants and older residents*
- *Use of health administrative data to identify patients with pulmonary hypertension*
- *Investigating mechanisms of cardiovascular injury to optimize care in cancer survivors*
- *Use of activity trackers to measure frailty transitions in older critical care survivors*
- *Use of intravenous Vitamin C in adults with sepsis*

Research Projects:

1. **Integration of Point of Care Ultrasound with Physical Examination Teaching for Internal Medicine Residents: A Pilot Study** Amer Wali (fellow) with Dr Marie Leung as supervisor.

2. **Gender Differences in the use of Point of Care Ultrasound in the Emergency Department- A Systematic Review**

Amer Wali (fellow) with PI iDr Almufleh.

3. **PROFLUIDS Study** — An international observational study of fluid administration practices in patients with acute respiratory failure. Aim is to compare practices between high resource settings and LMIC. Research activities would involve abstracting data from the charts of patients mechanically ventilated in the ICU, and contributing to analysis. PI D. Maslove

4. **Neutrophil mass cytometry in septic shock** — Data analysis using R to investigate differences in mass cytometry between patients enrolled in a septic shock study (D. Maslove PI)

Mass Cytometry Reveals Complex Neutrophil Heterogeneity in Patients With Septic Shock

Christina Yu[1,2], Patricia D.A. Lima[1,2], David M. Maslove[2,3,4]

1. Queen's CardioPulmonary Unit, Queen's University, Kingston, Ontario, Canada; 2. Department of Medicine, Queen's University, Kingston, Ontario, Canada; 3. Department of Critical Care Medicine, Queen's University, Kingston, Ontario, Canada; 4. Kingston Health Sciences Centre, Kingston, Ontario, Canada

Introduction

Characterizing the cellular and molecular heterogeneity of sepsis is key to enhancing treatment specificity and response. Building upon previous evidence of neutrophil heterogeneity within sepsis based on mRNA expression patterns, we investigated mass cytometry profiling of neutrophil heterogeneity and their key association with clinical outcomes. Known activation and maturation markers were used to distinguish between subtypes.

Methods

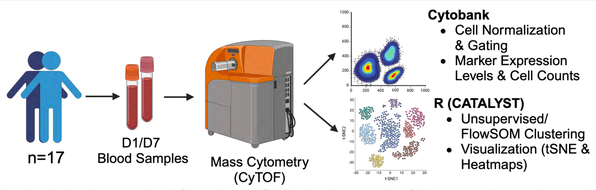


Fig 1: Patients enrolled from the LOVIT trial as part of this sub-study at day 1 (D1; first day in the ICU) and day 7 (D7). Blood cells were stained using antibodies conjugated with metals, and data were acquired using Helios (CyTOF). Neutrophils were selectively gated, and further analysis was conducted using Cytobank or R (CATALYST).

Results

CyTOF Workflow

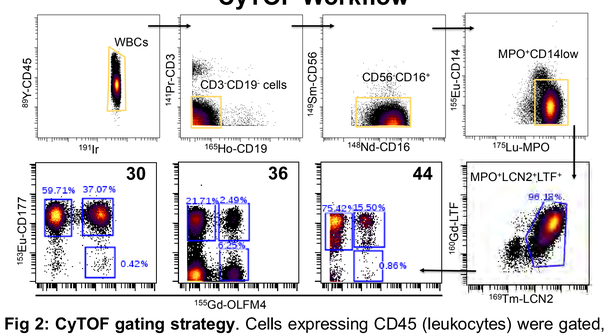


Fig 2: CyTOF gating strategy. Cells expressing CD45 (leukocytes) were gated, followed by a negative selection of cells expressing CD3 (T cells), CD19 (B cells), CD56/CD16 (NK cells). Neutrophils were identified via selecting cells highly expressing MPO and low CD14. Further gating identified neutrophils expressing Lipocalin-2 (LCN2) and Lactoferrin (LTF), followed by the identification of two major subsets: $CD177^{+}OLFM4^{+}$ and $CD177^{+}OLFM4^{-}$, and two small subsets: $CD177^{-}OLFM4^{-}$ and $CD177^{-}OLFM4^{+}$.

Results

Unsupervised Analysis Reveals 5 Distinct Neutrophil Clusters

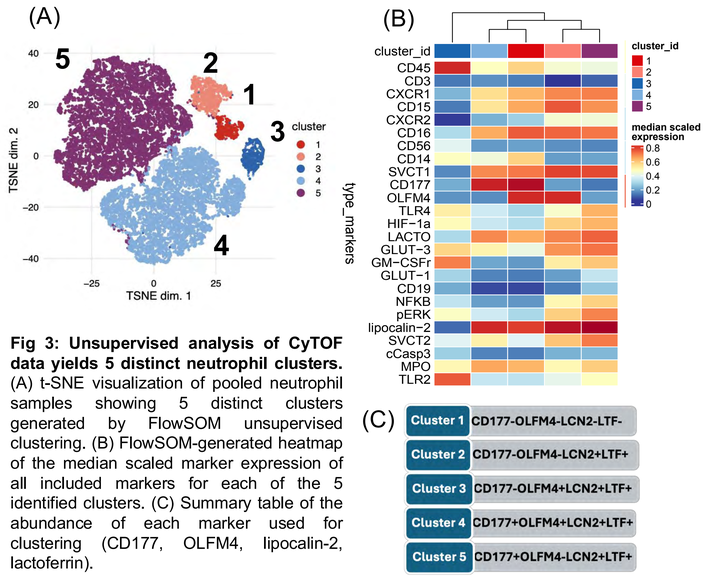


Fig 3: Unsupervised analysis of CyTOF data yields 5 distinct neutrophil clusters. (A) t-SNE visualization of pooled neutrophil samples showing 5 distinct clusters generated by FlowSOM unsupervised clustering. (B) FlowSOM-generated heatmap of the median scaled marker expression of all included markers for each of the 5 identified clusters. (C) Summary table of the abundance of each marker used for clustering (CD177, OLFM4, lipocalin-2, lactoferrin).

Flow Cytometric Quantification of $CD177^{+}OLFM4^{+}$ and $CD177^{+}OLFM4^{-}$

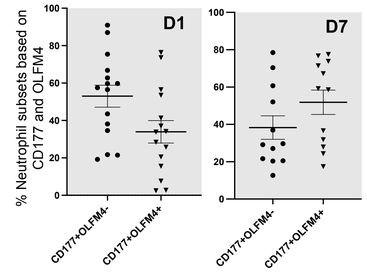


Fig 4: Prevalence (%) comparison of $CD177^{+}OLFM4^{+}$ vs. $CD177^{+}OLFM4^{-}$ neutrophils within D1 and D7. $CD177^{+}OLFM4^{-}$ neutrophils are more prevalent than $CD177^{+}OLFM4^{+}$ on D1, while $CD177^{+}OLFM4^{+}$ percentage seems to increase on D7. Data was normally distributed, and the paired t-test showed no statistical significance (D1 p = 0.095 and D7 p = 0.288). Mean±SD.

Cluster Connection to Clinical Outcome

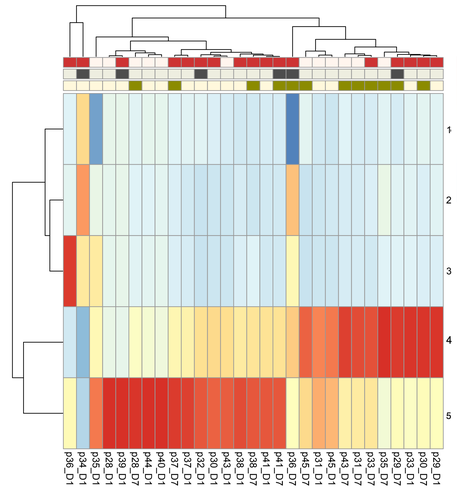


Fig 6: Heatmap of samples (columns) and outcomes sorted by cluster (rows). Samples clustered according to similarities using hierarchical clustering. Majority of samples are Cluster-4 or Cluster-5 predominant, with two outlier samples (D1 patients #34 and #36).

Relative Cluster Abundance Proportions

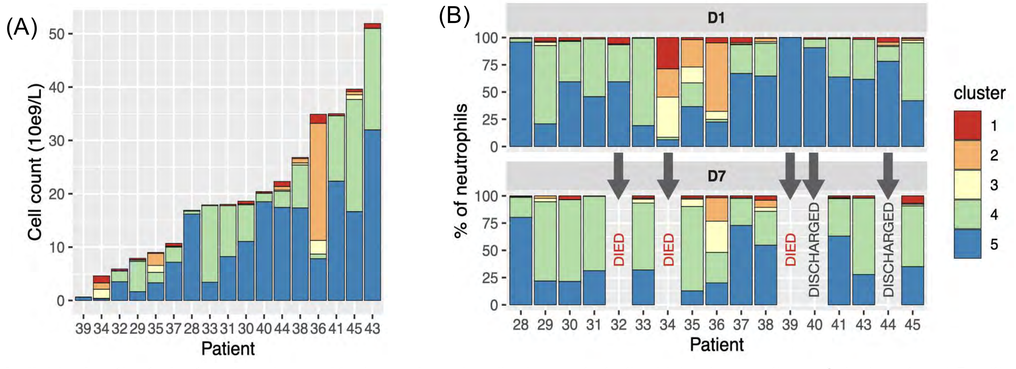


Fig 5: Individual patient cluster abundance. Most samples primarily demonstrate the highest proportions of clusters 4 and 5, with some exceptions. (A) Peak Day 1 white blood cell counts (WBC) colored by cluster proportions; no correlations between clusters and WBC counts are observed. Total WBC values ranged from $0.6x10^{9}$/L to $51.9x10^{9}$/L. (B) Each patient's cluster proportions for D1 vs. D7 time points. Lack of D7 sampling/analysis due to patient death or discharge is indicated.

Conclusion

- We identified distinct neutrophil clusters and subsets using mass cytometry with distinguishable marker expression and maturity.
- Five subsets are notable based on CD177, OLFM4, LCN2 and LTF expression.
- Neutrophil cluster incidence changes over time, with enrichment of cluster 5 ($CD177^{+}OLFM4^{+}$) on D7.
- Future research is needed to further explore these patterns and their correlation with clinical outcomes.

Acknowledgements

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Canadian Medical Education Journal

Black Ice

Five practical strategies to get a grip on large group cooperative virtual learning in medical education

Cinq stratégies pratiques pour réussir l'apprentissage coopératif virtuel en grand groupe dans programmes de médecine

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Abstract

The COVID-19 pandemic has led to the rapid replacement of in-person classroom learning with virtual large group learning. Done well, virtual large group learning can be an effective tool that provides flexibility, accessibility, and collaboration between learners. However, despite its potential benefits, human and technological challenges limit engagement and overall efficacy of large group virtual learning. The following account provides an evidence-based framework to maximize cooperative learning, learner engagement and retention of medical education in the virtual setting.

Résumé

La pandémie de la COVID-19 a rapidement entraîné le remplacement de l'apprentissage en classe en personne par l'apprentissage virtuel en grand groupe. Bien conçu, l'apprentissage virtuel en groupe peut être un outil efficace qui offre souplesse, accessibilité et possibilités de collaboration entre apprenants. Malgré ces avantages potentiels, les défis humains et technologiques limitent la participation à l'apprentissage virtuel en grand groupe et son efficacité générale. L'exposé suivant propose un cadre fondé sur des données probantes permettant de maximiser l'apprentissage coopératif, la participation des apprenants et la rétention des connaissances enseignées virtuellement dans les programmes de médecine.

Introduction

With the COVID-19 pandemic, medical education has rapidly transitioned, resulting in the accelerated uptake of virtual learning.[1,2] Done well, virtual large group learning can reach a broad audience,[1,3] provide flexibility for remote learners,[1] foster meaningful interactions,[2] and support multiple learning styles,[2] offering cost effective and efficient solutions even beyond the pandemic.

Outlined in the framework of cooperative learning, techniques that facilitate a culture of collaboration by cultivating positive interdependence, individual and group accountability, interpersonal and small-group skills , group processing, and face-to-face promotive interaction result in strong cooperative learning.[4] Learning processes that focus on cooperation rather than competition are seen to be more effective.[5] While large lecture environments erode this cooperative environment, virtual learning may further exacerbate the issue, decreasing interaction and immediate feedback between peers and teachers.[6] This is particularly troublesome in medical education, which unlike other branches of science, heavily incorporates peer-to-peer and student-teacher feedback through interactive simulations, case-based learning, and supervised patient interactions to teach communication, history, physical exam, and clinical reasoning skills that are unique.

Virtual learning may also be monotonous, have technical delays, and typically does not engage learners to the same degree as traditional face-to-face environments.[1-3] As student engagement with course material is an important predictor in their learning,[3] there is a need to make virtual

Training of Non-expert Users Using Remotely Delivered, Point-of-Care Tele-Ultrasound

A Proof-of-Concept Study in 2 Canadian Communities

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Abstract: Many physicians, particularly those practicing in remote regions, lack training opportunities to develop point-of-care ultrasound (POCUS) skills. This pretest-posttest study quantified the skill improvement of learners after participating in a virtual training program that used real-time, remotely delivered point-of-care tele-ultrasound (tele-POCUS) for teaching and learner feedback provision. Ten physicians practicing in an urban tertiary (Kingston, Ontario, Canada, n = 6) or remote care center (Moose Factory, Ontario, Canada, n = 4) completed a 3-week educational program that consisted of e-learning module review, independent image acquisition practice, and expert-guided tele-POCUS consultations. Pretraining and posttraining assessments were performed to evaluate skill enhancement in image acquisition, image quality, and image interpretation for cardiac and lung/pleura POCUS using a 5-point Likert scale. A total of 76 tele-POCUS consultations were performed during the study period. Significant improvements in image quality were noted following remotely delivered mentorship and guidance (all $P < 0.01$). In cardiac POCUS, pretraining and posttraining comparisons noted significant improvements in image acquisition (means, 2.69–4.33; $P < 0.02$), quality (means, 2.40–4.03; $P < 0.01$), and interpretation (means, 2.50–4.40; $P < 0.02$). In lung/pleura POCUS, significant improvements in image acquisition (means, 3.00–4.43; $P < 0.01$), quality (means, 3.23–4.37; $P < 0.01$), and interpretation (means, 3.00–4.40; $P < 0.01$) were demonstrated. Introductory ultrasound can be taught to novice users using a virtual, live-streamed training format with tele-POCUS while demonstrating significant enhancement in imaging skills.

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N.G. and D.J.B. contributed equally to this work.

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Key Words: point-of-care ultrasound, remote consultation, telecardiology, teleconsulting, tele-education.

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Over the past decade, point-of-care ultrasound (POCUS) has emerged as a frontline tool for cardiopulmonary assessment, providing treating physicians with real-time information to guide management.[1] Despite the clinical value of this tool, POCUS training and expertise are not universally available, mainly due to resource limitations, lack of training/supervision, and poor-quality assurance processes.[2] These barriers are further exacerbated in remote communities, where the lack of imaging resources, limited provider expertise, and significant geographic dispersion of communities may present significant barriers to care and POCUS uptake.[3,4]

To bridge this gap in care, tele-ultrasound has been used as a powerful alternative to formal imaging in resource-limited settings, allowing for rapid access to high-quality diagnostic services.[5] Evidence from a recent systematic review has shown that the quality of tele-ultrasound images obtained by nonexpert users is satisfactory for interpretation, clinical diagnosis, and management.[6] Despite its clinical utility, few opportunities exist for health care practitioners to gain practical POCUS skills outside of established residency programs.[7,8] Among those established programs, most are in person and lack the time and resource commitments necessary to integrate imaging skills into clinical practice, provide longitudinal learner feedback, and ensure ongoing quality assurance.[7,9] Furthermore, the COVID-19 pandemic has greatly disrupted traditional POCUS education and teaching, creating novel opportunities for training innovations that harness the power of virtual tools and platforms, such as tele-ultrasound.[9] With this in mind, recent survey data from Canada have indicated that trainees are not comfortable using telemedicine and desire specific clinical training that integrates expert supervision.[10] Given pandemic-related travel and physical distancing recommendations, there is an imminent need to offer virtual POCUS training to novice users that incorporates individualized feedback and longitudinal training.

The ARCTICA (Accelerated Remote Consultation by Tele-POCUS in Cardiopulmonary Assessment) program was designed to accelerate the virtual teaching of POCUS and

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Review

Screening and Management Recommendations for Type 2 Diabetes in Women With Breast Cancer

Laura Scott MD [a]; Lan-Linh Truong MD [a]; Robyn L. Houlden MD [b]; Don Thiwanka Wijeratne MD [a,c,d,*]

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Key Messages

- Breast cancer increases the risk of type 2 diabetes 1.07- to 4.27-fold depending on several factors (i.e. use of hormone therapy, adjuvant chemotherapy).
- Increased risk of diabetes begins at or just after diagnosis, and remains elevated for at least 10 to 15 years, with greatest risk in the first 2 years after diagnosis.
- This increased risk suggests that this population may benefit from more stringent screening, but further research is warranted before recommendations are made.

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ABSTRACT

Breast cancer increases the risk of type 2 diabetes 1.07- to 4.27-fold depending on patient and treatment characteristics, such as postmenopausal status, hormone therapy, and treatment with adjuvant chemotherapy. We evaluated the current evidence and considered the role of increased screening for type 2 diabetes in this at-risk population. This narrative review was conducted using Embase and MEDLINE databases. Keywords including diabetes and breast cancer were used. Articles were limited to those published in English between 2000 and 2022. It appears that the increased risk of diabetes begins at or just after breast cancer diagnosis, and remains elevated for at least 10 to 15 years, with greatest risk in the first 2 years after diagnosis. Subsets of patients with breast cancer appear to be at higher risk of developing type 2 diabetes, including those who were treated with adjuvant chemotherapy or hormone therapy. Further investigation is needed to develop specific screening recommendations for this population. If screening is performed with a glycated hemoglobin test during breast cancer treatment, then hemoglobin should be measured at the same time given the association of breast cancer therapy with anemia. Presence of breast cancer should not be a major factor when choosing among available antihyperglycemic agents. Overall, patients with breast cancer appear to be at an increased risk of developing type 2 diabetes. This increased risk suggests the need for further investigation to develop specific screening recommendations for this at-risk population.

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Mots clés:
diabète
dépistage
cancer du sein
pharmacothérapie

RÉSUMÉ

Le cancer du sein augmente le risque de diabète de type 2 de 1,07 à 4,27 fois en fonction des caractéristiques de la patiente et du traitement tels la postménopause, la thérapie hormonale et le traitement par chimiothérapie adjuvante. Nous avons évalué les données probantes actuelles et tenu compte du rôle du dépistage accru du diabète de type 2 dans cette population à risque. La présente revue narrative a été réalisée à partir des bases de données Embase et MEDLINE. Les mots clés, notamment le diabète et le cancer du sein, ont été utilisés. Les articles étaient limités aux articles publiés en anglais entre 2000 et

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RESEARCH/Original Article

Videoconferencing interventions and COPD patient outcomes: A systematic review

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SAGE

Meghan Bowman[1], Matthew Jalink[1,2], Isobel Sharpe[1], Siddhartha Srivastava[2] and Don Thiwanka Wijeratne[1,2]

Abstract

Introduction: Videoconferencing circumvents various physical and financial barriers associated with in-person care. Given this technology's potential benefits and timely nature, we conducted a systematic review to understand how videoconferencing for chronic obstructive pulmonary disease (COPD) follow-up care affects patient-related outcomes.

Methods: We included primary research evaluating the use of bidirectional videoconferencing for COPD patient follow-up. The outcomes of interest were resource utilization, mortality, lifestyle factors, patient satisfaction, barriers, and feasibility. We searched MEDLINE, EMBASE, EBM Reviews, and CINAHL databases for articles published from January 1, 2010, to August 2, 2021. Relevant information was extracted and presented descriptively and common themes and patterns were identified. The risk of bias for each study was assessed using design-specific validated tools.

Results: We included 39 studies of 18,194 patients (22 quantitative, 12 qualitative, and 5 mixed methods). The included studies were grouped by type of intervention; 18 studies explored videoconferencing for exercise, 19 explored videoconferencing for clinical assessment/monitoring, and 2 examined videoconferencing for education. Generally, videoconferencing was associated with high levels of patient satisfaction. There were mixed results in terms of its effects on resource utilization and lifestyle-related factors. Additionally, 12 studies were at high risk of bias, indicating that these results should be interpreted with caution.

Conclusions: The videoconferencing interventions resulted in high levels of patient satisfaction, despite facing technological issues. Overall, more research is needed to better understand the effects of videoconferencing interventions on resource utilization and other patient outcomes, quantifying their advantages over in-person care.

Keywords

ehealth, remote consultation, telecare, telehealth, teleconsulting, systematic review, COPD

Date received: 17 March 2022; Date accepted: 25 August 2022

Introduction

Chronic obstructive pulmonary disease (COPD) is a leading cause of global morbidity and mortality, accounting for 3.2 million deaths worldwide in 2019.[1–3] Furthermore, the European COPD Audit found a 90-day all-cause readmission rate of 35.1%.[4] In the United States, an analysis of Medicare claims data identified a 30-day all-cause readmission rate of 20.2%.[5] Researchers and policymakers have recently begun using telehealth, technology-based medical services where distance is a factor,[6] for COPD management.[7,8] Common applications of telehealth in COPD management include the monitoring of vital signs, patient education and self-management sessions, and pulmonary rehabilitation (PR) (i.e., supervised exercise and education sessions).[8] These technologies have the potential to benefit patients who experience barriers in access to care,[9] including rural,[10,11] elderly,[11,12] and Indigenous populations.[13]

Videoconferencing, a division of telehealth, provides bidirectional synchronous communication between providers and patients. It offers the benefits of face-to-face

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original reports abstract

Patient Satisfaction With Breast Cancer Care Delivery at the National Cancer Institute of Sri Lanka: Does Language Play a Role?

Susan J. Thanabalasingam, MD[1,2]; Sarith S. Ranawaka, MBBS[3]; Sathika S.C. Gunarathna, MBBS[3]; Bala Yathev, MBBS[3]; Christopher M. Booth, MD[4]; Sanjeewa Seneviratne, MBBS, MD, PhD[3,5]; Sanjeeva Gunasekera, MBBS, MD, MSc[5]; and Don Thiwanka Wijeratne, MBBS, MD, MSc[1,2]

PURPOSE This study sought to examine whether there was an association between language barriers and patient satisfaction with breast cancer care in Sri Lanka.

METHODS A telephone-based survey was conducted in the three official languages (Sinhala, Tamil, or English) among adult women (older than 18 years) who had been treated for breast cancer within 6-12 months of diagnosis at the National Cancer Institute of Sri Lanka. The European Organisation for Research and Treatment of Cancer Satisfaction with Cancer Care core questionnaire was adapted to assess three main domains (physicians, allied health care professionals, and the organization). All scores were linearly transformed to a 0-100 scale, and subscores for domains were summarized using means and standard deviations. These were also calculated for the Sinhalese and Tamil groups and compared.

RESULTS The study included 72 participants (32 ethnically Tamil and 40 Sinhalese, with 100% concordance with preferred language). The most commonly reported best aspect of care (n = 25) involved affective behaviors of the physicians and nurses. Ease of access to the hospital performed poorest overall, with a mean satisfaction score of 54 (30.5). Clinic-related concerns were highlighted as the worst aspect of the care (n = 10), including long waiting times during clinic visits. Sixty-three percent of Tamil patients reported receiving none of their care in Tamil and 18% reported experiencing language barriers during their care. Tamil patients were less satisfied overall and reported lower satisfaction with care coordination ($P = .005$) and higher financial burden ($P = 0.014$).

CONCLUSION Ethnically Tamil patients were significantly less satisfied than their Sinhalese counterparts and experienced more language barriers, suggesting there is a need to improve access to language-concordant care in Sri Lanka.

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INTRODUCTION

Breast cancer is the most common malignancy among females in Sri Lanka.[1,2] The incidence of breast cancer is rising, with a gradual increase of approximately 4% per year observed between 2001 and 2010.[3] Patient satisfaction with breast cancer care remains understudied in Sri Lanka, despite having a publicly funded health care system with universal access.[4]

Patient satisfaction is a valid, indispensable measure of quality of care.[5] It is an important quality indicator that may not necessarily align with other indicators of health care access and clinical outcomes. Several studies have reported there may be a relationship between patient satisfaction and perceived health care–related quality of life in the oncology setting.[6-8] Assessment of patient satisfaction is becoming increasingly important in oncology to optimize patient-centered care. Tools to evaluate patient experience to ascertain satisfaction are generally implemented with multidimensional surveys or questionnaires—these may help inform strategies to improve care delivery.[9]

The provision of patient-centered care is fundamentally tied to linguistically and culturally competent communication—when a health care provider and a patient do not share a common language or culture, communication difficulties that arise can have adverse consequences.[10] A demonstrated association between patient dissatisfaction with care and language barriers highlighted an unmet need among patients with cancer for linguistically sensitive care provision.[11] Health inequalities because of language barriers are mitigated when care providers are fluent in the patient's preferred language; hence, language-concordant care has been shown to improve outcomes.[12]

Sri Lanka is a multiethnic society including the Sinhalese majority, the Tamils, the Moors (a predominantly Muslim

ASSOCIATED CONTENT

Data Supplement

Author affiliations and support information (if applicable) appear at the end of this article.

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Systematic or Meta-analysis Studies

A systematic review of eHealth technologies for breast cancer supportive care

Bishal Gyawali [a,b], Meghan Bowman [b], Isobel Sharpe [b], Matthew Jalink [b,c], Siddhartha Srivastava [c], Don Thiwanka Wijeratne [b,c,*]

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Supportive care
Systematic review

ABSTRACT

Breast cancer places a substantial burden on patient physical and mental wellbeing, and the delivery of high-quality supportive care is essential at all stages of the disease. Given the increased uptake of technology in recent years, eHealth interventions may be a convenient and accessible method for supportive care. Within this context, we conducted a systematic review to describe and quantify the use of eHealth for breast cancer supportive care. We searched MEDLINE, EMBASE, and CINAHL databases for primary research studies published from 2016 to 2021 (present) that assessed the effects of eHealth interventions on adult patients with breast cancer. We explored the effects of the interventions on patient symptoms, lifestyle, satisfaction, and barriers, as well as factors related to feasibility and implementation. The risk of bias of each study was also assessed. Findings were presented according to stage of cancer care. We identified 43 relevant studies capturing n = 6,285 patients (30 randomized controlled trials and 13 non-randomized interventional studies); 5 evaluated patients who were newly diagnosed, 16 evaluated patients undergoing active treatment, and 22 evaluated patients in post-treatment follow-up. A total of 19 studies used mobile apps, 18 used online patient portals, 5 used text messaging, and 1 used both a patient portal and text messaging. We found that patients were broadly satisfied with the eHealth interventions; however, findings were less consistent for symptom and lifestyle-related outcomes. Eight studies were judged as high risk of bias. There was substantial between-study heterogeneity, which made it challenging to discern consistent trends. Overall, future research should continue to explore the use of eHealth for breast cancer supportive care, with a focus on improving patient symptoms.

Introduction

Managing the long-term care of patients with high-burden chronic conditions is a major challenge facing global healthcare today. Cancer is one of the most common chronic diseases worldwide [1] with breast cancer being the most common cancer among women [2]. In 2020, over 2 million women worldwide were newly diagnosed with breast cancer [2]. Beyond the burden that breast cancer itself poses, patients may also experience other comorbidities [3–5] requiring further support. Providing high quality supportive care to patients with breast cancer involves patient care management and providing relief from treatment side effects [6]. Strategies to manage breast cancer are important given the high global morbidity and mortality [7]. Breast cancer has a substantial burden on an individual's physical and mental wellbeing. Patients' quality of life (QoL) is impacted by psychological challenges and physical restrictions caused by both the disease and treatment side effects [8,9].

High-quality care is defined as effective, patient-centered, safe, timely, efficient, and equitable [10]. However, there are barriers and challenges preventing patients from receiving this care. Common examples include the distance to receive care, a lack of adequate or available transportation, and time constraints (i.e., travel time) [11]. Furthermore, these barriers may be more prevalent among elderly, rural, racialized, and socioeconomically disadvantaged individuals [12].

Electronic communication-based (eHealth) interventions are becoming a feasible option for providing supportive care to patients with breast cancer. eHealth is a cost-effective, bi-directional method of extending access to care for patients while providing healthcare workers

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Geriatric Medicine



Dr. Leah Nemiroff
Division Chair



Dr. Sudeep Gill
Research Lead

Summary

- *Improving care of the elderly, and the development of clinical teaching tools and education models*
- *Medical education on physical restraint use, end-of-life decision-making (e.g. determinants of code status), constipation, pressure ulcers, and Parkinson's disease treatment.*
- *Creation and assessment of a death certification module*
- *Investigating appropriate prescribing for medically complex older adults*
- *Assessment of rehabilitation potential and predictors of successful geriatric rehabilitation*
- *Pharmacoepidemiology including dementia treatment*
- *Perioperative geriatric care, polypharmacy and frailty*
- *Improving health care access with age friendly options in healthcare settings*
- *Improving the management of cognitive impairment and technology*
- *Modifying risk of frailty*
- *Reducing isolation and loneliness through intergenerational programming*

Division of Geriatrics
Department of Medicine, Queen's University

Geriatric Medicine Faculty Available to Mentor Resident Research Projects

Dr. Christopher Frank:
Dr. Frank's research interests relate to clinical work in Geriatrics and Palliative Care. Research topics could include medical education, physical restraint use, end-of-life decision-making (e.g. determinants of code status), constipation, pressure ulcers, and Parkinson's disease treatment.

Dr. Michelle Gibson:
Dr. Gibson could offer medical education opportunities for interested residents (e.g. prior project focused on assessing a death certification module).

Dr. Sean Goldhar:
Dr. Goldhar is interested in research as it pertains to medical education in Care of the Elderly, and the development of clinical teaching tools.

Dr. Sudeep Gill:
Research interests include: appropriate prescribing among older adults; medications and other health services utilization by medically complex older adults; assessment of rehabilitation potential and predictors of successful geriatric rehabilitation; pharmacoepidemiology including dementia treatment.

Dr. Taleen Haddad:
Dr. Haddad could discuss resident research opportunities focused on geriatrics topics. Research interests include perioperative geriatric are, polypharmacy and frailty.

Dr. Leah Nemiroff:
Dr. Nemiroff can offer medical education opportunities, with ideas that could be launched with an interested resident.

Dr. John Puxty (Division Chair):
Dr. Puxty has interests in age friendly communities, intergenerational interactions, frailty and cognitive impairment. Research opportunities include: 1) Age friendly healthcare - primary care settings and ER; 2) Cognitive impairment and technology; 3) Developing eBooks linked to common geriatric issues; 4) Modifying risk of frailty; 5) Reducing isolation and loneliness through intergenerational programming.

Dr. Kathryn Trebuss:
Dr. Trebuss could discuss resident research opportunities focused on geriatrics themes.

Dr. Erica Weir:
Dr. Weir could discuss resident research opportunities focused on geriatrics and/or public health.

We would be happy to discuss potential research projects with interested residents. Please feel free to contact individual faculty directly or Dr. Gill at (613) 544-4900 ext. 53257 or gills@providencecare.ca.

Generative AI to reduce EHR-related documentation burden: a multi-center implementation study
PI: S. Srivastava
Co-I: L. Nemiroff, L. Flynn, J. Matthews, M. Jaeger, R. Beveridge, D. Richardson, J. Drover, D. Leybourne, H. Braund, G. Wendt, L. Goonartne, V. O' Leary, S. Grin
Funding: Unburdening health care CMA grant ($1M)

Leveraging Simulation to Increase Competence in Assessment of Capacity in Psychiatry and Geriatric Psychiatry Training
PI: M. Hussain
Co-I: L. Nemiroff, S. O'Brien, M. Andrew, E. St. Denis, J. Kirkham, J. Pipitone, H. Braund
Funding: SEAMO endowed scholarship and education fund ($14,794)

Implementing a Standardized Triage Pathway in Geriatric Medicine to Improve Communication and Access to Appropriate Care
PI: K. Trebuss
Co-I: L. Nemiroff, C. Frank
Funding: SEAMO Quality Improvement Project Fund ($3,000)

Why Choose Two when One will Do? QI project on blood transfusion usage on the inpatient Geriatric Unit at PCH
PI: C. Frank

Implementing and sustaining a National GrandPals Program
PI: J. Puxty
Funding: $753,136 over 3 years from the Waltons Trust

Designing and implementing a collaborative Geriatric Medicine-Surgical Oncology clinic
PI: T. Haddad
Co-I: S. Merchant

ORIGINAL RESEARCH

Identifying the Priority Topics for the Assessment of Competence in Care of the Elderly

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ABSTRACT

Background

With Canada's senior population increasing, there is greater demand for family physicians with enhanced skills in Care of the Elderly (COE). The College of Family Physicians Canada (CFPC) has introduced Certifi ates of Added Competence (CACs), one being in COE. Our objective is to summarize the process used to determine the Priority Topics for the assessment of competence in COE.

Methods

A modified Delphi technique was used, with online surveys and face-to-face meetings. The Working Group (WG) of six physicians acted as the nominal group, and a larger group of randomly selected practitioners from across Canada acted as the Validation Group (VG). The WG, and then the VG, completed electronic write-in surveys that asked them to identify the Priority Topics. Responses were compiled, coded, and tabulated to identify the topics and to calculate the frequencies of their selection. The WG used face-to-face meetings and iterative discussion to decide on the final topic names.

Results

The correlation between the initial Priority Topic list identifie by the VG and that identified by the WG is 0.6793. The final list has 18 Priority Topics.

Conclusion

Defining the required competencies is a first step to establishing national standards in COE.

Key words: priority topics, key features, enhanced skills, care of the elderly, core competencies

INTRODUCTION

The average age of Canada's population is changing dramatically. The number of seniors has increased from 8% of the population in 1971 to 14.8% in 2012.[1,2] By 2020, family physicians can expect at least 30% of outpatients, 60% of inpatients, and 95% of nursing home patients to be aged over 65 years.[3,4]

Family physicians provide the largest share of care for older patients, but have variable training and experience with this population.[3,5] The College of Family Physicians of Canada (CFPC) has accredited enhanced skills training in 'Care of the Elderly' (COE) since 1992. Two hundred and forty-five family physicians had successfully completed this training by 2014, either as residents or via re-entry to training from practice.[6] These physicians provide both comprehensive care to seniors and advanced care to frail patients, often in collaboration with geriatric medicine specialists and geriatric psychiatrists. Given the well-recognized shortage of physicians trained in geriatric care, there will be an increasing demand for family physicians with enhanced skills and added competency in COE.[7]

There has been a shift towards competency-based medical education (CBME) of residents. A core competency (CC)

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Canadian Medical Education Journal

Brief Reports

Prescribing competency assessment for Canadian medical students: a pilot evaluation

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Abstract

Background: The knowledge and ability to prescribe safely and effectively is a core competency for every graduating medical student. Our previous research suggested concerns about medical student prescribing abilities, and interest in a standardized assessment process.

Methods: A multi-year cross-sectional study evaluating the feasibility, acceptability, and discriminative ability of an online prescribing competency assessment for final year Canadian medical students was conducted. Students at nine sites of four Ontario medical schools were invited to participate in an online one-hour exam of eight domains related to prescribing safely. Student feedback on perceived fairness, clarity, and ease of use formed the primary outcome. Exam performance and parity between schools were the secondary outcome.

Results: A total of 714 students completed the assessment during spring final review courses between 2016 and 2018. Student feedback was more favourable than not for appropriateness of content (53.5% agreement vs 18.3% disagreement), clarity of questions (65.5% agreement vs 11.6% disagreement), question layout and presentation (70.8% agreement vs 12.2% disagreement), and ease of use of online interface (67.1% agreement vs 13.6%

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We can do better: Addressing ageism against older adults in healthcare

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Abstract

Ageism in healthcare is a pervasive reality that leads to negative health outcomes for older adults. While it is often implicit, the COVID-19 pandemic threw explicit age discrimination in healthcare into sharp relief globally. In medicine, ageism translates into myriad forms of age discrimination that impact the provision of ethical care and range from 'micro' individual issues like paternalistic medicine or therapeutic nihilism to 'macro' system issues including barriers to timely and effective healthcare or exclusion from research trials. The culture of ageism in medicine can be unintentionally transmitted through role-modelling and the hidden curriculum. Strategies to combat ageism and provide ethical healthcare include intergenerational learning, educational programs, and strong leadership from organizations to enact policy and practice changes.

Introduction

Ageism is the stereotyping (how we think), prejudice (how we feel), and discrimination (how we act) against people solely on the basis of their chronological age.[1,2] For those of us in medicine who work with older adults, this is an undeniable and pervasive reality, an added challenge to the already often complex health and wellness battle our patients face daily. Although we aim to provide ethics-based care, ageism leads to a prevalent form of discrimination that is socially accepted and mainly unchallenged, possibly because it is most often implicit and subconscious.[1,2] In many contexts, age alone may be considered adequate justification for disregarding medical ethics by treating older adults unequally and limiting their access to resources or meaningful engagement in healthcare decisions – even when the patient has capacity (contrary to the principles of beneficence, justice, and patient autonomy).[1,3]

The COVID-19 pandemic exposed the grave consequences of age discrimination explicitly to the world – with age (rather than individual risks) being used as a firm cut-off for rationing care in some areas,[4] along with disproportionate physical and social isolation and lack of access to healthcare.[5] Healthcare workers, older adults, and their families have witnessed the consequences, with widespread precipitous declines in health, frailty, cognition, and mental health.[6,7] Rabheru[5] posits that the combination of deeply entrenched societal ageism and the COVID-19 pandemic 'has created a dual pandemic, leading to a widespread and devastating impact on older persons' lives everywhere'.

Ageism is considered by the WHO to be a human rights violation.[8] The pandemic has highlighted the urgency and gravity of addressing age discrimination in healthcare. Although ageism can affect any age group,[9] this article will focus on medical ageism towards older adults, how it impacts the provision of ethical and equitable healthcare, and consider strategies that leaders in medicine can apply to address age discrimination in healthcare.

Sources and consequences of ageism in healthcare

Older adults are a heterogenous group, and many of us who practice in Geriatric Medicine or Care of the Elderly advocate that chronological age is an inaccurate measure of health or prognosis.[4] Alternative measures, like the Clinical Frailty Scale, take into account multiple factors and are often better predictors of clinical outcomes.[4,10] However, stereotypes against older adults based on age alone develop early, with an onslaught of exposures to the negative aspects of ageing from movies, television, music, and social media.[1] We also pick up on implicit bias by observing the language and behaviour of those around us.[1] The positive or negative experiences we have had with older people throughout our lifetimes are also robust predictors of ageism directed at others.[11] The quality of contact with older adults, both personally and professionally, even goes so far as to impact the likelihood that medical and nursing students would consider a career in geriatrics.[12-15] Personal anxiety about one's own ageing, or fear about death and dying, also predict negative attitudes towards older people.[16,17]

In healthcare, negative attitudes towards older adults translate to age discrimination with lapses in ethics-based care in myriad forms, which can be seen from the 'micro' individual level to the 'macro' structural and systemic level. Ageism at the provider and patient level can manifest through paternalistic or infantilizing approaches, limited involvement in consent discussions, cognitive bias (e.g. attributing patient concerns/symptoms to 'old age'), exclusion from recommended screening, investigation and/or treatment guidelines, and therapeutic nihilism.[12,18] We have all seen examples of these kind of breaches of medical ethics – confidential information or

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The MedSafer Study—Electronic Decision Support for Deprescribing in Hospitalized Older Adults
A Cluster Randomized Clinical Trial

Emily G. McDonald, MD, MSc; Peter E. Wu, MD, MSc; Babak Rashidi, MD, MHI; Marnie Goodwin Wilson, MD, MPH; Émilie Bortolussi-Courval, CPN; Anika Atique, MDCM; Kiran Battu, RPh, PharmD; Andre Bonnici, BPharm; Sarah Elsayed, BSc; Allison Goodwin Wilson, PharmD; Louise Papillon-Ferland, BPharm, MSc; Louise Pilote, MD, PhD; Sandra Porter, BPharm; Johanna Murphy, MD; Sydney B. Ross, MSc; Jennifer Shiu, PharmD; Robyn Tamblyn, PhD; Rachel Whitty, RPh, MHSc; Jieqing Xu, MD; Gabriel Fabreau, MD, MPH; Taleen Haddad, MD; Anita Palepu, MD; Nadia Khan, MD; Finlay A. McAlister, MD; James Downar, MD, MHSc; Allen R. Huang, MDCM; Thomas E. MacMillan, MD, MSc; Rodrigo B. Cavalcanti, MD, MSc; Todd C. Lee, MD, MPH

IMPORTANCE Scalable deprescribing interventions may reduce polypharmacy and the use of potentially inappropriate medications (PIMs); however, few studies have been large enough to evaluate the impact that deprescribing may have on adverse drug events (ADEs).

OBJECTIVE To evaluate the effect of an electronic deprescribing decision support tool on ADEs after hospital discharge among older adults with polypharmacy.

DESIGN, SETTING, AND PARTICIPANTS This was a cluster randomized clinical trial of older (≥65 years) hospitalized patients with an expected survival of more than 3 months who were admitted to 1 of 11 acute care hospitals in Canada from August 22, 2017, to January 13, 2020. At admission, participants were taking 5 or more medications per day. Data analyses were performed from January 3, 2021, to September 23, 2021.

INTERVENTIONS Personalized reports of deprescribing opportunities generated by MedSafer software to address usual home medications and measures of prognosis and frailty. Deprescribing reports provided to the treating team were compared with usual care (medication reconciliation).

MAIN OUTCOMES AND MEASURES The primary outcome was a reduction of ADEs within the first 30 days postdischarge (including adverse drug withdrawal events) captured through structured telephone surveys and adjudicated blinded to intervention status. Secondary outcomes were the proportion of patients with 1 or more PIMs deprescribed at discharge and the proportion of patients with an adverse drug withdrawal event (ADWE).

RESULTS A total of 5698 participants (median [range] age, 78 [72-85] years; 2858 [50.2%] women; race and ethnicity data were not collected) were enrolled in 3 clusters and were adjudicated for the primary outcome (control, 3204; intervention, 2494). Despite cluster randomization, there were group imbalances, eg, the participants in the intervention arm were older and had more PIMS prescribed at baseline. After hospital discharge, 4989 (87.6%) participants completed an ADE interview. There was no significant difference in ADEs within 30 days of discharge (138 [5.0%] of 2742 control vs 111 [4.9%] of 2247 intervention participants; adjusted risk difference [aRD] −0.8%; 95% CI, −2.9% to 1.3%). Deprescribing increased from 795 (29.8%) of 2667 control to 1249 (55.4%) of 2256 intervention participants [aRD, 22.2%; 95% CI, 16.9% to 27.4%]. There was no difference in ADWEs between groups. Several post hoc sensitivity analyses, including the use of a nonparametric test to address the low cluster number, group imbalances, and potential biases, did not alter study conclusions.

CONCLUSIONS AND RELEVANCE This cluster randomized clinical trial showed that providing deprescribing clinical decision support during acute hospitalization had no demonstrable impact on ADEs, although the intervention was safe and led to improvements in deprescribing.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT03272607

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Supplemental content

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COMMENTARY

WILEY

Beta testing the potential link between the alpha antagonist tamsulosin and dementia

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COMMENTARY

Driven by increases in average life expectancy and the baby boomer bulge, the prevalence of Alzheimer's disease and related dementias is expected to soar in coming decades.[1,2] The costs of caring for this large and growing number of individuals with dementia are colossal and rival the financial burden imposed by conditions such as heart disease and cancer.[3] Of course, monetary costs alone do not capture the full impact of dementia on affected individuals and their families.

Only a handful of modestly effective medications are currently available to treat Alzheimer's disease and related dementias, and no new medications to treat dementia have been approved in well over a decade.[4] As a result, new insights into possible contributors to dementia pathogenesis are desperately needed. In this context, the study by Duan and colleagues in this issue of *Pharmacoepidemiology and Drug Safety* is a welcome addition to the literature.[5]

Duan and colleagues report a thoughtfully executed retrospective cohort study that evaluates the link between exposure to the alpha-adrenergic antagonist tamsulosin and the subsequent development of dementia. They use administrative data from US Medicare and focus on older male beneficiaries who were diagnosed with benign prostatic hyperplasia (BPH) to evaluate the relationship between tamsulosin and dementia. They present a variety of sensitivity analyses to make their case more persuasive, and results demonstrate a modest but statistically significant relationship that appears robust in a variety of comparisons (ie, against other alpha-adrenergic antagonists, against other drugs with a similar prescribing indication, and against no use of any BPH medication).

Duan and colleagues should be congratulated for presenting a compelling pharmacoepidemiology study, which builds on existing basic science that they cite in their introductory comments. This is the first study to report an association between exposure to tamsulosin and the development of dementia, and hopefully, it will spur other investigations using other datasets. At this early stage, however, clinicians and researchers might ask how they should incorporate this new information into their framework for understanding dementia pathogenesis. Should the causal inference suggested by this association be embraced or rejected, pursued vigorously, or monitored cautiously? Could the association between tamsulosin use and dementia be explained away by residual confounding that persists despite the investigators' use of various analytic techniques? And assuming that the link between tamsulosin and dementia is real, how big of a threat does it represent to individuals taking this alpha-adrenergic antagonist?

Analogous questions have been raised about the association between use of proton pump inhibitors (PPIs) and the development of dementia. Yang recently published a thoughtful critique that attempts to explain the inconsistent findings from the studies published so far that evaluate the association between PPIs and dementia.[6] However, in the case of the association between tamsulosin and dementia, we currently have only the report of Duan and colleagues to guide us.[5] They have produced a well-argued first test (or *alpha test*) to address methodologic questions about the observed association between tamsulosin and dementia and make the case that it represents an insight worth exploring further to clarify aspects of dementia pathophysiology.

We offer the following approach as a sort of *beta test*, using three helpful metrics to quantitatively gauge our confidence in their findings.

A first metric, cited by Duan et al. themselves, was introduced by Swaen and van Amelsvoort.[7] These authors propose an intriguing approach to weight the Bradford Hill criteria in a quantitative manner to produce an estimate of the probability that an observed association represents valid causal inference. Applying the method proposed by Swaen and van Amelsvoort to the findings of Duan et al, we generated a probability of 38% (ie, the probability that the association between tamsulosin use and development of dementia is causal). It would be inappropriate to focus solely on this probability estimate (and others may reasonably plug in slightly different numbers when using Swaen and van Amelsvoort's method and thereby arrive at a slightly different

Commentary on manuscript ID: PDS-16-0431.R1: "Tamsulosin and the risk of death in older men with benign prostatic hyperplasia" by Duan and colleagues

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Hematology



Dr. Annette Hay
Division Chair
Research Lead

Summary

- *Research into the patients with known vascular disorders to determine if patient had an undiagnosed bleeding disorder*
- *Investigations of the genetic origin of hematological disorders and cancer*
- *Impact of exogenous hormones on patients with bleeding disorders*
- *Development of bleeding assessment tools for patients with bleeding disorders and uterine pathologies*
- *Clinical trials on improving transfusion practice for patients undergoing chemotherapy and stem cell transplants*
- *Assessment of thrombotic disorders in emergency departments*
- *Improving assessment of various anemias in refugees and new immigrant populations*
- *Case studies on rare diseases and presentations of hemotological pathologies*
- *Affective therapies for multiple myeloma*
- *Use of medical devices to prevent pulmonary embolism in high risk patients*

Resident Research Projects –
Hematology Current/Past Projects 2024

Potential opportunities

1. Clonal hematopoiesis

Clonal hematopoiesis of indeterminate potential (CHIP) is increasingly being revealed to be associated with development of hematological malignancies and a host of other systemic, non-cancer disorders. Myeloid cancers such as acute myeloid leukemia and myelodysplasia often arise from multiple genetic mutations, which may occur over many years. Dr. Rauh's research is focused on the origins and clinical consequences of clonal hematopoiesis, and the application of next generation sequencing (NGS) in the clinical setting. He would be happy to talk with residents and try to match them with a project of interest.
Website: https://www.queensu.ca/rauhlab/home
Supervisor: Dr. Michael Rauh (rauhm@queensu.ca)

2. Bleeding Disorders

Dr. Paula James leads the Inherited Bleeding Disorders Program of Southeastern Ontario, along with Dr. Jennifer Leung. The research program spans laboratory and clinical research, including bleeding assessment tools. The James Lab are working on the use of menstrual effluent (ME) samples to isolate and culture human endometrial endothelial cells (HEECs) which will give insight into variability in heavy menstrual bleeding and other uterine pathologies in patients with von Willebrand disease. They are also working to validate the PBAC (pictorial bleeding assessment chart) score using a menstrual cup. This is laboratory based, wet-bench research, suitable for a resident with a reasonable amount of research time to dedicate to the project.
Website: https://letstalkperiod.ca/
Supervisor: Dr. Paula James (jamesp@queensu.ca)

3. Blood Transfusion

Transfusion of red blood cells, platelets, plasma and other products is an integral part of medicine. Multiple randomized clinical trials and guidelines inform practice. Dr. Callum's research is focussed on optimizing transfusion practice within the hospital setting. Interested residents can reach out to her to explore potential projects.
Supervisor: Dr. Jeannie Callum (Jeannie.callum@kingstonhsc.ca)

4. Thrombosis

Thrombotic disorders, including deep vein thrombosis and pulmonary embolism, are common. They are associated with morbidity, mortality and health care utilization. Dr.

Kerstin de Wit's research is focussed on clotting disorders, particularly in the emergency department. Interested residents can reach out to her to explore potential projects.
Supervisor: Dr. Kerstin de Wit (Kerstin.deWit@kingstonhsc.ca)

5. Inherited red blood cell disorders

Thalassemia and sickle cell disease are a major global cause of anemia and morbidity. In the Kingston region, prevalence is increasing with immigration. Dr. Natasha Satkunam established a hemoglobinopathy clinic in 2021 to serve the needs of this population. It is in its early phases and anticipated to grow, integrating with pediatrics and existing services for refugees and new immigrants. Interested residents can reach out to explore potential projects.
Supervisor(s): Dr. Natasha Satkunam (natasha.satkunam@kingstonhsc.ca) and Dr. Laura Wheaton (laura.wheaton@kingstonhsc.ca)

Current projects

6. Primary care patient management pathways

a) Elevated lymphocyte counts occur for a variety of reasons. Infection, smoking, splenectomy, chronic lymphocytic leukemia and other underlying causes may be present. A hospital wide initiative to "eliminate wait times" was launched in 2020. As part of this, primary care physicians and specialists are working together to develop primary care patient management pathways for commonly encountered conditions where long specialist wait times exist. A resident developed a new pathway to aid with diagnosis and management of low-risk cases in the community, and rapid identification of high risk features meriting urgent referral and specialist assessment.
b) Monoclonal gammopathy of undetermined significance – abstract submitted
c) Iron deficiency anemia – developed in collaboration with General Internal Medicine
d) Potential future pathways include erythrocytosis and thrombocytosis

https://kingstonhsc.ca/refer/hematology
Supervisors: Dr. Annette Hay (ahay@ctq.queensu.ca) and Dr. Bethany Monteith (Bethany.monteith@kingstonhsc.ca). Resident. Dr. Pallavi Ganguli.

Examples of completed projects

7. Refractory Hypercalcemia: Rare Presentation of a Common Disease

Hypercalcemia can be seen in patients with hematologic malignancies, but is rarely described in diffuse large B cell lymphoma. In this case report, an 81 year-old woman is described who presented to the ER with weakness, fatigue, weight loss and decreased appetite as we all increased thirst. She was discovered to be hypercalcemic and to have an intra-abdominal mass. Pathology showed a double hit (BCL2 and MYC) diffuse large B cell lymphoma. She was treated with R-CHOP and although experienced a

complicated course, eventually responded to chemotherapy. Key learning points about hypercalcemia are reviewed in this poster presentation.
Supervisor: Dr. Annette Hay (ahay@ctg.queensu.ca), Resident: Dr. Ali Tahir

8. Carfilzomib Toxicity: A Second Generation Proteosome Inhibitor Used in the Treatment of Relapsed and Refractory Multiple Myeloma

Multiple myeloma (MM) is a malignant clonal disorder of plasma cells with associated immunoglobulins or light chain production. The prevalence of MM is increasing, and the treatment landscape has changed drastically in the last decade. Novel agents such as carfilzomib and pomalidomide have been developed and show promise in clinical trials, however known and unknown toxicities must be carefully studied in order to optimize drug combinations and patient outcomes. This specific study is part of the larger MYX1 clinical trial, which is a single arm phase II, investigator initiated, multi-centre trial run through the Myeloma Cancer Research Network and the Canadian Cancer Trials Group (CCTG). The objectives are to determine the incidence of thrombotic microangiopathy, classify the suspected mechanisms of this toxicity and conduct a cost analysis to determine the financial toxicity of this novel agent.
Supervisor: Dr. Annette Hay (ahay@ctg.queensu.ca), Resident: Dr. Bethany Monteith

9. Can We Transfuse Wisely in Patients Undergoing Chemotherapy or Autologous Stem Cell Transplantation?

Current practice for many Canadian leukemia and bone marrow transplant centers is a liberal transfusion threshold of 2 units of PRBCs for a hemoglobin < 80 g/L, however there is little evidence assessing optimal transfusion targets, and a restrictive strategy appears feasible. In this study, the objective was to evaluate if a more restrictive (1 unit for Hgb $\leq$ 70 g/L) vs. liberal (2 units for Hgb $\leq$ 80g/L) RBC transfusion strategy reduces the overall RBC utilization without an increase in morbidity or mortality in patients receiving intensive inpatient induction chemotherapy for acute leukemia or conditioning for autologous stem cell transplant (ASCT). A total of 132 treatments involving 121 patients were included, and a significant decrease in RBC utilization was shown in both leukemia and ASCT patients, without an increase in morbidity or mortality. Cost savings of $3330.50 per cycle of induction chemotherapy and $666.10 per ASCT were also shown.
Supervisor: Dr. Sita Bhella, Residents: Dr. Michelle Lamarche and Dr. Danielle Hammond

10. Inferior Vena Cava Filter Utilization: A Comparison of Practice with Guidelines at KGH

Inferior Vena Cava (IVC) filters offer mechanical protection against pulmonary embolism in high risk patients; guidelines are specific about their use. The objective of this study was to determine compliance with current recommendations at Kingston Health Sciences Centre (KHSC). During the study period, 95 IVC filters were implanted at KHSC, with the decision to insert being consistent with recommendations in 58 patients (61.1%).

Complications were also documented, and arose in 21 patients (22.1%). Educational initiatives are underway at KHSC to optimize the use of IVC filters.
Supervisors: Dr. Janet Lui (janet.lui@queensu.ca) and Dr. Annette Hay (ahay@ctg.queensu.ca), Resident: Dr. Alex Trussler

11. Are We Choosing Mobilization Regimens for Autologous Stem Cell Transplantation in Multiple Myeloma Wisely?: A Single Centre Comparison of GCSF+/-Plerixafor vs. Cyclophosphamide/GCSF+/-Plerixafor

Multiple strategies are employed for mobilization of stem cells in autologous stem cell transplantation (ASCT). Cyclophosphamide/GCSF is an effective standard regimen, although there are reported toxicities associated with cyclophosphamide. Since Plerixafor was introduced in Canada, this mobilization agent has been increasingly used as needed with GCSF at Kingston Health Science Centre (KHSC), with elimination of cyclophosphamide. There is however high cost associated with Plerixafor. This retrospective review evaluated ASCT outcomes of multiple myeloma (MM) patients who had undergone stem cell mobilization with GCSF+/-plerixafor (G) vs cyclophosphamide/GCSF+/-plerixafor (CyG) at KHSC. 97 patients were included (47 in the G group and 50 in CyG) and showed that stem cell mobilization with CyG resulted in significantly higher total collection cell count and more efficient collection with higher yield on the first day of apheresis. It did not lead to less use of plerixafor as rescue, and was possibly associated with higher rates of febrile neutropenia. The “wise” mobilization regimen may vary depending on institutional resources for apheresis, cellular processing and to treat febrile neutropenia.
Supervisor: Dr. Sita Bhella, Residents: Dr. Chloe Yang and Dr. Mina Dehghani Mohammadabadi

Challenges and Knowledge Gaps facing Haemophilia Carriers: Perspectives from Patients and Healthcare Providers

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LET'S TALK PERIOD

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INTRODUCTION

- It is clear that carriers of hemophilia experience abnormal bleeding.[1]
- Knowledge gaps remain about the existence of abnormal bleeding in carriers causing mismanagement and a reduced quality of life.[1,2,3]

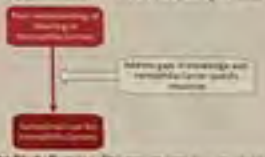


Figure 1. **The Study Purpose.** This project aims to uncover/add more knowledge to improve care for carriers.

AIM

- **Primary Objective:** Describe the major challenges and knowledge gaps facing hemophilia carriers from the perspective of both hemophilia carriers and healthcare providers.
- **Secondary Objective:** Produce educational materials targeting the challenges and knowledge gaps identified.

METHOD

- Participants: 11 Hemophilia Carriers, 11 Physicians, 8 Nurses
- Carriers participated in semi-structured, hour-long focus groups and completed a short-survey after.
- HCPs participated in only surveys.
- Questions asked were as follows:



Statistical Analyses:

- Opinions of participant groups on timing of testing FVIII/FIX levels for carriers, and circumstances for genetic testing for those under the age of consent, were compared using the Fisher's Exact test.
- P-values of <0.05 were used as the cut-point for statistical significance.

RESULTS

- 11 carriers participated in the study
- Carrier participants ranged from 21 to 69 years of age and were affiliated with five different Hemophilia Treatment Centres (HTC) in three different provinces across Canada
- Focus group discussions yielded four areas identified as major challenges



Survey Results:

- Similar beliefs regarding when factor testing should be done.
- Misalignment in beliefs regarding genetic testing (Table 1). When both study groups were asked about the circumstances under which genetic testing for a hemophilia carrier under the age of consent should be considered, hemophilia carriers were significantly more in favour of genetic testing than health care providers in all scenarios (Table 1).

CONCLUSIONS

- Interventions needed include:

1. Educational initiatives targeting healthcare providers outside of HTCs about abnormal bleeding in hemophilia carriers.
2. Educational initiatives targeting hemophilia carriers themselves to provide clear guidance on what constitutes abnormal bleeding and when to seek care.
3. Concrete treatment recommendations for abnormal bleeding symptoms in carriers.
4. Consensus on testing recommendations for young girls which accounts for the increased bleeding phenotype of hemophilia carriers.

- Educational materials addressing the issues identified, were created on the Let's Talk Period website (www.letstalkperiod.ca) and disseminated through our social media channels.
- Future projects will focus on the testing concerns identified by carriers and work towards establishing treatment recommendations specific to hemophilia carriers and the abnormal bleeding symptoms they experience.

REFERENCES

1. Gilbert L, Parnham A, Gerlach D, Debaun MR, Jacobs R. Haemophilia A carriers experience reduced health-related quality of life. Haemophilia. 2017;23(5):767-769.
2. Renaud M, Howell R, Robinson K, Greer W. Qualitative assessment of the emotional and behavioural responses of haemophilia A carriers to negative experiences in their medical care. Haemophilia. 2011;17(2):237-241.
3. Young J, Gilbert J, Tuttle A, et al. Evaluation of the self-administered bleeding assessment tool (Self-BAT) in haemophilia carriers and correlations with quality of life. Haemophilia: the Official Journal of the World Federation of Hemophilia. 2017;23(5):e536-e539.

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BAYER

PP-82

Poster Session Online

Does the use of an online screening tool affect referral outcomes? Preliminary results of the Let's Talk Period project

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INTRODUCTION

•Classification of bleeding symptoms as normal or abnormal is a challenge for both patients and physicians yet is critical in the diagnosis of an inherited bleeding disorder.
•An online Self-Administered Bleeding Assessment Tool (Self-BAT) is freely accessible via the Let's Talk Period website (www.letstalkperiod.ca). It can be used by patients to quantify their bleeding history and generate a final Bleeding Score (BS).

OBJECTIVE

•To determine if patients seen in a tertiary care clinic in Kingston, Ontario were more likely to be diagnosed with an inherited bleeding disorder and require more clinical intervention when initially referred due to an abnormal Self-BAT BS (normal ≤ 5 for women, ≤ 3 for men), as opposed to patients referred without the prior use of the Self-BAT as a screening tool.

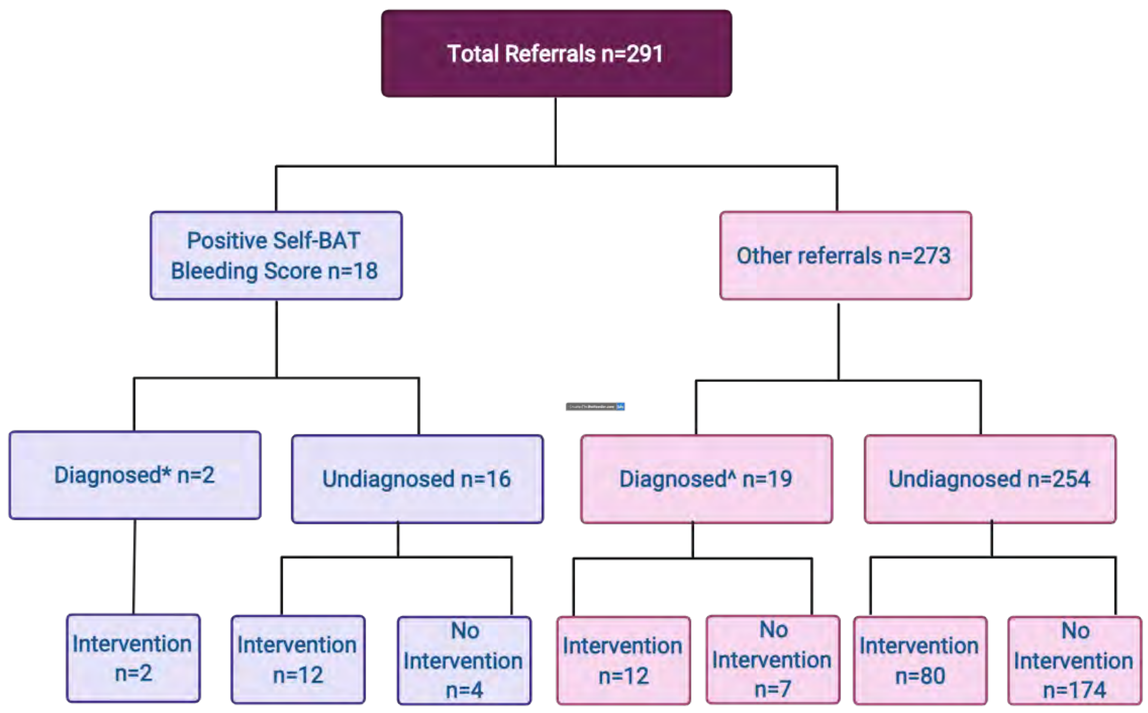
METHODS

•A retrospective, observational study
•REB approval was obtained
•Chart review of all clinic patients assessed for suspicion of an inherited bleeding disorder during a 5-year period
•Clinical assessment of bleeding symptoms was by expert administered Condensed MCMDM-1VWD Bleeding Score (BS)
•Subjects were divided into two groups: 1: Referred for abnormal Self-BAT BS or 2: Referred for other reasons; mucocutaneous bleeding, abnormal laboratory results or family history of an inherited bleeding disorder
•Further intervention is defined as: referral to other specialist, iron replacement or surgical/procedural management.

Subject Characteristics

	Referred for +Self-BAT BS n=18	Referred for other reasons n=273	*p*
Females (%)	18 (100.0)	245 (91.1)	0.233
Mean Age (range)	36.8 (19-74)	42.9 (18-82)	0.123
Median Expert Administered BS (range) *Reference range	8 (2-19) *0-56	4 (-2-19) *0-56	0.001
Hemoglobin (g/L), mean (range) *Reference range	131.7 (100-149) *115-155	135.8 (77-171) *115-155	0.251
Ferritin (ug/L), mean (range) *Reference range	30.1 (4-87) *11-307	56.1 (1-438) *11-307	0.106
Diagnosed with Inherited Bleeding Disorder (%)	2 (11.1)	19 (0.7)	0.379
Required Intervention (%)	14 (77.8)	92 (34.2)	<0.001

Flow Diagram of Referrals and Results



*Type 1 VWD ^11 x Type 1 VWD, 1 mild Hemophilia A, 3 Platelet Function Disorder (PFD); 3 Hemophilia A carrier; 1 FXI deficiency

SUMMARY

•Of 291 patients referred for investigation of a bleeding disorder 18 were referred for abnormal Self-BAT BS (6.2%)
•2/18 (11.1%) were diagnosed with an Inherited Bleeding Disorder and 16/18 required further intervention (88.9%)
•The median BS and the need for intervention was significantly higher in the +Self-BAT BS group than the other referrals group

CONCLUSION

•Results of this ongoing study suggest that the Self-BAT at letstalkperiod.ca may be a useful tool for patients and physicians in identifying those in need of referrals to hematology clinics for assessment and management of bleeding symptoms

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CSL Behring

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Enrichment of variants in platelet genes in patients with bleeding of unknown cause

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INTRODUCTION

Despite extensive laboratory investigations, ~50% of patients seen in hematology clinics with a significant bleeding history remain undiagnosed.[1] These patients are referred to as bleeders of unknown cause (BUC). Understanding the underlying pathogenesis would inform management.

AIM

To use whole exome sequencing (WES) to identify pathogenic variants associated with a significant bleeding history in BUC.

METHODS

Adults (≥18 years) referred to tertiary care hematology clinics for query bleeding disorder were recruited. Research Ethics Board approval and informed consent from all participants was obtained.

Detailed hemostatic investigations were carried out including CBC, aPTT, PT, VWF levels, coagulation factor levels, and platelet function testing. Bleeding scores (BS) were obtained using the Condensed MCMDM-1VWD bleeding questionnaire.

To prioritize sequencing, patients with a positive BS (≥4), with a positive family history of bleeding and a non-diagnostic work-up were sent for WES. To enrich for potentially causal variants, we compared the frequency of rare (≤1% in gnomAD) variants with a ClinVar assignment of pathogenic or likely pathogenic, and rare stop-gain, frameshift or splice-site variants in platelet genes from the curated list of Tier 1 genes[2] in cases versus controls.

RESULTS

540 patients were enrolled and 86 met the criteria to have WES performed (Fig 1). Of the 86, there were 81 females and 5 males, with a median age of 42 years (range 18-73 years).

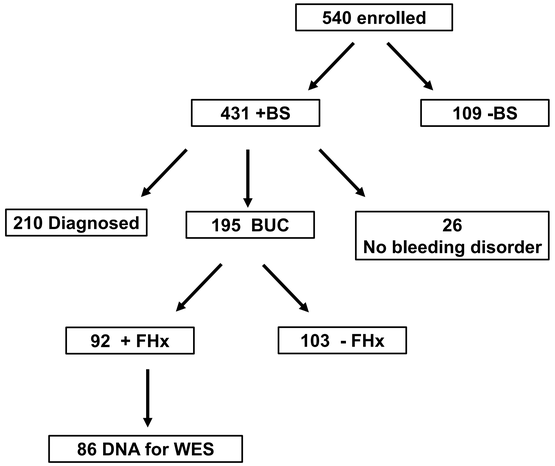


Figure 1: Flow diagram showing the number of patients enrolled in overall study and the prioritization of BUC with +FHx for WES.
BS: bleeding score; BUC: bleeding of unknown cause; FHx: family history of bleeding; WES: whole exome sequencing

In 37 of the 86 patients (43%), 39 rare variants were identified in 19 platelet genes. 34 were rare missense variants and five were potentially causal. The potentially causal variants, BS and platelet investigations for the five patients are shown in Table 1.

When cases were compared to control exomes (n=22,344) the frequency of these potentially causal variants was statistically significant (0.029 v. 0.015, respectively; Fisher's exact p=0.02, Odds Ratio=1.94).

Table 1: The potentially causal platelet variants and laboratory investigations for the five patients.

Patient ID	Bleeding score	Platelet count (x10⁹/L)^	Mean platelet volume (fL)#	Platelet aggregation studies	Gene symbol	Gene name	Associated Disease(s)	Inheritance	Amino Acid change	Genotype
GWC-101	4	264	n/a	normal	*HPS1*	HPS1 biogenesis of lysosomal organelles complex 3 subunit 1	Hermansky-Pudlak syndrome	AR	p.Pro324fs	Heterozygous
GWK-023	13	177	11.2	normal	*ITGA2B*	integrin subunit alpha 2b	Platelet-type bleeding disorder 16, Glanzmann thrombasthenia	AD, AR	p.Gln852fs	Heterozygous
GWK-195	4	170	11.5	normal	*ITGA2B*	integrin subunit alpha 2b	Platelet-type bleeding disorder 16, Glanzmann thrombasthenia	AD, AR	p.Arg889fs	Heterozygous
GWK-182	6	146	8.9	normal	*MYH9*	myosin heavy chain 9	May-Hegglin	AD	p.Glu1350del	Heterozygous
GWC-063	9	209	n/a	normal	*NBEAL2*	neurobeachin like 2	Gray platelet syndrome	AR	p.Arg2187fs	Heterozygous

Bleeding score (BS) obtained using Condensed MCMDM1-VWD (BS ≥ 4 = positive); ^ Platelet count normal range = 150-400; #Mean platelet volume normal range = 6.5-10.3; n/a = not available; AR = Autosomal Recessive; AD = Autosomal Dominant.

CONCLUSIONS

In BUC, rare Clinvar pathogenic variants and rare frameshift variants in genes related to platelet function were identified. Individuals heterozygous for variants in genes known to cause AR disease are carriers and the effect of this on bleeding is unknown. In some cases co-inheritance with variants in other genes, especially variants of unknown significance (VUS), may contribute to the bleeding phenotype. The clinical significance of these variants requires further investigation.

REFERENCES

1. **Quiroga T**, et al. High prevalence of bleeders of unknown cause among patients with inherited mucocutaneous bleeding. A prospective study of 280 patients and 299 controls. *Haematologica* 2007; **92**: 357-65.
2. **Megy K**, et al. Curated disease-causing genes for bleeding, thrombotic, and platelet disorders: Communication from the SSC of the ISTH. *J Thromb Haemost* 2019; **17**:1253-60.

ACKNOWLEDGEMENTS

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Evaluation of von Willebrand Factor (VWF) Replacement on *in vivo* Angiogenesis in VWF-deficient Mice

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PB0906

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INTRODUCTION

Gastrointestinal (GI) bleeding from angiodysplasia is a common problem in patients with inherited and acquired abnormalities of von Willebrand factor (VWF) and can be challenging to manage[1,2]. Recent studies have demonstrated a negative regulatory role of VWF in angiogenesis[3].

AIM

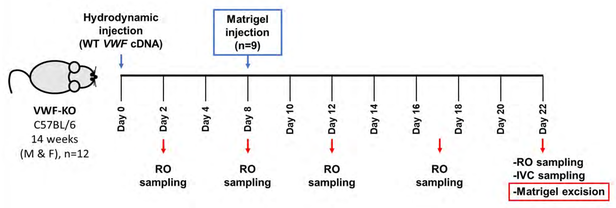
To examine the effect of VWF replacement on *in vivo* angiogenesis in a mouse model of VWF deficiency.

METHODS

The Matrigel plug assay was performed in 14 to 16-week old C57Bl/6 *VWF*-knockout (KO) mice of both genders (N=9) that expressed VWF antigen (VWF:Ag) levels of ≥20U/ml at 48-hours following hydrodynamic injection with wild type (WT) murine VWF cDNA[4].

On day eight post-hydrodynamic injection, Matrigel mixed with fibroblast growth factor (FGF) and vascular endothelial growth factor (VEGF) was injected subcutaneously in the right back flank of each mouse. In the left back flank, an equal volume of Matrigel with phosphate buffered saline (PBS) was injected as a control. After 14 days, plugs were harvested and processed for hematoxylin and eosin (H&E) and immunohistochemical staining (IHC). Retro-orbital (RO) sampling was performed at specific timepoints during the 14-day incubation period, to assess VWF:Ag and multimer structure. Inferior vena cava (IVC) sampling was performed prior to euthanization on the final day.

Experimental timeline



RESULTS

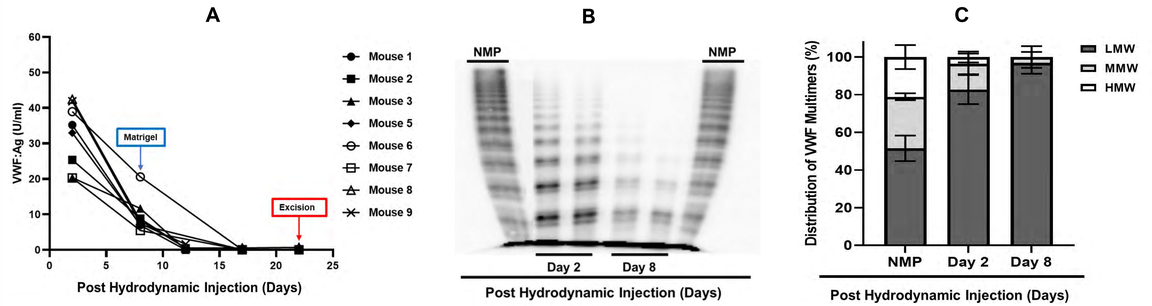


Figure 1 *(A) VWF:Ag of each mouse from day 2 to 22 post hydrodynamic injection. (B) Representative multimers are shown for C57Bl/6 normal plasma pool (NMP; lane 1 & 6), day 2 (lane 2 & 3), and day 8 (4 & 5) post-hydrodynamic injection. (C) Densitometric analysis of multimers shown as mean ± SD; N=9 (NMP & Day 2), N=8 (Day 8). Low molecular weight (LMW), intermediate molecular weight (IMW), high molecular weight (HMW).*

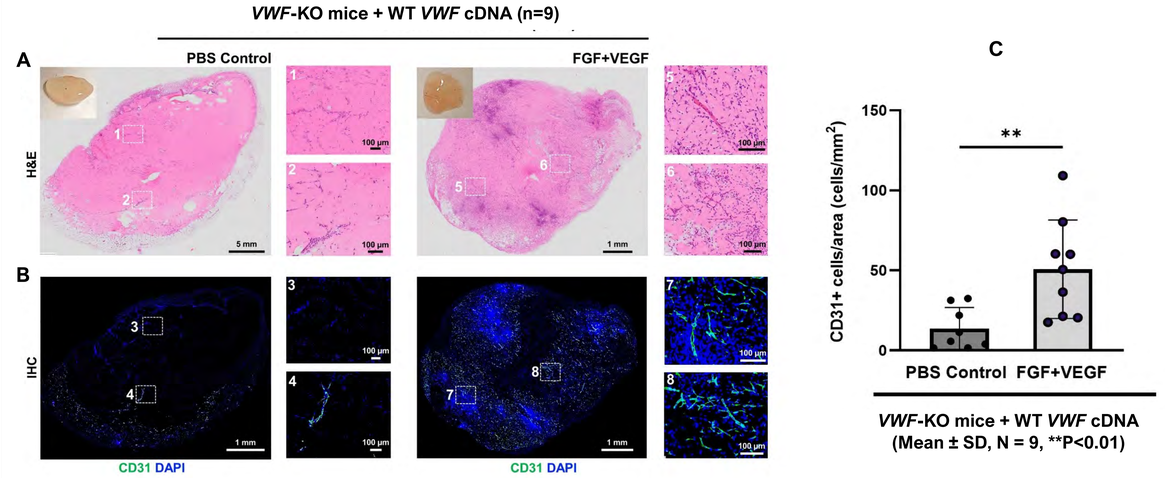


Figure 2*. Sections from FGF + VEGF supplemented plugs and PBS controls were stained for (A) H&E and (B) IHC: DAPI (blue), and CD31 (green). (C) The number of CD31+ cells in the entire area of each plug section were quantified and is shown as mean ± SD; PBS Control: dark gray and FGF + VEGF: light gray. N= 9 for each group, **P<0.01.*

CONCLUSIONS

Although hydrodynamic VWF replacement was successful but short-lived in VWF-deficient mice, liver expressed murine VWF was predominantly low MWM and did not prevent angiogenesis in the Matrigel plug assay.

Further research is needed to evaluate the role of VWF in *in-vivo* angiogenesis.

REFERENCES

1. **Makris, M., et al.** The natural history of occult or angiodysplastic gastrointestinal bleeding in von Willebrand disease. *Haemophilia* 21.3 (2015): 338-342.
2. **Vincentelli, A., et al.** Acquired von Willebrand syndrome in aortic stenosis. *New England Journal of Medicine* 349.4 (2003): 343-349.
3. **Starke, RD., et al.** Endothelial von Willebrand factor regulates angiogenesis. *Blood* 117.3 (2011): 1071-1080.
4. **Pruss, CM., et al.** Pathologic mechanisms of type 1 VWD mutations R1205H and Y1584C through in vitro and in vivo mouse models. *Blood, The Journal of the American Society of Hematology* 117.16 (2011): 4358-4366.

ACKNOWLEDGEMENTS

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Infectious Disease



Dr. Gerald Evans
Division Chair



Dr. Tony Bai
Research Lead

Summary

- *Staphylococcus aureus bacteraemia mortality asystematic review and meta-analysis*
- *Improving access and education for HIV prophylaxis*
- *Therapeutics to prevent recurrent c. Difficile infections*
- *Serological evidence of COVID-19 in healthcare workers*
- *Creation of database of track outpatient antibiotic treatment for performance improvements and appropriateness*
- *Assessment of bacteraemia consultations and long-term survival in patients*
- *Anaerobe coverage in aspiration pneumonia*
- *Local evaluation of peritoneal dialysis related to peritonitis*
- *Targeted testing for self-reported penicillin allergic in-patients*
- *Prevalence surveillance on antimicrobial use*
- *Improving management of Lyme's Disease locally*

Project 1. Effectiveness of chronic suppressive therapy for patients with prosthetic joint infection undergoing DAIR.

Principal investigator: Dr. Jorge Martinez-Cajas (email: jm209@queensu.ca)

Methods: Chart review case series study

Summary
Objective 1: to estimate the effectiveness and durability of clinical response to antimicrobial chronic suppressive therapy in patients undergoing DAIR for prosthetic joint infection in a single centre.
Objective 2: to explore the factors that determine success/failure of DAIR and chronic suppressive therapy

This is a retrospective descriptive study of all patients who underwent DAIR in the KHSC in the last 5-10 years. The main outcome is relapse of clinical/microbiologic findings of prosthetic joint infection; need for further surgical treatment after original DAIR + chronic suppressive therapy

Resident role: 1. Refine study protocol; 2. Research Ethics application; 3. Chart review; 4. Descriptive statistical analysis; 5. Preparation of manuscript/publication

Time frame: 2 years

Project 2. Building the HIV database for the IIC clinic

Principal investigator: Dr. Santiago Perez Patrigeon (email: santiago.perez@queensu.ca)

Methods: Chart review case series study

Summary
This is a retrospective cohort study of HIV patients currently being followed at the Hotel Dieu Hospital HIV clinic. The objectives include: 1) make a descriptive analysis of the cohort; 2) participant identification for future trials; 3) collaboration with other cohorts

Resident role: Chart review and data entry

Time frame: 1 year

Project 3. Mandatory infectious diseases consultation for *Staphylococcus aureus* bacteraemia: A retrospective cohort study

Principal Investigator: Dr. Anthony Bai (email: tony.bai@queensu.ca)

Methods: Retrospective chart review cohort study

Summary: This quality improvement study will collect information on outcomes for *S. aureus* bacteremia for 1 year before and after implementation of mandatory *S. aureus* bacteremia. The study will analyze if mandatory infectious diseases consultation improves patient outcomes.

Resident role: Chart review and data entry. Participate in analysis and writing up manuscript as a co-author.

Time frame: 1 year

Project 4. Microbiology for aspiration pneumonia: A systematic review

Principal Investigator: Dr. Anthony Bai (email: tony.bai@queensu.ca)

Methods: Systematic review

Summary: This is a systematic review to describe the bacterial pathogens isolated in aspiration pneumonia in prior studies.

Resident role: Assist with title / abstract screening, full-text reading and data extraction. Participate in writing of manuscript as co-author.

Timeframe: 2 years

Project 5. Oseltamivir for treatment of influenza requiring hospitalization: A target trial emulation

Principal Investigator: Dr. Anthony Bai (email: tony.bai@queensu.ca)

Methods: Target trial emulation using GEMINI database

Summary: This is a target trial emulation that compares oseltamivir to no treatment in patients hospitalized for influenza to determine if there is any benefit for oseltamivir treatment in terms of in-hospital mortality or length-of-stay in hospital.

Resident role: Resident will assist with performing a background literature search, forming a statistical analysis plan and writing up of manuscript as a co-author.

Timeframe: 1 year

Project 6. Long term mortality and morbidity for bacterial meningitis: A population-based study

Principal Investigator: Dr. Anthony Bai (email: tony.bai@queensu.ca)

Methods: Population-based cohort study using ICES database

Summary: This is a population-based study using ICES database to describe the 1-year mortality and morbidity for patients with bacterial meningitis.

Resident role: Resident will assist with performing a background literature search and help write-up of the manuscript as a co-author.

Time frame: 1 year

Nephrology



Dr. David Holland
Division Chair



Dr. Rachel Holden
Research Lead

Summary

- *Identifying predictors and development of clinical testing of phosphate intolerance and handling*
- *Analysis of vascular calcification and therapeutic options for chronic kidney disease*
- *Dialysis frequency and quality of life in elderly patients*
- *Investigation on vitamin D metabolism in kidney disease*
- *Indigenous health research in non-communicable disease*
- *Global and population health research in low and middle-income countries in prevention of chronic and acute non-communicable diseases (such as stroke, cancer, kidney injury and disease)*
- *Exposure to environmental stress of sugar cane workers in Tanzania and prevalence of chronic kidney disease*
- *Smartphone app development for tracking patient lab results and 'protocolizing' disease management*
- *Quality improvement interventions for patients with acute kidney injury*

Division of Nephrology

Faculty	Research interests	Potential projects
Dr. Karen Yeates	• Global health/population health • Community based research in Indigenous health • Mobile health interventions to improve provision of health care • Non-communicable disease in East Africa	• Prevalence of chronic disease in sugar cane workers • Smartphone applications for tracking patient lab results and protocolized diabetes and BP management in remote living Indigenous patients in Canada
Dr. Khaled Shamseddin	• Kidney transplant research	Narrative reviews • GLP1 agonist use in kidney transplant • Adrenal insufficiency in kidney transplant • FSGS recurrence and management in kidney transplant • Lab frequency and potential cost saving in post-kidney transplant recipients • Patient satisfaction
Dr. Christine White	• GFR measurement • Less frequent dialysis in the elderly	• Comparison of bloodwork values in twice weekly dialysis compared to thrice weekly dialysis • Mineral metabolism management in twice weekly dialysis compared to thrice weekly dialysis • Anemia management in twice weekly dialysis compared to thrice weekly dialysis
Dr. Rachel Holden	• Mineral metabolism • Vascular calcification • Vitamin D metabolism	• Impact of obesity on vitamin D and mineral metabolism management in ESKD
Dr. Sam Silver	• Acute kidney injury • Health Services research	

The Abdominal Aortic Calcium Score could Increase Access to Non-calcium Based Phosphate Binders in Hemodialysis patients

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Department of Biomedical and Molecular Sciences[1], Radiology[2], and Medicine[3], Public Health Sciences[4], Critical Care Medicine[5], Clinical Evaluation Research Unit Kingston Health Sciences Center[6], Queen's University, Kingston, Ontario, Canada. Department or Medicine, University of Ottawa, Ottawa, Ontario Canada[7], Department of Medicine, Schulich School of Medicine and Dentistry, Western University, London, Ontario Canada[8]

BACKGROUND

- Calcification of the vasculature is associated with excess mortality in patients with end stage kidney disease (ESKD) requiring hemodialysis (HD).[1]
- The presence of abdominal aortic calcification (AAC) is associated with greater risk of cardiovascular events and mortality[2]
- In HD patients, compared to non-calcium based PBs (NCPBs), calcium phosphate binders (CPB) increase progression of:
  - coronary artery calcification (CAC)[3]
  - abdominal aortic calcification (AAC)[4]
- NCPBs are covered by the Exceptional Access Program (EAP) where, in addition to sustained hyperphosphatemia (two phosphate values > 1.8 mmol/L), patients must have demonstrated CAC or hypercalcemia (Ca ≥ 2.7 mmol/L).[5]

OBJECTIVES

- To determine the association between CAC score measured by multidetector computer tomography (MDCT) and AAC Framingham score obtained from lumbar x-ray in 50 participants of the iPACK-HD clinical trial.
- To compare the degree of progression in CAC and AAC among patients.
- To determine the percentage of patients with AAC that qualify for NCPBs based on EAP criteria and those that were prescribed CBPs and NCPBs during the study.

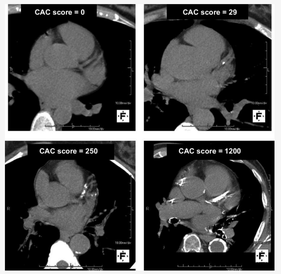
METHODS

- The iPACK-HD trial was a double-blind placebo controlled trial in 86 HD patients from three centres randomized to 10mg of Vitamin K treatment 3 times a week or placebo for 12 months.
- Lumbar x-rays at baseline and study exit were obtained for 50 participants of the trial. AAC was determined using the Framingham method to assess calcification severity (0-24).
- 35 participants with baseline and exit CAC and AAC were grouped by the median change in CAC and AAC into rapid and slow progressors.

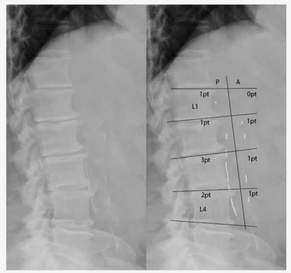
RESULTS

Inclusion Criteria: ≥ 18 years old, on hemodialysis, irreversible end stage kidney disease

Exclusion Criteria: warfarin treatment, reversible kidney injury, previous coronary artery bypass grafting or coronary stents, severe co-morbid conditions, pregnant, life expectancy < 1



Non-contrast CT at the base of the heart used calcified plaque density to measure CAC score in Agatson units.[6]



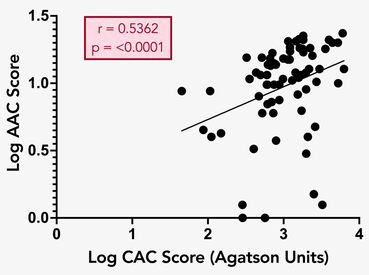
From a lateral lumbar x-ray, the extent of abdominal aortic calcification is graded from 0-3 for 4 posterior and anterior segments to obtain a AAC score of 0-24.[7]

Baseline Characteristics

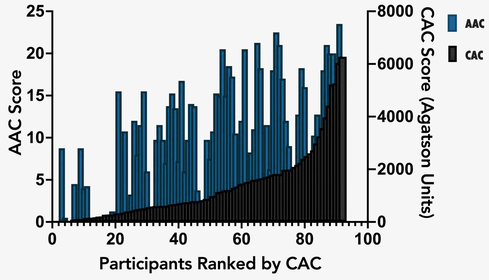
	Mean/ Median/ Count	Correlations	
		CAC	AAC
Age	65 ± 14	0.36	0.49
Diabetes	29 (55%)	0.24	-0.015
HD Vintage (days)	719 (1832)	0.12	0.039
Serum Ca (mM)	2.3 (0.21)	0.18	0.22
Serum PO_4 (mM)	1.6 (0.5)	0.029	-0.15
25(OH)D (ng/mL)	0.5 ± 0.39	-0.16	-0.24
$1,25(OH)_2D$ (pg/mL)	13 (12)	-0.21	-0.016
PTH (pmol/L)	36 (39)	0.048	0.034
FGF-23 (pg/mL)	1276 (3562)	0.086	-0.079
Alkaline Phosphatase (IU/L)	97 (55)	0.057	-0.21

Variables presented as mean ± SD or median (IQR). Categorical variable reported as count, %. Spearman R values. HD: hemodialysis vintage p<0.01 (yellow) p<0.0001 (red).

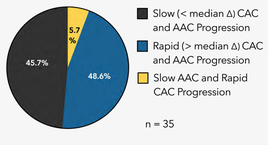
CAC and AAC Correlation



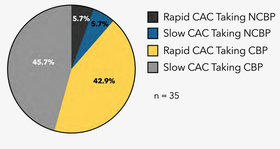
CAC and AAC Scores



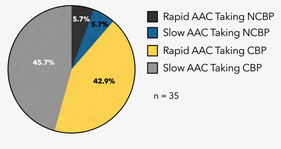
Degree of CAC and AAC Progression in Patients



CAC Progression and Phosphate Binders



AAC Progression and Phosphate Binders



- AAC and CAC were present in 90.6% patients at either baseline or exit.
- 81.3% of patients with AAC > 0 (n=47) were prescribed CBPs during the study.
- All patients prescribed NCBPs (n=7) during the study had AAC > 0.
- 75% of patients with sustained hyperphosphatemia (n=33) would qualify for NCPBs if EAP criteria included AAC.
- No patients had slow CAC progression and rapid AAC progression.

CONCLUSIONS

There was a significant correlation between CAC and AAC (p<0.0001).

When grouped by rapid and slow progression, there was 94.3% concordance between CAC and AAC.

If an AAC > 0 was used to identify patients for NCBPs qualification, 75% of patients who meet EAP criteria would qualify.

49% of patients prescribed CBPs during the study were rapid CAC and AAC progressors.

AAC obtained from lumbar x-ray costs 80% less and exposes patients to 2-3 times less radiation than CAC, therefore the use of AAC to confirm arterial calcification would increase the accessibility of NCPBs for Ontarians.

References

1. A Go AS. Cardiovascular Disease Consequences of CKD. [Review]. Seminars in Nephrology. 2016;36(4):293-304.
2. Leow K, Szulc P, Schousboe JT et al. Prognostic Value of Abdominal Aortic Calcification: A Systematic Review and Meta-Analysis of Observational Studies. Journal of the American Heart Association. 2021;10:17-205.
3. Liu L, Wang Y, Chen H et al. The effects of non-calcium-based phosphate binders versus calcium-based phosphate binders on cardiovascular calcification and bone remodeling among dialysis patients: a meta-analysis of randomized trials. Ren Fail. 2014 Sep;36(8):1244-52.
4. Toussaint ND, Lau KK, Polkinghorne KR, Kerr PG. Attenuation of aortic calcification with lanthanum carbonate versus calcium-based phosphate binders in haemodialysis: A pilot randomized controlled trial. Nephrology (Carlton). 2011 Mar;16(3):290-8.
5. Ontario Ministry of Health. Exceptional Access Program Reimbursement Criteria for Frequently Requested Drugs. 2022 May.
6. Rumberger JA. Using noncontrast cardiac CT and coronary artery calcification measurements for cardiovascular risk assessment and management in asymptomatic adults. Vasc Health Risk Manag. 2010 Aug 9;6:579-91.
7. de Bie, M.K., Buiten, M.S., Rotmans, J.I. et al. Abdominal aortic calcification on a plain X-ray and the relation with significant coronary artery disease in asymptomatic chronic dialysis patients. BMC Nephrol 18, 82 (2017)

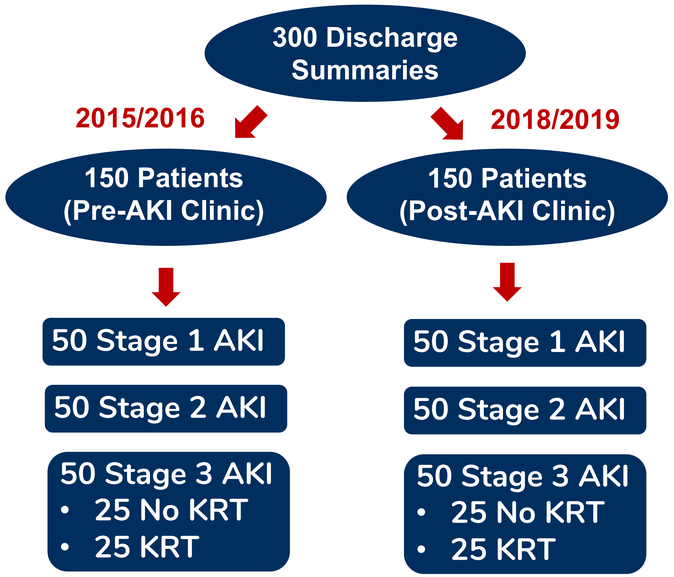
The Quality of Discharge Summaries After Acute Kidney Injury

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Background

- **Acute kidney injury (AKI) increases the risk of hospital readmission, chronic kidney disease (CKD), and death**
- **High quality communication needed in discharge summaries for patients who survive AKI**

Methods



Assessed discharge summaries for **9 key elements → composite score /10 to determine discharge summary quality**
- AKI course
- Follow-up recommendations

Objectives

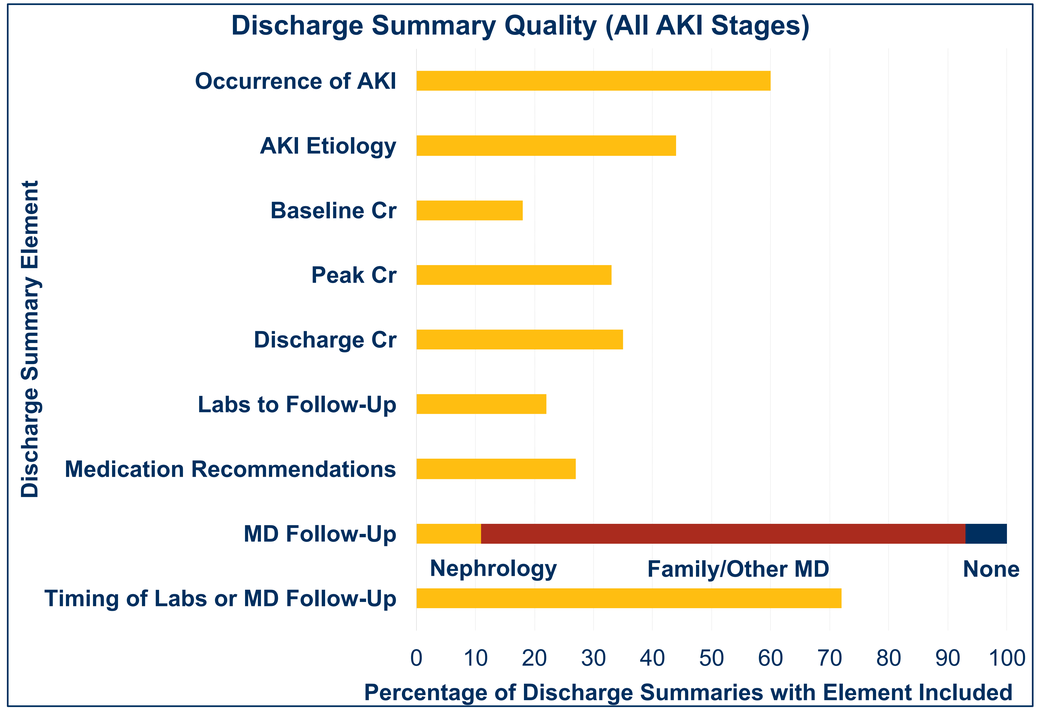
1. **Determine how often key elements of AKI were mentioned in discharge summaries**
2. **Identify predictors of discharge summary quality after AKI**

Results

Predictors of Discharge Summary Quality

Patient Characteristic	Odds Ratio for Composite Score ≥4/10 (95% CI)	P Value
Era		
2015-2016	Ref	
2018-2019	0.76 (0.44-1.31)	0.33
Age, per decade	0.96 (0.80-1.15)	0.64
Sex		
Male	0.73 (0.41-1.28)	0.27
Female	Ref	
Baseline Cr, per 25 umol/L	1.86 (1.42-2.43)	**< 0.001***
Discharge Cr % Above Baseline[a]		
<50% Above Baseline Cr	Ref	
50 to <100% Above Baseline Cr	2.12 (0.99-4.57)	0.06
≥100% Above Baseline Cr	4.88 (1.80-13.26)	**0.002***
AKI Stage		
Stage 1	Ref	
Stage 2	3.96 (1.97-7.96)	**< 0.001***
Stage 3 No KRT	6.85 (2.83-16.59)	**< 0.001***
Stage 3 KRT	4.39 (1.53-12.58)	**0.01***
AKI Etiology		
Pre-Renal	Ref	
ATN/Other	2.33 (1.23-4.41)	**0.01***
Post-Renal/Obstructive	1.19 (0.36-3.99)	0.78
Hospital-Acquired AKI		
Yes	0.77 (0.41-1.42)	0.40
No	Ref	
Inpatient Nephrology Consult[a]		
Yes	10.53 (4.82-22.98)	**< 0.001***
No	Ref	

[a]Univariate analysis. Excluded from multivariable regression model due to collinearity with AKI stage.
* P < 0.05 considered statistically significant



Conclusion

- **Discharge summary quality in AKI survivors is poor**
- **Higher quality discharge summary for patients with:**
  - Baseline CKD
  - Intrarenal etiology
  - Severe AKI
  - Higher discharge Cr
  - Inpatient nephrology involvement
- **Most discharge summaries are missing key elements**
  - Cr trajectory
  - AKI-specific follow-up recommendations
- **Opportunity exists to improve discharge summary communication for patients with AKI**

Contact: 14crg3@queensu.ca

Efficacy of Evusheld (Tixagevimab/Cilgavimab) Preventing Breakthrough COVID-19 Infection among Vaccinated Kidney Transplant Patients

Arezou Shahmoradi, MD[1,2], Wilma Hopman , MA[2], Jessy Donelle, MSc[2], Gail V. Dean, B.Com[2], Anne Dumais, B.Sc.OT[2], Lori Van Manen, RN, BNSc, MSc[2], David Holland, MD, MSc[1,2], and M. Khaled Shamseddin, MD, MSc[1,2]

Division of Nephrology, Department of Medicine, Queen's University[1], Kingston Health Sciences Centre[2], Kingston, ON

INTRODUCTION & AIM

Transplant patients are at high risk of COVID-19 infection and its complications.

The aim of this study was to evaluate the efficacy of Evusheld pre-exposure prophylaxis in preventing breakthrough COVID-19 infection among vaccinated kidney transplant patients in a single center study.

METHODS AND COHORT

RETROSPECTIVE SINGLE CENTER STUDY
Aug 1st, 2022 – Jan 30th, 2023

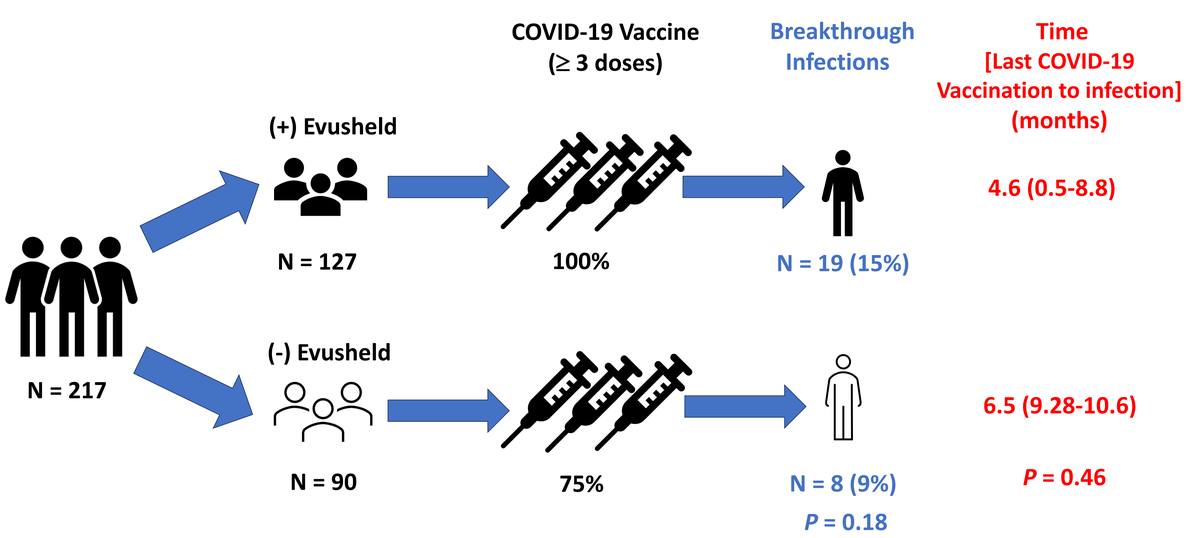
Kingston Kidney Transplant Program (KKTP)

217 Kidney Transplant Patients
127 (58%) Consented to Evusheld Use

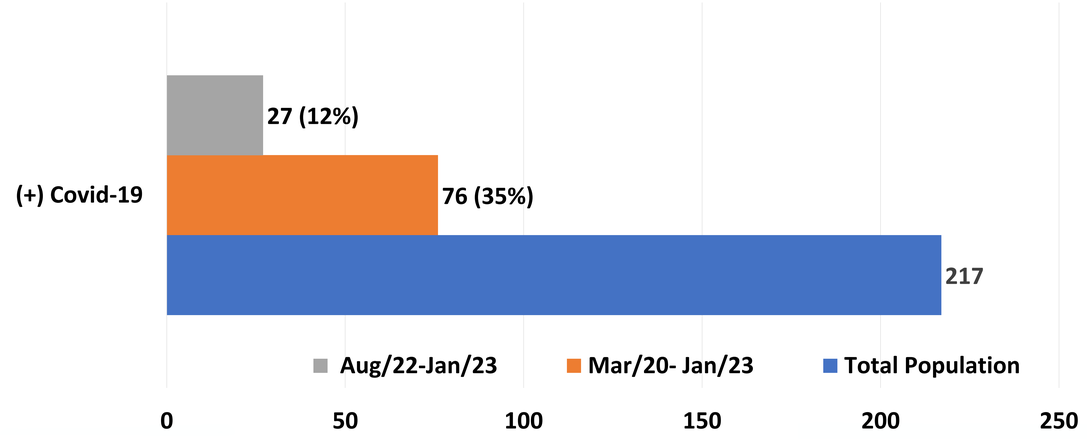
Evusheld Clinic
August 1st – November 30th, 2022

♀ 33.2% ♂ 66.8%

Age: 57 ± 14 years



PREVALENCE OF COVID-19 INFECTION



CONCLUSION

Evusheld 300 mg did not decrease the risk of breakthrough COVID-19 infection among fully vaccinated kidney transplant patients.

Studies with higher doses of Evusheld and further COVID-19 vaccination are still required to determine efficacy of prevention of breakthrough COVID-19 infection among transplant patients.

ACKNOWLEDGMENT

We would like to acknowledge the efforts and dedication of our KKTP Medical Team and Administration in establishing an excellent care for our kidney transplant patients.

CONTACT INFORMATION

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FACILITATING COVID-19 VACCINATION FOR KIDNEY TRANSPLANT PATIENTS USING A DEDICATED OUTREACH PROGTRAM

Arezou Shahmoradi, MD[1,2], Wilma Hopman , MA [2], Margaret Lacey, RN [2], Natalie Witton, RN, BScN [2], Jessy Donelle, MSc [2], Lori Van Manen, RN, BNSc, MSc [2], David Holland, MD, MSc [1,2], Sam Silver, MD, MSc [1,2] , and M. Khaled Shamseddin, MD, MSc [1,2]

Division of Nephrology, Department of Medicine, Queen's University[1], Kingston Health Sciences Centre[2], Kingston, ON

INTRODUCTION

Transplant patients are at high risk of COVID-19 infection and its complications. Due to importance of timely vaccination, we launched an Outreach Program (OP) and a Vaccine Clinic (VC) for transplant patients in early April 2021, as part of Ontario's phase II roll out policy.

METHODS AND COHORT

RETROSPECTIVE SINGLE CENTER STUDY
April 2021 – April 2022

Kingston Kidney Transplant Program (KKTP)

Outreach Program
- Clerk
- Nurse
- Transplant Nephrologist
- Vaccine Clinic

External Vaccination

213 Kidney Transplant Patients

35.7% ♀ 64.3% ♂

Age: 57±14 years

RESULTS

VACCINE RATE AND % FACILITATED BY OUTREACH PROGRAM COMPARED TO ONTARIO %

(N= 213)	207	204	179	152
	(97.2%)	(95.8%)	(84%)	(71.4%)
	145	165	171	152
	(70%)	(80.9%)	(95.5%)	(100%)
ONTARIO	17,779	17585	15,045	7,756
	(91.7%)	(90.7%)	(77.6%)	(40%)

All Solid Organ Transplant Recipients (N =19,389) as per June 5th, 2022

TIME BETWEEN VACCINE DOSES: OUTREACH PROGRAM VS EXTERNAL VACCINATION

	DAY # Median (IQR)	DAY # Median (IQR)	DAY # Median (IQR)
	23 (21-24)	106 (98-126)	153 (140-158)
	35 (26-67)	134 (102-173)	
	P < 0.001	*P* = 0.046	

CONCLUSION

1) Our outreach program improved the rate of COVID-19 vaccination rate of our kidney transplant patients compared with the provincial rate of all immunocompromised patients.

2) Patient's personal choices not to be immunized was the main reason not to achieve a 100% vaccine rate (*Data is not presented*).

3) An outreach program for kidney transplant patients shortened the time between COVID-19 immunizations compared with external vaccination.

ACKNOWLEDGMENT

We would like to acknowledge the efforts and dedication of our medical team and outreach program in establishing excellent care for our kidney transplant patients.

CONTACT INFORMATION

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Palliative Medicine



Dr. Danielle Kain
Division Co-Chair



Dr. Jean Mathew
Research Lead

Summary

- *Use of standardized tool to improve communication between specialist palliative care physicians and family physicians regarding new consults*
- *Phone app and remote-care accessibility tools for improving at home care*
- *Cannabis and psilocybin therapy for symptom and anxiety management in palliative and cancer patients*
- *Identifying palliative care needs in heart failure patients*
- *Screening for aberrant opioid use behaviour in care clinics*
- *Use of opioids for improved outcomes in pulmonary rehabilitation*
- *The development of an end-of-life medication de-prescribing and conversion guide for trainee use*
- *Educational evaluation of teaching point-of-care ultrasound to improve health worker skillset*
- *Implementation of Compassionate Community Innovation in Kingston study*

**Refer to Topics table below to determine Resident Recruitment*

Systematic Screening for Risk of Aberrant Opioid Use Behaviour with the Opioid Risk Tool: a Quality Improvement initiative

Emily Lee (Presenter), Dr. Michael Brundage, Dr. Aynharan Sinnarajah, Dr. Danielle Kain, Wilma Hopman, Dr. Jean Mathews (PI)
Department of Oncology and Department of Medicine/Palliative Medicine, Queen's University

Background

- Cancer patients are often prescribed opioids for symptom management (e.g., pain, dyspnea), and evidence suggests that they may be at risk of opioid-related health harms.
  - **Aberrant opioid use behaviours (AOUB):** use of prescription opioids in a manner not intended by the prescriber.
  - **Opioid use disorder (OUD)**: problematic patterns of opioid use resulting in clinically significant impairment or distress.

- The **Opioid Risk Tool (ORT)** is the most common screening tool for aberrant opioid use behaviours in palliative care.

- The **ORT is under-utilized in the Palliative Care Oncology Clinic** as it is **clinician-initiated and not systematically implemented**.
  - Systematic screening permits **early identification of patients who are at high risk** of AOUB, which allows clinicians to **mitigate this risk through guidelines for safe opioid prescribing.**

Primary objective:
to implement systematic screening with the ORT in the palliative care clinic and measure improvement in the identification of patients at risk of developing opioid-related health harms.

Secondary objectives:
to assess the feasibility and acceptability of implementing the ORT, as perceived and reported by healthcare providers and patients.

Methods

Retrospective sample: all new consults from May 1, 2023, to June 30, 2023

Chart abstraction guide: drafted, pilot-tested, implemented

Retrospective chart review and data collection

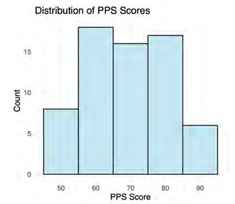
Create acceptability surveys for prospective data collection

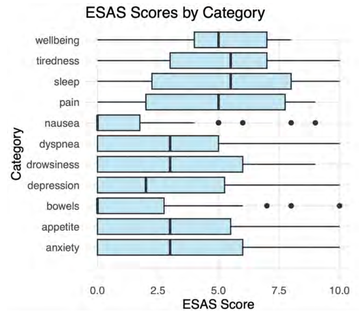
Results from Retrospective Chart Review

- $n = 68$
- Median age was **72.5 years**, **57% were female**, **57% were married**.
- Most common cancer diagnoses were lung and gastrointestinal, and 69% were at an advanced stage.
- 32% of patients were on a scheduled opioid at time of their consult.
- **1 out of 68** patients was documented as **positive for risk of aberrant opioid use behavior.**
  - A 63-year-old female with advanced lung cancer, who **increased opioid dose without medical guidance; risk mitigated with more frequent follow-up and lower quantities of opioids prescribed.**

	Number (%)
Smoking Status (%), $n = 68$	
Never	9 (13.2)
Former	9 (13.2)
Current	9 (13.2)
Missing	41 (60.3)
Tumour Site (%), $n = 68$	
Breast	0
Gastrointestinal	12 (17.6)
Genitourinary	6 (8.8)
Gynecologic	5 (7.4)
Head and Neck	3 (4.4)
Hematologic	7 (10.3)
Lung	21 (30.9)
Neurologic	3 (4.4)
Other	2 (2.9)
Tumour Stage* (%), $n = 61$	
Early	9 (14.8)
Advanced	48 (68.7)
Remission	0
Unavailable	4 (6.6)

*Hematologic malignancies were excluded due to the complicated nature of staging.





	Number of Patients (%)
Pre-consult Scheduled Opioid, $n = 68$	
Buprenorphine	1 (1.5)
Codeine	1 (1.5)
Fentanyl	0
Hydromorphone	17 (25.0)
Methadone	1 (1.5)
Morphine	3 (4.4)
Oxycodone	2 (2.9)
None	46 (67.6)
Addition of Scheduled Opioid Post-consult in Opioid-Naïve patients, $n = 46$	15 (32.6)
Post-consult Scheduled Opioid Dose Change, $n = 22$	
None	12 (54.5)
Increase	7 (31.8)
Decrease	1 (4.5)
Opioid Rotation	1 (4.5)
Other	1 (4.5)
Addition of Methadone, $n = 68$	4 (5.9)

Next Steps

- Since the ORT is not currently systematically implemented in the palliative care oncology clinic, **it is possible that some patients with high risk are not being identified** and strategies to address that risk are not being communicated to the care team.

- **Implementation of ORT screening** (feasibility, adherence, acceptability) and **prospective data collection.**

The development of an end-of-life medication deprescribing and conversion guide for trainee use

Arun Agha, MD, FRCPC and Craig Goldie, MD, FRCPC
Division of Palliative Medicine (Department of Medicine), Queen's University, Kingston, ON

BACKGROUND

Patients with life-limiting diseases often remain on medications with little to no short-term benefit in primary or secondary prevention (Fede et al 2011). This can contribute to pill burden, potential adverse drug effects, and has a financial impact (Lindsay et al 2014). In contrast, in scenarios where patients lose the ability to swallow medications orally, many medications important for symptom management often do not have readily-available parenteral formulations.

The inability to administer these medications can exacerbate pre-existing symptoms (e.g. pain, nausea, rigidity) or may result in withdrawal symptoms if abruptly discontinued (e.g. anti-depressants, anti-hypertensives). Non-oral versions of medications of a similar class or for similar indications may exist but may be unfamiliar to prescribers, especially trainees. The purpose of our project was to develop an end-of-life medication deprescribing and conversion guide for trainee use during palliative medicine clinical experiences at Queen's University.

METHODS

We performed a database search for pre-existing deprescribing and conversion tools in the context of palliative care. Expert opinion was sought from palliative medicine specialists and a pharmacist at Queen's University. We utilized the 2022 European Pharmaceutical Marketing Research Association (EphMRA) Classification Guideline to ensure a systematic approach to drug classes and to minimize inadvertent omissions.

TABLE 1: SIGNS OF IMPENDING LOSS OF ORAL ROUTE

Palliative Performance Scale (PPS) of 30% or lower
Rapid reduction in PPS
New dysphagia/odynophagia
Underlying morbidity: Head and neck cancer and no alternative enteral route (i.e. g-tube), history of stroke, seizures, dementia, or other cognitive impairments.
Presence of aspiration clinical risk factors (pocketing food in the mouth/cheeks, clearing the throat or coughing while eating, drooling, or displaying any difficulty breathing with eating or drinking) (Kollmeier and Keenaghan 2023)
Delirium
Nausea and/or vomiting

TABLE 2: END-OF-LIFE MEDICATION GUIDE (PORTION OF CARDIOVASCULAR SECTION)

Medication	Common Indications	Deprescribing Considerations	Comfort-Focused Administration Considerations
Hyperlipidemia Medications (statins, fibrates, ezetimibe)	Primary or secondary prevention of CV events	Consider stopping as unlikely to have short term benefits. No tapering required.	No recommended options
Non-Diuretic Antihypertensives (e.g. ACEi, BB, nitro)	Hypertension, secondary prevention of CV events.	Consider stopping unless indication is for angina (e.g. Betablockers, CCB, and nitrates are sometimes used for recurrent angina) or for hypertensive urgency or emergency. Taper gradually and monitor for symptomatic hypertension after discontinuation (chest pain, acute severe back pain, dyspnea, focal neuro symptoms). Beta-blockers in particular should be gradually tapered to avoid tachycardia, hypertension, or ischemia	Nitroglycerin Spray or patch
Diuretics (e.g. Lasix, spironolactone, HCTZ)	CHF, ascites from cirrhosis, anasarca, HTN, secondary prevention for CV events	Consider stopping for mild hypertension or secondary prevention (no tapering required if used for these indications)	Consider Furosemide subcutaneous (single administration should not exceed 20 mg)
Anti-arrhythmics (e.g. amiodarone, procainamide)	Afib, SVT	Consider stopping unless for Symptomatic afib or SVT. Taper gradually and monitor for palpitations, chest pain, dyspnea, etc.	No known non-po/iv options available
Ivabredine	HFrEF	Would not recommend as may have symptom benefit	No known non-po/iv options available

RESULTS

Key literature assisting in the development of this guide included the OncPal Deprescribing Guideline (2014) as well as the National Hospice and Palliative Care Organization Hospice Medication Deprescribing Toolkit (2020). This data and expert opinion were incorporated into our End of Life Medication Guide (see Table 2 for excerpt). This guide utilized the EphMRA classification of drugs.

It provides *deprescribing considerations*, that is, scenarios when deprescribing should be considered, and *comfort-focused administration considerations* if a patient's swallowing is impaired or uncomfortable. This guide also incorporates clinical signs to monitor for potential impending loss of oral route (Table 1) which may be pertinent if concerns for medication withdrawal exist, in order to contemplate a taper to avoid sudden discontinuation.

DISCUSSION

We anticipate this guide will act as a useful reference tool for trainees undergoing palliative medicine learning experiences at Queen's University and help provide excellent symptom-directed care in medically complex palliative care patients by helping guide discontinuing non-comfort-focused medications and avoiding sudden discontinuation of certain medications due to loss of regular oral route of administration.

We aim to incorporate this guide into the pre-existing Queen's Palliative Care Symptom Management Pocket Guide (Heidman and Goldie 2015) with potential distribution across other Canadian training sites. We will also work with the Canadian Deprescribing Network to further develop and disseminate this unique palliative-focused deprescribing guide

REFERENCES

- Fede, A., Miranda, M., Antonangelo, D., Trevizan, L., Schaffhausser, H., Hamermesz, B., Zimmermann, C., Del Giglio, A., & Riechelmann, R. P. (2011). Use of unnecessary medications by patients with advanced cancer: cross-sectional survey. *Supportive Care in Cancer*, *19*, 1313-1318.
- Lindsay, J., Dooley, M., Martin, J., Fay, M., Kearney, A., Khatun, M., & Barras, M. (2015). The development and evaluation of an oncological palliative care deprescribing guideline: the 'OncPal deprescribing guideline'. *Supportive care in cancer*, *23*, 71-78.
- National Hospice and Palliative Care Organization . (2020). *Hospice Medication Deprescribing Toolkit* https://www.nhpco.org/wp-content/uploads/NHPCO_Deprescribing_Toolkit.pdf
- European Pharmaceutical Marketing Research Association (EphMRA). (2022). *Anatomical Classification Guidelines* https://www.ephmra.org/sites/default/files/2022-01/2022%20ATC%20Guidelines.pdf
- Heidman, J.G., and Goldie, C. (Queen's University). (2015). *Palliative Care Symptom Management Pocket Guide.*

Using a standardized letter to improve communication between specialist palliative care physicians and family physicians regarding new consults to the Palliative Oncology Clinic at the Cancer Centre of Southeastern Ontario

Jonathan Tam, Leonie Herx, Aynharan Sinnarajah, Abigail Berube, Justyna Nowak, Jean Mathews

Division of Palliative Medicine, Department of Medicine, Queen's University, Kingston, Ontario, Canada

Background and Rationale

Palliative care improves the quality of life of patients with life-limiting illnesses. For patients with advanced cancer, it is recommended that palliative care should be integrated early in the course of the illness, ideally in an ambulatory clinic setting. However, it is neither necessary nor sustainable for specialist palliative care teams to be involved indefinitely in the care of all patients with advanced cancer. Systematic symptom screening can identify patients who can benefit from targeted early specialist palliative care, while patients with stable or mild symptoms can benefit from primary palliative care provided by their family physicians.

Studies in other jurisdictions in Canada have identified several barriers to family physicians providing palliative care, including lack of time, inadequate compensation, and lack of awareness of community palliative care resources. A survey from Ontario reported that one-third of family physicians provide home palliative care, and that increasing support and collaboration with specialist palliative care teams may improve the engagement of family physicians with palliative care. A systematic review of barriers and enablers to the delivery of palliative care by family physicians reported that communication between healthcare professionals was a barrier and better communication would enable family physicians to deliver palliative care.

A qualitative study to optimize communication between family physicians and specialist palliative care teams reported on the following key components of such communication: clarifying role boundaries; providing education about the clinical scenarios that require specialist input and those that can be managed by family physicians; and opportunities for ongoing and structured communication between family physicians and specialist palliative care teams. A standardized letter template has been used by oncologists in other jurisdictions in Canada to improve communication with family physicians.

Patients with cancer can lose contact with their family physicians due to poor communication and care coordination, and patients receiving palliative oncology care value their family physicians being involved for ongoing primary care. Their family physicians also value being involved at all stages of cancer care and being able to clarify their roles throughout the illness trajectory. At present, there is lack of a structured communication between the specialist team at the palliative oncology clinic at the CCSEO and family physicians. An informal survey of local family physicians, conducted by our team, identified lack of communication at the time when oncologists refer their patients to specialist palliative care as a barrier to them providing primary palliative care for their patients.

Aims and Objectives

The primary objective of this quality improvement initiative is to evaluate the pilot implementation of a standardized letter to improve communication between specialist palliative care teams at the CCSEO and family physicians, regarding their patients with cancer. This letter will clarify shared care role boundaries and indications for specialist palliative care involvement, provide information about our local palliative care resources, and provide contact information for ongoing 24/7 communication with the specialist palliative care team about their patients. The secondary objective is to follow these patients longitudinally to track their contacts with family physicians, home care, specialist palliative care teams, and with acute care services. This will inform the next phase of this study which will occur at multiple sites and will measure differences in patient-reported outcomes depending on level of involvement with primary and specialist palliative care.

Letter

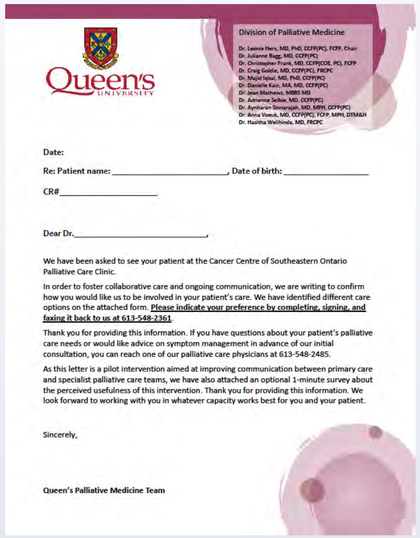
Pages 1-4 comprise the standardized letter sent out to local family physicians.

Page 1 is the introductory page introducing the intervention

Page 2 outlines the different shared care options for the family physician to choose from and asks for the best contact information for the family physician to be reached

Page 3 is the family physician survey using a Likert-scale to collect data on the perceived usefulness of the intervention

Page 4 provides additional information about the Queen's Palliative Medicine Team and the services that we provide to our patients including home visits from our Community Consult team and direct admission to Kingston General Hospital and the Palliative Care Unit at Providence Care Hospital



Division of Palliative Medicine

Dr. Leonie Herx, MD, PhD, CCFP(PC), FCFP, Chair
Dr. Julianne Bagg, MD, CCFP(PC)
Dr. Christopher Frank, MD, CCFP(COE, PC), FCFP
Dr. Craig Gokiert, MD, CCFP(PC), FRCPC
Dr. Majid Iqbal, MD, PhD, CCFP(PC)
Dr. Daniela Kain, MA, MD, CCFP(PC)
Dr. Jean Mathews, MBBS MD
Dr. Adrienne Selkie, MD, CCFP(PC)
Dr. Aynharan Sinnarajah, MD, MPH, CCFP(PC)
Dr. Anna Vowles, MD, CCFP(PC), FCFP, MPH, DTM&H
Dr. Hashka Welthiwia, MD, FRCPC

Date:

Re: Patient name: _____, Date of birth: _____

CR#_____

Dear Dr._____,

We have been asked to see your patient at the Cancer Centre of Southeastern Ontario Palliative Care Clinic.

In order to foster collaborative care and ongoing communication, we are writing to confirm how you would like us to be involved in your patient's care. We have identified different care options on the attached form. **Please indicate your preference by completing, signing, and faxing it back to us at 613-548-2361**

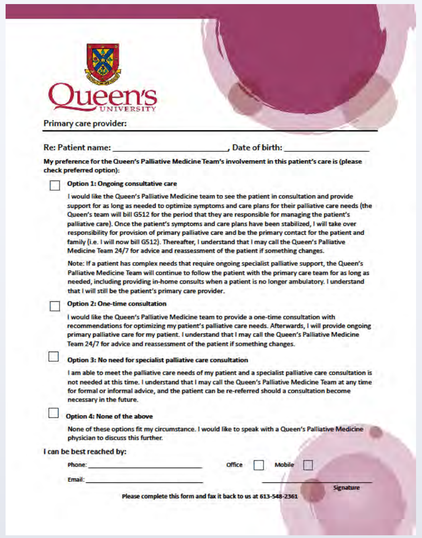
Thank you for providing this information. If you have questions about your patient's palliative care needs or would like advice on symptom management in advance of our initial consultation, you can reach one of our palliative care physicians at 613-548-2485.

As this letter is a pilot intervention aimed at improving communication between primary care and specialist palliative care teams, we have also attached an optional 1-minute survey about the perceived usefulness of this intervention. Thank you for providing this information. We look forward to working with you in whatever capacity works best for you and your patient.

Sincerely,

Queen's Palliative Medicine Team

Page 1: Introduction



Primary care provider:

Re: Patient name: _____, Date of birth: _____

My preference for the Queen's Palliative Medicine Team's involvement in this patient's care is (please check preferred option):

☐ **Option 1: Ongoing consultative care**

I would like the Queen's Palliative Medicine team to see the patient in consultation and provide support for as long as needed to optimize symptoms and care plans for their palliative care needs (the Queen's team will bill GS12 for the period that they are responsible for managing the patient's palliative care). Once the patient's symptoms and care plans have been stabilized, I will take over responsibility for provision of primary palliative care and be the primary contact for the patient and family (i.e. I will now bill GS12). Thereafter, I understand that I may call the Queen's Palliative Medicine Team 24/7 for advice and reassessment of the patient if something changes.

Note: If a patient has complex needs that require ongoing specialist palliative support, the Queen's Palliative Medicine Team will continue to follow the patient with the primary care team for as long as needed, including providing in-home consults when a patient is no longer ambulatory. I understand that I will still be the patient's primary care provider.

☐ **Option 2: One-time consultation**

I would like the Queen's Palliative Medicine team to provide a one-time consultation with recommendations for optimizing my patient's palliative care needs. Afterwards, I will provide ongoing primary palliative care for my patient. I understand that I may call the Queen's Palliative Medicine Team 24/7 for advice and reassessment of the patient if something changes.

☐ **Option 3: No need for specialist palliative care consultation**

I am able to meet the palliative care needs of my patient and a specialist palliative care consultation is not needed at this time. I understand that I may call the Queen's Palliative Medicine Team at any time for formal or informal advice, and the patient can be re-referred should a consultation become necessary in the future.

☐ **Option 4: None of the above**

None of these options fit my circumstance. I would like to speak with a Queen's Palliative Medicine physician to discuss this further.

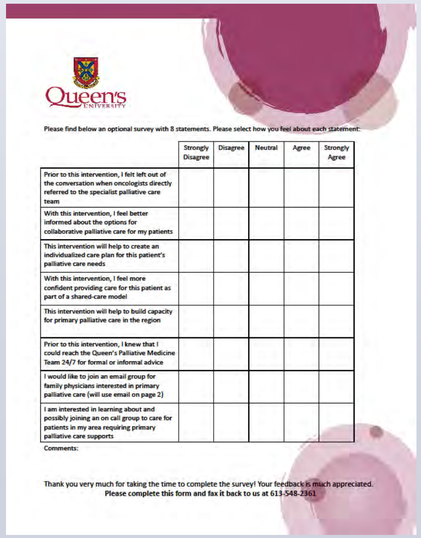
I can be best reached by:

Phone: _____ Office ☐ Mobile ☐

Email: _____ _____ Signature

Please complete this form and fax it back to us at 613-548-2361

Page 2: Options for shared care



Please find below an optional survey with 8 statements. Please select how you feel about each statement:

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
Prior to this intervention, I felt left out of the conversation when oncologists directly referred to the specialist palliative care team					
With this intervention, I feel better informed about the options for collaborative palliative care for my patients					
This intervention will help to create an individualized care plan for this patient's palliative care needs					
With this intervention, I feel more confident providing care for this patient as part of a shared-care model					
This intervention will help to build capacity for primary palliative care in the region					
Prior to this intervention, I knew that I could reach the Queen's Palliative Medicine Team 24/7 for formal or informal advice					
I would like to join an email group for family physicians interested in primary palliative care [will use email on page 2]					
I am interested in learning about and possibly joining an on call group to care for patients in my area requiring primary palliative care supports					

Comments:

Thank you very much for taking the time to complete the survey! Your feedback is much appreciated.
Please complete this form and fax it back to us at 613-548-2361

Page 3: Family physician survey



Additional Information About Our Team

Our specialist palliative care team sees ambulatory patients at the Cancer Centre of Southeastern Ontario (CCSEO) and in our outreach clinic at Quinte Health Centre (QHC). We provide consultative support for cancer-related symptom management and care planning, and offer palliative procedures such as therapeutic paracentesis at our CCSEO site.

We follow patients as long as needed to optimize symptoms and we work closely with a patient's oncology and primary care teams who provide ongoing cancer-based and primary care. Our nurse navigator supports a symptom triage line that patients, families and healthcare professionals can call during working hours. After hours, primary care providers can call the palliative medicine physician on call for formal or informal advice.

When patients with ongoing or intermittent need for specialist palliative care supports become homebound, our Community Consult team can continue to provide home-based assessments (in person or virtual, depending on patient location) as needed. The patient's family physician remains the patient's primary care provider.

When necessary, our team provides direct admissions to Kingston General Hospital for patients seen in our program with complex palliative symptom management issues requiring acute care supports. We also provide direct admission to the palliative care unit (PCU) at Providence Care Hospital for patients at end of life whose comfort-focused care needs cannot be managed in their home setting.

Further information about our team can be found on our website at:
https://deptmed.queensu.ca/divisions/palliative-medicine/clinical

Page 4: Additional information about the Queen's Palliative Medicine Team

Methods

A standardized letter template was created with inputs and several rounds of review from local family physicians and specialist palliative care team members. This letter includes the following components: information about local palliative care resources and contact information for the specialist palliative care team at Queen's University; a one-page survey to clarify shared care role boundaries, that family physicians will be requested to complete and fax back to the specialist team; a one-page survey using a Likert-scale to collect data on the family physicians' perceptions regarding the usefulness of this intervention to improve their engagement with palliative care.

This letter will be sent to family physicians whenever their patients are referred to the palliative oncology clinic by their oncologist. When responses are received from family physicians for the survey clarifying shared care role boundaries, this will be documented in the electronic patient record by the clinic team. Family physician input regarding their preferred level of engagement with palliative care (fully engaged for primary palliative care and specialist consult not required; one-time consult with specialist team and ongoing primary palliative care by family physician; ongoing specialist palliative care involvement while family physician continues to provide for other primary care needs) will determine further care planning in the palliative oncology clinic, and will be discussed with the patient at the next visit to arrive at a shared decision for managing ongoing palliative care needs.

Phase 1 of this project will include a 6-month pilot implementation at the CCSEO site. Relevant outcomes that will be measured include: feasibility (ratio of letters sent out over number of new consults received); response rate for the survey clarifying role boundaries (ratio of survey responses received from family physicians over number of letters sent out); descriptive summary of family physicians' preference for shared care roles; and family physician responses to the survey regarding their perceptions of the usefulness of this intervention. Patients will be followed longitudinally during the implementation period and data will be collected on number of contacts with family physicians, specialist palliative care, healthcare utilization, and place of care at the end-of-life.

We are already collaborating with other specialist palliative care teams in Ontario and Alberta to develop a multi-site project to improve communication between family physicians and specialist palliative care teams, pending findings from the pilot implementation. At the multi-site level, patients will be followed longitudinally in three prospective cohorts based on level of shared care- primary palliative care by family physician alone, one-time consult with specialist team and ongoing primary palliative care by family physician, and ongoing specialist palliative care follow-up. Relevant outcomes will be measured including symptom burden, quality of life, survival, number of contacts with family physicians and specialist palliative care, healthcare utilization, place of care at the end-of-life, and patient and family caregiver satisfaction with care.

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Educational Interventions to Improve Medical Learners' Competency in Goals Of Care Discussions– A Scoping Review

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Queen's UNIVERSITY

Department of Family Medicine

Introduction

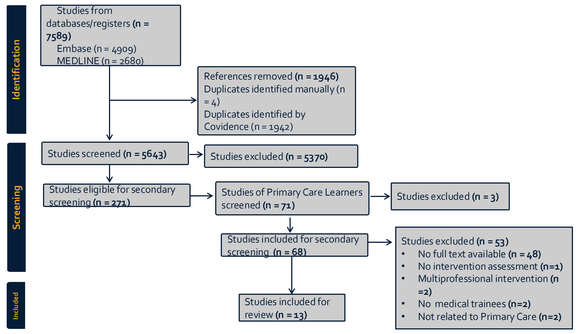
Advance care planning (ACP) is the process by which clinicians engage patients in conversations about illness understanding, elicit their wishes and values for their care, and designate a substitute decision-maker (SDM). Goals of care (GOC) discussions incorporate a patient's current wishes and values into preferences regarding specific medical interventions, place of care, and focus of care.

A Canadian survey found that only 9% of elderly patients discuss their values regarding care with their primary care providers. The main barrier reported by primary care residents in engaging patients in GOC discussions is a lack of confidence and skill. Leading GOC discussions is a teachable skill. However, it is not known what are the components of an effective educational intervention to improve learner competency in leading GOC discussions.

This study aimed to review the evidence for educational interventions to improve medical trainees' competency in conducting GOC discussions.

Methods

MEDLINE and EMBASE databases were searched on November 8 2023, and studies were uploaded into Covidence for screening. Inclusion criteria were studies targeting primary care residents (defined as Family Medicine, General Internal Medicine and General Pediatrics) that reported on details of the educational intervention, including mode of delivery, duration and frequency, and evaluation methods. Exclusion criteria: Non-English language articles, editorials, abstracts without full papers, and studies that did not report intervention details.



CENTRE FOR STUDIES IN PRIMARY CARE

Results

First Author, Year, Country	Study Design	N / Training program	Components of Intervention	Duration/ Frequency	Significant Results
Allen, 2015, USA	Pre-post surveys	95 / IM residents	Formalized continuity clinic curriculum including didactic session, role-play scenarios, and point-of-care tools to facilitate clinic workflow.	One-hour didactic and role-play/one-time	Improved confidence in ACP and increased number of ACP discussions.
Blomberg, 2020, USA	Pre-post surveys	34 / IM incoming residents	Workshop including lecture, patient-oriented decision aids, prognostication tools, small-group discussion, and case-based role-play.	3 hours/one-time	Self-reported knowledge and comfort regarding ACP improved. The workshop was well received. Participants found the role-play especially valuable.
Brown, 2012, USA	Secondary analysis of RCT	472 / IM residents, subspecialty fellows, NP students, advanced practice nurses	Simulation-based multisession workshop, including didactic overview with demonstration of role-play; skills practice with standardized patients; and reflective discussions. Control group: usual education	4 hours / 8 sessions	Intervention was associated with improved trainees' self-assessment of competence in communication skills.
Day, 2022, Canada	Qualitative	11 / IM Residents	E-learning module with 5 step approach to GOC discussions, including fictional patient cases, frequent reflective questions and exercises, and video role modeling.	1.5 hours /one-time	There was a shift in residents' perspectives from physician-centered GOC discussions focused on code status to a more patient-centered approach
Kam-Madruger, 2019, USA	Mixed methods	52 / FM residents	Interprofessional and multispecialty clinic curriculum including didactic session, resident-led multidisciplinary patient review, supervised resident-led patient encounter	3 hours / not specified	Improved resident self-assessed knowledge and confidence in ACP. Patients reported satisfaction with ACP discussion.
Kurahashi, 2020, Canada	Qualitative	15 / FM residents	Palliative care rotation including weekly didactic seminars, 2 weeks of home visits and 2 weeks of inpatient consultations	4 weeks	Participants reported more comfort with GOC discussions after the rotation. Adequate time for GOC discussions and preceptor modeling and supervision were facilitators.
Nagpal, 2021, USA	Pre-post surveys	84 / IM residents	Didactic sessions and simulation training with SPs, followed at least 3 months later by mini-Clinical Evaluation Exercise including direct feedback from real patients.	3 hours simulation/ once, followed by GOC discussion with real patients	Participants felt more prepared to conduct GOC conversations after simulation. Resident skills were retained or improved during the real patient interaction. Patients and families reported being heard and feeling satisfied with the conversation
Nassikas, 2020, USA	Pre-post surveys	24 / IM residents	Resident primary care clinic intervention including slideshow presentation on ACP, educational video, and 10-minute role-play	30-minute educational session / once	Improved resident confidence in ACP and increased number of ACP discussions.
Pekmazaris, 2011, USA	Pre-post surveys with control group comparison	150 / IM residents	Intensive end-of-life communications training over 2 weeks, including 6 didactic sessions, role-play with SPs , feedback and discussion regarding end-of-life. Outcomes were measured 2 weeks later.	2 hours / 6 sessions	Due to pre-test heterogeneity between intervention and control groups, data regarding competence in GOC discussions were analyzed in quartiles. In the intermediate quartile there was improved competence after the intervention.
Pettit, 2019, USA	Pre-post surveys	15 / FM Residents	Curriculum co-developed by clinicians and attorneys, including didactic session, direct observation of patient interaction, and feedback, videos (EPEC) and handout. They used a 5-point developmental scale to score residents' performance.	1-hour didactic + 30-minute observed patient interactions x2-3 interactions over an year	Residents' ACP discussions improved after each observed discussion, from "beginner" at first observed session to "developing" at third observed session. Residents rated their performance as good or excellent and felt confident in discussing ACP.
Tung, 2014, USA	Pre-post surveys	106 / IM residents	ACP quality improvement workshop in the continuity clinic, including didactic learning, case-based reflections, chart audit of resident's patients, and small group discussions.	half-day / once	At baseline, only 24% of audited patients had an advance directive, and 28% of the ACP-documentation was of no clinical utility. Residents reported significantly improved confidence with ACP after the intervention.
Von Guten, 2017, USA	Mixed methods with control group comparison	448 / Internal Medicine (IM) and Family Medicine (FM) residents	Palliative care clinical rotation including didactic content from 4 EPEC online modules, video-taped interview with an SP, reflection exercises and supervised care for patients in the hospice setting.	4 weeks	Improved scores in knowledge test and improved self-assessed confidence in palliative care communication skills. Large effect size in improved knowledge when compared to a national reference cohort. The rate of hospice referral for physicians trained in the program were similar to a control group, but those trained in the program referred patients to hospice earlier.
Wu, 2019, USA	Pre-post surveys	22 / IM residents	3-Act model for narrative approach to GOC discussions, including two small group sessions with didactic learning, narrative reflections, and video demonstration; 10 role-play sessions with 360-degree reflection; and grading using a novel GOC Communication Assessment Tool.	Two 3-hour workshops including didactic + role-play	Proficiency increased from 30% pre-test to 100% after final role-play. 96% of participants felt ready to lead GOC discussions independently.

Discussion

Intervention Demographics

11/13 studies were from the US, and 8/13 studies were published in the last 5 years. 9/13 studies targeted IM residents, 3/13 targeted FM residents, and 1 study targeted both. 7/13 studies had a pre-post survey design. The mean number of participants in the included studies was 117.5, ranging from 11-to 472.

Teaching Modalities

The majority of the studies utilized multimodal approaches. While it is challenging to determine the comparative effectiveness of simulation versus real-patient encounters due to heterogeneity in study designs, the integration of both approaches was perceived as beneficial by trainees.

Length of Interventions

7/13 studies used a one-time workshop design. Studies that measured the impact of longitudinal interventions reported that performance improved after follow-up sessions. It is likely these interventions will need multiple sessions for knowledge retention, reinforcement of desirable behaviours in engaging in GOC discussions, and ultimately to ensure a positive impact on patient care.

Assessment Methods

All 13 studies used a self-assessed learning metric: confidence, comfort, or competence. Three studies used independent measures of performance on knowledge tests or assessment of residents' GOC discussions. Two studies measured improved resident behavior in conducting more GOC discussions. Three studies measured results of the training on referrals to hospice and patient satisfaction.

Overall, while these interventions showed promise to improve trainee competency in GOC discussions, further research is needed to standardize evaluation methods and ensure comprehensive coverage of relevant domains of GOC discussions.

Conclusion

The current landscape of GOC teaching initiatives in primary care settings is characterized by studies from high-income countries, with a pre-post survey design, using a one-time multi-modal workshop model, and measuring impact on self-assessed learner atitudes to conducting GOC discussions.

While most studies show positive impacts on medical trainees, further research should study interventions in high- and low-and-middle-income countries, including simulated and real patient encounters, covering all domains of ACP and GOC, delivered longitudinally, and assessed using a mix of methods.

Respirology & Sleep Medicine



Dr. Genevieve Digby
Division Co-Chair



Dr. Nicolle Domnik
Research Lead

Summary

- *Impact of continuous positive airway pressure (CPAP) on ventilatory neural control and respiratory mechanics during cardiopulmonary exercise testing (CPET) in chronic obstructive pulmonary disease (COPD) and Obstructive sleep apnea (OSA) patients*
- *Impact of CPAP on physical activity and fatigue in COPD-OSA patients*
- *Assessment of sleep quality on physical activity and exercise capacity of patients*
- *Impact of vaping historic/acute vaping in young adults on cardiovascular regulation and sleep*

Division of Respirology and Sleep Medicine – Resident Research Fair Submission

Active Projects

Principal Investigator: Dr. J Alberto Neder, alberto.neder@queensu.ca

Novel paradigms on clinical cardiopulmonary exercise testing interpretation: using machine-learning approaches to develop and validate the first software for dynamic assessment of dyspnea and ventilation during exercise testing (DyVe-X)

In this ongoing study, we aim to develop the first software (DyVe-X) to quantify exertional dyspnea severity while exposing its mechanical-ventilatory underpinnings across progressively higher ventilatory demands during incremental cardiopulmonary exercise testing (CPET). We will also innovate using machine-learning approaches to build on our previous and current work on novel paradigms to present and interpret the CPET data founded on key neurophysiological and psychophysical concepts of exertional dyspnea. The successful candidate should have solid IT and big data analysis skills/experience to achieve tangible outcomes in a timely fashion.

Principal Investigator: Dr. Vanessa Martelli, vanessa.martelli@mail.mcgill.ca

Project Title: Correlation and Agreement between two Health-Related Quality of Life Measures in Patients with Obstructive Sleep Apnea

Randomized controlled trials in patients with obstructive sleep apnea have attempted to assess whether continuous positive airway pressure improves health-related quality of life (HRQOL), with positive findings using certain HRQOL questionnaires, such as the OSA-specific Functional Outcomes of Sleep Questionnaire (FOSQ), but not the generic EQ-5D health utility. OSA-specific HRQOL questionnaires have a more appropriate distribution of health states for the main impacts of the disease; however, cannot be converted to a health utility for quality-adjusted life-years measurement. This study will use correlation statistics and Bland Altman analysis to determine the correlation and agreement between the FOSQ-10 and the EQ-5D-5L in 200 adult patients with treated and untreated obstructive sleep apnea.

Principal Investigator: Dr. M Diane Lougheed, diane.lougheed@kingstonhsc.ca

Active Areas of Research:

- Asthma health services research, using existing observational databases and/or IC/ES data
- Knowledge translation using EMRs – integrating guidelines into practice, focused on asthma and COPD

- Clinical physiology – symptom perception of asthma and cough.

Principal Investigator: Dr. Onofre Moran, morano@queensu.ca

Research Projects and Opportunities:

- Clinical characteristics and prognosis of patients with UIP pattern and BAL lymphocytosis.
- Evaluation of dyspnea by the Brief King's Dyspnea questionnaire and dyspnea VAS.
- Description of CT patterns on presentation in patients with CTD related ILD.
- Description of clinical, radiological and serologic domains in IPAF.
- Validation of CTD questionnaire used in ILD clinic.
- BAL comparisons after discarding 20 ml randomly.
- Prognosis of patients with chronic HP when an extensive exposure questionnaire is applied.
- Assessment of the diagnosis and prognosis of ILD radiologic patterns on chest

Principal Investigator: Dr. Sebastián Rodriguez,
sebastian.rodriguezllamazares@kingstonhsc.ca

PLEURAL SPACE RESEARCH

The pleural space clinic manages over 20 patients with Malignant Pleural Effusion (MPE) monthly. Currently looking towards expanding its services towards ultrasound diagnosis, PleurX guided pleurodesis and medical thoracoscopy, the Pleural Space is proud to host the following opportunities:

A. Improving oncological care through a one-stop shop model of care.

- **Objective:** Redesign clinical pathways and processes to provide multiple interventions in patients with MPE within a single timeframe.
- **Profile:**
  - A maximum of two PGY-1 or PGY-2 residents
  - Interest in quality improvement initiatives
- **Expected gains:**
  - Become proficient in point-of-care thoracic ultrasound
  - Harness hands-on ability for minimal invasive pleural interventions
  - (At least) one quality-improvement related publication

B. Linking Pleural Physiology to clinical care

- **Objective:** Use pleural physiology measures (i.e. pleural manometry, ultrasound-guided atelectasis displacement measurements) to improve clinical outcomes during pleural procedures.

- **Profile:**
    - One PGY-1 or PGY-2 resident
    - Interest in translational research and pleural procedures.
- **Expected gains:**
    - Become proficient in point-of-care thoracic ultrasound
    - Harness hands-on ability for minimal invasive pleural interventions
    - (At least) one translational research publication.

Principal Investigator: Dr. Nicolle Domnik, PhD, Biomedical and Molecular Sciences with Cross-Appointment to Division of Respirology and Sleep Medicine, n.j.domnik@queensu.ca

Resident Research Opportunities:

1. Characterization of sleep via MUSE headband, and associations between typical sleep and susceptibility to sleep deprivation-related impacts on cardiopulmonary exercise testing
   OR
   Impact of sleep deprivation on cardiovascular and metabolic circulatory markers
    - Both are sister-studies to an ongoing project examining effects of sleep deprivation on CPET and perceptual/physiologic responses to exercise
    - Opportunity to either analyse sleep data obtained by MUSE headband and qualitative sleep data OR circulatory biomarkers to investigate associations with sleep deprivation-related effects
2. Quantifying the prevalence of oral nicotine pouch use in Canadian post-secondary students
3. Does a metronome-paced tachypnea protocol adequately induce dynamic hyperinflation (in COPD, in health), enabling its use as a test for bronchodilator efficacy?
4. Wildcard! Feel free to reach out if you have ideas for retrospective (e.g., using internal resources like chart review, sleep lab database, our research team's database) or prospective inquiry you wish to pursue in the general domain of cardiopulmonary (patho)physiology, sleep, and exercise from either a quantitative or qualitative lens, and I'd be happy to chat.

Resident-Led Projects and Manuscripts

1: Saint-Pierre MD, Abdulnour J, Sabbagh R, Neder JA. Low D_{LCO} predicts all-cause hospital admissions in patients with reduced left ventricular ejection fraction or diastolic dysfunction. ERJ Open Res. 2020 Jul 20;6(2):00095-2020. doi: 10.1183/23120541.00095-2020. PMID: 32714956; PMCID: PMC7369432.

2: Saint-Pierre M, Ladha J, Berton DC, Reimao G, Castelli G, Marillier M, Bernard AC, O'Donnell DE, Neder JA. Is the Slow Vital Capacity Clinically Useful to Uncover Airflow Limitation in Subjects With Preserved FEV₁/FVC Ratio? Chest. 2019 Sep;156(3):497-506. doi: 10.1016/j.chest.2019.02.001. Epub 2019 Feb 12. PMID: 30768928.

3. Marillier M, Bernard AC, Reimao G, Castelli G, Alqurashi H, O'Donnell DE, Neder JA. Breathing at Extremes: The Restrictive Consequences of Super- and Super-Super Obesity in Men and Women. Chest. 2020 Oct;158(4):1576-1585. doi: 10.1016/j.chest.2020.04.006. Epub 2020 Apr 15. PMID: 32304775.

4. Attalla M, AlGhamdi S, Digby G, Neder JA. A "Bloody" Surprise: When Having Two Lungs Is Providential Ann Am Thorac Soc . 2022 Aug;19(8):1419-1427. doi: 10.1513/AnnalsATS.202203-184CC.

5. D'Cruz J, Neder-Serafini I, Zapotichny A, Neder JA. Ann Am Thorac Soc. 2024 Feb;21(2):343-Exposing the Roots of Restriction: When the Transfer Coefficient Makes the Difference. 350. doi: 10.1513/AnnalsATS.202305-484CC.

6. Alqurashi H, Marillier M, Neder-Serafini I, Bernard AC, Moran-Mendoza O, Neder JA. Impact of obesity progression or regression on the longitudinal assessment of fibrosing interstitial lung disease. Eur Respir J. 2024 Apr 18;63(4):2301864. doi: 10.1183/13993003.01864-2023. PMID: 38514096.

7. Al Sa'idi L, Berton DC, Neder JA. Eur Respir J. 2024 Jul 26:2301960. doi: The 2022 ERS/ATS z-score classification to grade airflow obstruction: relationship with exercise outcomes across the spectrum of COPD severity. 10.1183/13993003.01960-2023. Online ahead of print. PMID: 38936965

Characterizing Adult Asthma: Insights from the Canadian Primary Care Sentinel Surveillance Network

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BACKGROUND

- National statistics on asthma prevalence is based upon population health surveys or administrative data[1].
- However, as most of the care provided to patients with asthma in Canada is through family physicians[2], primary care electronic medical records (EMRs) may provide complementary information on asthma epidemiology and practice patterns.
- The Canadian Primary Care Sentinel Surveillance Network (CPCSSN) is a national database comprising of data sourced from 12 primary care networks across Canada, making it a valuable resource for obtaining information on the care of adults with asthma.
- Our study aimed to further characterize adult asthma in Canada based on our recently validated CPCSSN case definition for suspected or confirmed asthma[3]
  - Patients meet this case definition if their chart contains either the ICD-9 code for asthma or the text string "asthma" in one or more of the billing, encounter diagnosis, or health condition sections, and excludes variations of the text string "query asthma" in encounter diagnosis.

OBJECTIVES

1. To estimate the prevalence of adult asthma across Canada using the validated CPCSSN case definition.
2. To characterize the demographic variables and comorbidities of adults with asthma in Canada.
3. To provide an overview of national prescribing practices in primary care.

METHODS

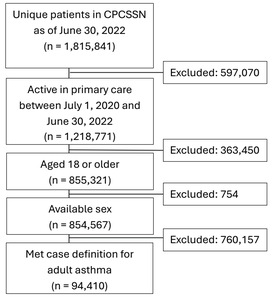
- For all unique patients with an active visit at a participating CPCSSN clinic in the 2-year period from July 1, 2020 to June 30, 2022, charts were screened to include patients who were aged 18 years or older with available sex recorded.
- The CPCSSN adult asthma case definition was applied to identify cases of confirmed or suspected adult asthma.
- Using these data, the prevalence of confirmed or suspected asthma was estimated, and further stratified by age, sex and BMI.
  - The number of comorbidities were compared in cohorts with or without asthma, and between males and females with asthma.
  - The age and sex distribution from the Statistics Canada 2021 census profile[4] was used to estimate the age- and sex-adjusted prevalence for adults aged 20 years and older.
- For all patients in the sample, medication prescriptions were collected across the patient's lifetime.
  - Prescriptions were grouped by class using Anatomical Therapeutic Chemical (ATC) codes.

FUNDING

Funded by the Government of Ontario's Academic Health Sciences Centre Alternate Funding Plan Innovation Fund.

RESULTS

Sample derivation

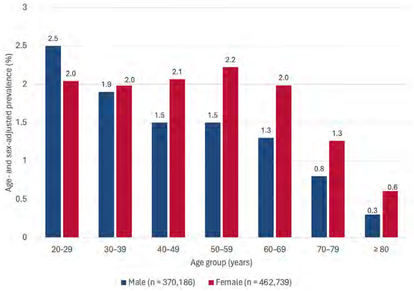


- 854,567 charts with available demographic information were identified as active adult patients in the 2-year study period.
  - 94,410 charts met criteria for suspected or confirmed asthma.

Prevalence

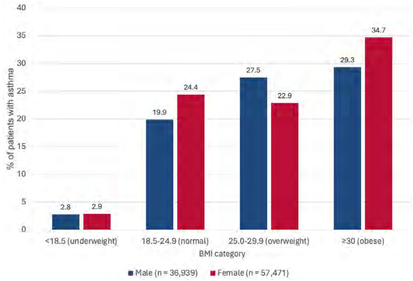
- The overall prevalence of adult asthma is 11%.
- Asthma prevalence decreases with increasing age (14% in adults aged 18-29 years compared to 8% in adults aged ≥ 80 years).
- Asthma is more common in females (12%) vs. males (10%).

Age and sex-standardized prevalence



- Asthma is more common in females compared to males across every age category, except for adults aged 20-29 years.

BMI category of male and female patients with asthma



- A greater proportion of females with asthma are obese (BMI ≥ 30 kg/m^2) compared to males with asthma (35% vs. 29%, respectively; p <0.0001).
  - This was most apparent in obesity class III (BMI ≥ 30 kg/m^2) (9% vs. 5%, female vs. male).

Comorbidities

- The prevalence of 3 or ≥ 4 comorbidities is higher in females with asthma than without asthma (33% vs. 27%, respectively for ≥ 4 comorbidities).
  - Females with asthma are more likely to have 2, 3 or ≥ 4 comorbidities compared to males with asthma.

Age- and sex-adjusted prevalence ratios for comorbidities in adults with asthma

Comorbidity	Adjusted prevalence ratio (95% CI)
Chronic Obstructive Pulmonary Disease	2.40 (2.33-2.46)
Chronic Heart Failure	1.63 (1.57-1.69)
Depression	1.56 (1.54-1.58)
Coronary Artery Disease	1.53 (1.49-1.58)
Diabetes	1.33 (1.31-1.36)
Hypertension	1.42 (1.40-1.45)

- Adults with asthma are more likely to also hold a diagnosis of chronic obstructive pulmonary disease, heart failure, coronary artery disease, diabetes, hypertension and depression.

Prescription of medication classes (lifetime) in patients with asthma

Medication class	No. of patients prescribed medication	% (n=94,410)
Short-acting bronchodilators	70,952	75.2
ICS[a]	44554	47.2
ICS/LABA[b]	42521	45.0
Budesonide/formoterol	27756	29.4
ICS/LABA/LAMA[c]	5103	5.4
LTRA[d]	9596	10.2
Biologics	291	0.3
Confirmed chronic macrolides (>50% of year)	1089	1.2
Prednisone		
- Chronic *(>50% of year)*	1561	1.7
- 2 or more courses in the last year (including duration not available)	8946	9.5

[a]ICS: inhaled corticosteroid; [b]LABA: long-acting beta-agonist; [c]LAMA: long-acting muscarinic antagonist; [d]LTRA: leukotriene receptor antagonist

- Most patients (75%) have been prescribed short-acting bronchodilators in their lifetime.
- Very few patients in the primary care setting were prescribed chronic macrolides or chronic prednisone (1.2% and 1.7%, respectively).

Prescription of unique medication classes (lifetime) in patients with asthma

Medication class	No. of patients prescribed medication	% (n=94,410)
SABA[a] monotherapy	11886	12.6
SAMA[b] monotherapy	101	0.2
SABA/SAMA Combination	369	0.4
ICS monotherapy[‡]	21405	22.7
ICS/LABA[‡]	28106	29.8
Budesonide/formoterol monotherapy	4275	4.5
ICS/LABA/LAMA[‡]	2312	2.45
LTRA‡	772	0.8
ICS/LABA/LTRA[‡]	4342	4.6
Triple Therapy/LTRA[‡]	2798	3.0

[a]SABA: short-acting beta-agonist; [b]SAMA: short-acting muscarinic antagonist
‡: ± any SABA, SAMA, or SABA/SAMA

- Only a small percentage patients on asthma therapies were on SABA or SAMA monotherapy.
- Overall, approximately 30% of patients with asthma were never prescribed a steroid-containing inhaler.
  - Of patients who were prescribed medication for asthma, approximately 17% were never prescribed a steroid-containing inhaler.

CONCLUSIONS

- The estimated prevalence of suspected or confirmed asthma is 11% based on a national sample of EMR data, similar to prior Canadians estimates based on self-reported survey data[5, 6].
- Asthma is more prevalent in females than males across all age groups other than 20-29 years.
- Patients with asthma are at greater risk of having of multiple major comorbidities.
- Multi-morbidity is increased in females with asthma when compared both to females without asthma, as well as to males with asthma.
- Obesity is highly prevalent in both males and females with asthma.
- Most patients with asthma have been prescribed multiple classes of inhalers. However, approximately 30% have never been prescribed a steroid-containing inhaler.

REFERENCES

1. Statistics Canada (2023). Table 13-10-0096-08: Asthma, by age group.
2. Minard JP, et al. Development and implementation of an electronic asthma record for primary care: Integrating guidelines into practice. *J Asthma.* 2014;51:58–68.
3. Moloney M, et al. Validation of adult asthma case definitions for primary care sentinel surveillance. *Allergy Asthma Clin Immunol.* 2023;19(95).
4. Statistics Canada (2022). Tables 98-26-0009: Special Interest Profile, 2021 Census of Population.
5. Chu LM, Pahwa P. Prevalence and associated factors for self-reported asthma in a Canadian population: The Canadian Community Health Survey, 2014. *J Asthma.* 2018;55(1):26-34.
6. Nasreen S, et al. Age, period, and cohort effects on asthma prevalence in Canadian adults, 1994-2011. *Ann Epidemiol.* 2020;41:49-55.

Effects of Asthma Management Resources on Health Services Utilization in Ontario Emergency Departments

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Abstract

Background: Emergency departments (EDs) play important roles in the management of asthma exacerbations. ED return-visit rates provide a measure of the quality of acute asthma care. We sought to assess the impact of access to ED asthma management resources and specialists on return ED visits within 72 hours and hospital admissions.

Methods: 173 Ontario hospitals were surveyed regarding their access to community and ED asthma specialists, and ED asthma management resources. Survey data were linked to Ontario's administrative health databases to quantify acute health services utilization. Multi-variable logistic regression models adjusted for potential patient- and hospital-level confounders.

Results: 119 (69%) sites responded to the online survey, six were excluded from analysis due to incomplete responses. The majority of respondents were community hospitals (53%). There were no significant differences in hospital characteristics based on survey completion status and no significant associations between the availability (within a 100km radius) of community-based asthma specialists and return ED visits or hospital admissions (Table 1). Availability was not universal across all sites. Access to consultant Respirologists in the ED was associated with a 39% (p=0.0092) increased odds of return ED visits. The availability of peak expiratory flow testing and spirometry were associated with 34% (p=0.0071) and 23% (p=0.028) reductions in the odds of return ED visits, respectively. These measures were only available at 77% and 45% of sites, respectively.

Conclusions: Important gaps in ED asthma management resources were identified in many centres, notably limited access to spirometry, Respirologists, asthma education, and other specialists with expertise in asthma management. Increased return visits at sites where Respirologists are available for consult may be indicative of more severe asthma patients seen at larger centres, despite attempting to control for more severe patient characteristics. Peak expiratory flow testing and spirometry, which are associated with reduced ED return visits, were not universally available despite their low costs and portability. These results support the need for continued efforts to implement strategies demonstrated to improve ED asthma care and outcomes.

Table 1: Adjusted ORs[f] for Return ED Visit Within 72 Hours and Hospital Admission, by Asthma Management Specialists and Resources (N=113)[g]

ED Management strategy	Number of sites (%)	Return ED Visit Within 72 hours		Hospital Admission	
		OR (95% CI)	*p*-Value	OR (95% CI)	*p*-Value
Community Asthma Specialists					
Allergist	78 (65.5)	0.93 (0.69-1.27)	0.6561	0.78 (0.54-1.11)	0.165
Asthma Educator	66 (55.5)	1.20 (0.96-1.50)	0.115	1.07 (0.83-1.38)	0.5879
General Internist	95 (79.8)	0.87 (0.58-1.30)	0.5001	0.64 (0.41-1.02)	0.0618
Respirologist	82 (68.9)	0.95 (0.66-1.37)	0.7961	0.98 (0.65-1.46)	0.9039
ED Asthma Specialists					
Anesthesiology	92 (77.3)	0.88 (0.58-1.33)	0.5353	0.61 (0.34-1.11)	0.1052
General Internal Medicine	75 (63.0)	0.84 (0.61-1.16)	0.2973	1.09 (0.73-1.63)	0.6589
Respirology	35 (29.4)	**1.39 (1.08-1.78)**	**0.0092**	0.82 (0.63-1.07)	0.1442
Respiratory Therapy	75 (63.0)	0.92 (0.63-1.32)	0.6386	1.34 (0.81-2.24)	0.2559
ED Asthma Resources					
Peak Expiratory Flow Testing	92 (77.3)	**0.66 (0.49-0.89)**	**0.0071**	1.38 (0.97-1.97)	0.0728
Spirometry	54 (45.4)	**0.77 (0.62-0.97)**	**0.028**	1.22 (0.95-1.55)	0.1159
Advanced medical directives for bronchodilators	76 (63.9)	0.93 (0.70-1.24)	0.6285	0.82 (0.61-1.11)	0.2047
Advanced medical directives for steroids	27 (22.7)	1.17 (0.89-1.54)	0.2688	1.10 (0.84-1.43)	0.499
Pre-printed orders	66 (55.5)	1.01 (0.81-1.26)	0.9403	1.19 (0.93-1.51)	0.1632
Written discharge instructions	45 (37.8)	0.98 (0.76-1.25)	0.847	0.82 (0.63-1.05)	0.1192

[f]*Adjusted for age, sex, triage level, ED visit for asthma in the previous 12 months, hospital admission for asthma in the previous 12 months, ED visit volume, proportion of all ED visits with asthma, propensity to admit.*
[g]*Data not provided by six survey respondents*

Background

- Exacerbations of asthma reflect suboptimal control of this disease, contributing substantially to its morbidity and costs.
- Asthma management guidelines[1,2,3] summarize evidence-based asthma care.
  - Adoption of guidelines hinges upon successful knowledge translation and implementation initiatives[4].
- ED asthma management strategies include access to tests and specialists, use of medical directives and order sets, patient education and discharge instructions and follow-up.
  - Clinical pathways can be an effective means of supporting best practice for a variety of conditions and settings, including asthma.
- As part of a provincial asthma strategy[4], the Government of Ontario funded the development of a standardized ED asthma care pathway (EDACP) for adult asthma to enable adherence to best practice and be suitable for province-wide implementation.
- Following a successful pilot study[5], the Government of Ontario funded The Lung Association - Ontario to design and support a 'roll-out' of the EDACP making it available to all Ontario EDs through regional workshops between 2008 to 2011.

Objective

- To assess the impact of access to ED asthma management resources and specialists on return ED visits within 72 hours and hospital admissions

Methods

- This is an institution-cohort study of all ED or Urgent Care Centres (UCC) in Ontario, Canada. This study was approved by the institutional review board at Sunnybrook Health Sciences Centre, Toronto, Canada and Queen's University, Kingston, Canada.

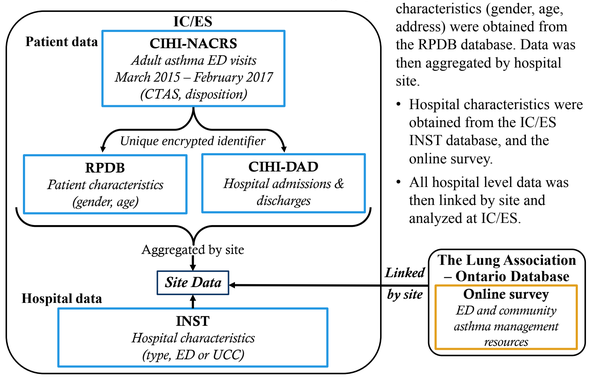
Data Sources

- All Ontario EDs and UCCs were invited by The Lung Association – Ontario to complete an online survey about their current EDACP implementation status, and access to ED asthma management resources, consultants and outpatient specialists.

	Institute for Clinical Evaluative Sciences (IC/ES)	The Lung Association-Ontario Database
Patient	• Canadian Institute for Health Information-National Ambulatory Care Reporting System (CIHI-NACRS) • Canadian Institute for Health Information-Registered Persons Database (CIHI-RPDB) • Canadian Institute for Health Information-Discharge Abstract Database (CIHI-DAD)	
Hospital	• Institution Database (INST)	• Online survey

Data linkage

- All ED or UCC visits for asthma for individuals aged 20 to 64 between March 1, 2015 - February 28, 2017 were obtained from the CIHI-NACRS database. Hospital admissions were collected from the CIHI-DAD database. Using unique encoded identifiers, patient characteristics (gender, age, address) were obtained from the RPDB database. Data was then aggregated by hospital site.
- Hospital characteristics were obtained from the IC/ES INST database, and the online survey.
- All hospital level data was then linked by site and analyzed at IC/ES.



Statistical Analysis

- Multi-variate logistic regression models investigated the association between asthma management strategies and resources and:
  i) return ED visits within 72 hours;
  ii) hospital admission following an index ED visit.
- Potential patient-level confounders (age, sex, triage level, ED visit for asthma in the previous 12 months, hospital admission for asthma in the previous 12 months) and ED-level confounders (ED visit volume, proportion of all ED visits with asthma, propensity to admit) were assessed in the modeling.

Results

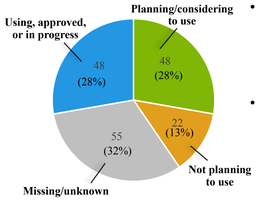
- 35,954 individuals presented at 173 different institutions for asthma between March 2015 - February 2017.
- 119 (69%) sites responded to the online survey (Table 1).
  - The majority of respondents were community hospitals.
  - There were no significant differences in the characteristics of sites that did and did not respond to the survey.

Table 1: Characteristics of Sites by Survey Completion Status

Characteristic	Survey Completion		*p*-Value
	Yes (n, %) N=119	No (n, %) N=54	
Hospital Type			<0.989
Small	41 (34.5)	18 (33.3)	
Community	63 (52.9)	29 (53.7)	
Teaching	15 (12.6)	7 (13.0)	
Urgent Care Centre	9 (7.6)	≤ 5	0.705
Has Acute Beds	111 (93.3)	52 (96.3)	0.43
Medical Beds (Mean±SD)	58.06 ±84.71	39.67±66.27	0.17
ICU Beds (Mean±SD)	11.69 ±18.97	8.65 ±16.52	0.324
Total Beds (Mean±SD)	129.29 ±177.41	95.73 ±136.81	0.23
ED Visit Volume (Mean±SD)*	35,714.98 ±27,542.13	28,784 ±28,348.30	0.131
Hospital Admission Volume (Mean±SD)*	7,834.45 ±10,334.29	5,800.12 ±9,125.92	0.23
Open 24/7	114 (95.8)	51 (94.4)	0.694

**Number per year*

Implementation Status



- As of April 2017, implementation status was known for 118 sites.
- 41% of sites who responded to the survey (representing 28% of all sites) were using or in the process of approving the EDACP. Of these sites, the majority were using the updated 2012 version.
- Implementation status was significantly different across sites by hospital type ($p = 0.047$)
  - Teaching hospitals were more likely to be using, have approved, or be in the process of implementing the EDACP.
  - Small and community hospitals were more likely to be planning/considering using the EDACP at their sites.

Community Asthma Specialists

Table 2: Adjusted ORs[f] for Return ED Visits Within 72 Hours and Hospital Admission, by Community Asthma Specialists (N=113)[g]

Community Asthma Specialists	Number of sites (%)	Return ED Visit Within 72 hours		Hospital Admission	
		OR (95% CI)	*p*-Value	OR (95% CI)	*p*-Value
Allergist	78 (65.5)	0.93 (0.69-1.27)	0.6561	0.78 (0.54-1.11)	0.165
Asthma Educator	66 (55.5)	1.20 (0.96-1.50)	0.115	1.07 (0.83-1.38)	0.5879
General Internist	95 (79.8)	0.87 (0.58-1.30)	0.5001	0.64 (0.41-1.02)	0.0618
Respirologist	82 (68.9)	0.95 (0.66-1.37)	0.7961	0.98 (0.65-1.46)	0.9039

[f]*Adjusted for age, sex, triage level, ED visit for asthma in the previous 12 months, hospital admission for asthma in the previous 12 months, ED visit volume, proportion of all ED visits with asthma, propensity to admit.*
[g]*Data not provided by six survey respondents*

ED Asthma Management Strategies

Table 3: Adjusted ORs[f] for Return ED Visit Within 72 Hours and Hospital Admission, by ED Asthma Management Strategies and Services (N=113)[g]

ED Management strategy	Number of sites (%)	Return ED Visit Within 72 hours		Hospital Admission	
		OR (95% CI)	*p*-Value	OR (95% CI)	*p*-Value
ED Asthma Specialists					
Anesthesiology	92 (77.3)	0.88 (0.58-1.33)	0.5353	0.61 (0.34-1.11)	0.1052
General Internal Medicine	75 (63.0)	0.84 (0.61-1.16)	0.2973	1.09 (0.73-1.63)	0.6589
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ED Asthma Resources					
Peak Expiratory Flow Testing	92 (77.3)	**0.66 (0.49-0.89)**	**0.0071**	1.38 (0.97-1.97)	0.0728
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Written discharge instructions	45 (37.8)	0.98 (0.76-1.25)	0.847	0.82 (0.63-1.05)	0.1192

[f]*Adjusted for age, sex, triage level, ED visit for asthma in the previous 12 months, hospital admission for asthma in the previous 12 months, ED visit volume, proportion of all ED visits with asthma, propensity to admit.*
[g]*Data not provided by six survey respondents*

Conclusions

- 41% of reporting Ontario EDs (representing 28% of all sites) were using or in the process of approving the EDACP, primarily the updated 2012 version.
- Important gaps in ED asthma management resources were identified in many centres, notably limited access to spirometry, respirologists, asthma education, and other specialists with expertise in asthma management.
- Peak expiratory flow testing and spirometry, which are associated with reduced ED return visits, were not universally available.
- Future interrupted time-series analysis will assess the impact of implementation of the multiple asthma management strategies addressed by the EDACP on patient outcomes and health services utilization, including repeat ED visits and hospital admissions.

Acknowledgements

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- Parts of this material are based on data and information compiled and provided by CIHI. However, the analyses, conclusions, opinions and statements expressed herein are those of the author, and not necessarily those of CIHI.

References

1. Lougheed MD, Lemiere C, Ducharme FM, Licskai C, Dell SD, Rowe BH, FitzGerald M, Leigh R, Watson W, Boulet LP, Canadian Thoracic Society Asthma Clinical Assembly. Canadian Thoracic Society 2012 guideline update: diagnosis and management of asthma in preschoolers, children and adults. *Can. Respir. J.* 2012;19(2):127-64.
2. 3. Hodder R, Lougheed MD, Rowe BH, FitzGerald JM, Kaplan AG, McIvor RA. Management of acute asthma in adults in the emergency department: nonventilatory management. *CMAJ.* 2010 Feb 9;182(2):E55-67.
4. Garvey N, Lougheed MD. Asthma in Ontario: Ontario's Asthma Plan of Action. In: Boulet et al. Implementing Practice Guidelines: A workshop on guidelines dissemination and implementation with a focus on asthma and COPD. *Can Respir J.* 2006;13(Suppl A):32A-34A.
5. Lougheed MD, Olajos-Clow J, Szpiro K, *et al*. Multicentre evaluation of an emergency department asthma care pathway for adults. *CJEM* 2009; 11:215-229.

Funded by: Government of Ontario, The Lung Association – Ontario, Queen's University William M. Spear Endowment/Start Memorial Fund, Queen's University Department of Medicine Innovation Fund

Improving Access to Care through a Lung Cancer Rapid Assessment Clinic: Impact of an Outreach Clinic – Interim Evaluation

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BACKGROUND

- The Lung Diagnostic Assessment Program (LDAP) in Southeastern (SE) Ontario is a rapid assessment clinic that expedites the care of patients with suspected lung cancer (LC).
- LDAP management is associated with improved 2-year survival for patients with LC in SE Ontario; increased distance from the LDAP is associated with lower likelihood of LDAP management and worse survival.
- We implemented an LDAP outreach clinic at the Lennox & Addington County General Hospital (LACGH) that mirrors the tertiary care model with added capacity for small nodule (SN) patient assessments.
- We sought to determine the impact of the outreach clinic on:

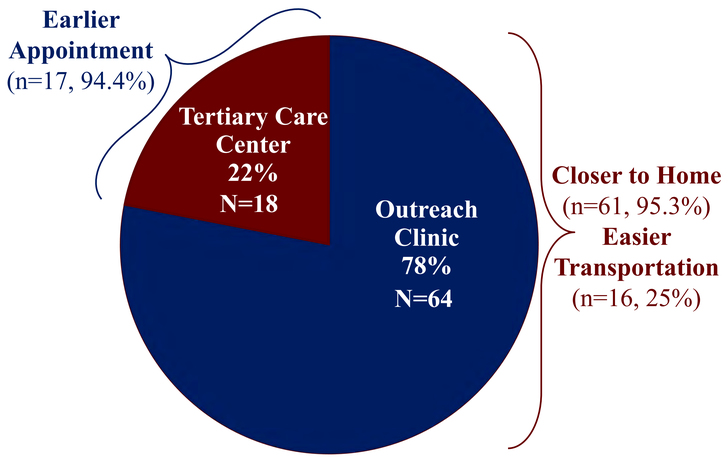
Clinic Capacity | Out-of-Pocket Patient Costs | Timeliness of Assessment | Environmental Outcomes

METHODS

- Retrospective chart review before outreach clinic implementation (Aug - Nov 2021) (N=234)
- Prospective chart review to assess for improvement (Nov 2021 - Jul 2022) (N=555)
- Data include:
  - Patient preferred site for physician consultation & rationale
  - Dates of LDAP referral & assessment
  - Distance travelled

RESULTS

Patient Preferred Site of Assessment and Rationale



RESULTS

Figure 1a: Number of New Patient Referrals Triaged to Respirology Pathway per Month (c Chart)

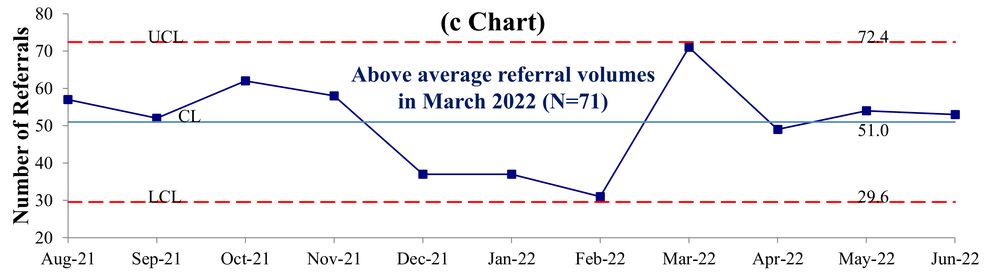


Figure 1b: Number of New Patients Assessed in Tertiary Care LDAP and Outreach LDAP per Month (c Chart)

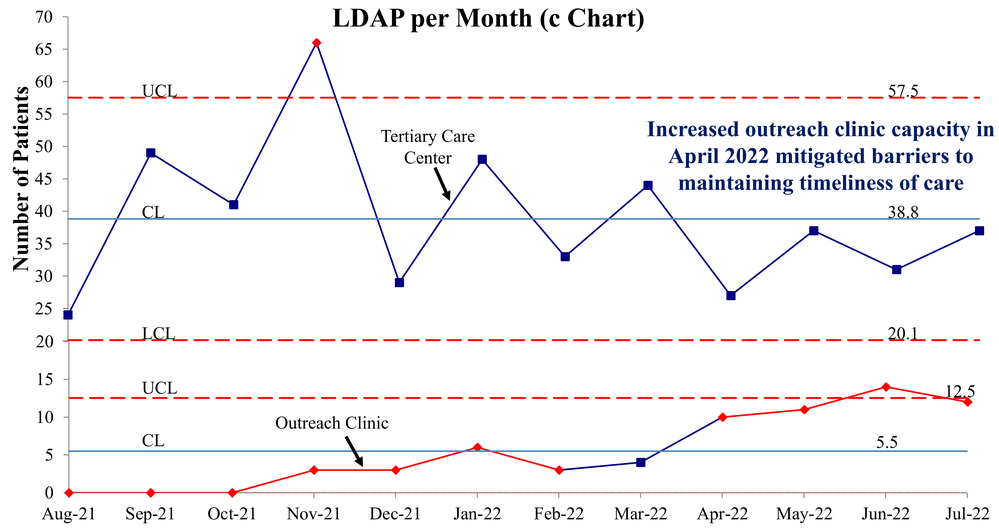
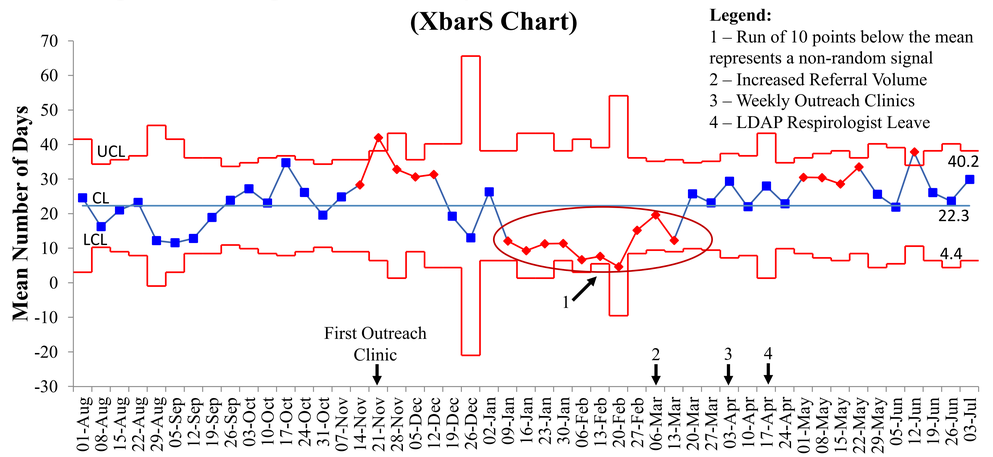
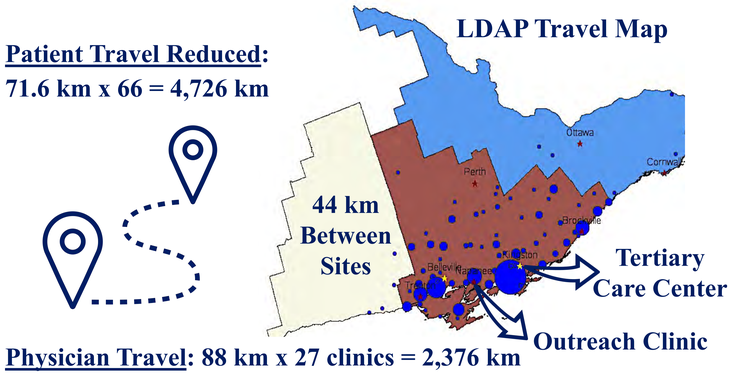


Figure 2: Average Number of Days from Referral to LDAP Assessment (XbarS Chart)



RESULTS

Patient Travel Reduced:
71.6 km x 66 = 4,726 km



Physician Travel: 88 km x 27 clinics = 2,376 km

- 66 patients were assessed in the outreach clinic from Nov 2021 to Jul 2022 (SN N=6; LDAP N=60)
  - Patient driving & parking costs saved = **$2,969.08** ($44.99/patient)
  - Patient travel reduced by **4,726 km** (71.6 km/patient)
  - Total travel reduced by **2,350 km***
  - CO_2 emissions saved = **0.768 tCO_2***

= emissions from 327L of gasoline

*accounting for physician travel to the outreach clinic

CONCLUSIONS

- Implementation of an LDAP outreach clinic led to:

Capacity to accommodate higher referral volumes | Carbon Footprint Out-of-Pocket Patient Costs

LC care for patients in their local community

NEXT STEPS

Characterize the impact of the outreach clinic on timeliness of diagnosis and treatment of LC

Assess for differences in LC diagnostic milestones between the outreach clinic and tertiary care center

Financial Support: Merck/MaRS Lung Cancer Innovation Challenge

Abbreviations: SE: Southeastern, LC: Lung Cancer, LDAP: Lung Diagnostic Assessment Program, LACGH: Lennox & Addington County General Hospital, SN: Small Nodule, CO_2: Carbon Dioxide, tCO_2: tonne of Carbon Dioxide

Poor Perception of Bronchoconstriction and Hyperinflation and Risk of Acute Asthma Exacerbations: A Data Linkage Analysis

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Abstract

Background: Perceptual acuity scores from bronchoprovocation testing may be useful clinically to identify individuals at risk of life-threatening asthma.
Aim: To determine whether poor perception of bronchoconstriction (BC) and/or dynamic hyperinflation (DH) are independently significant risk factors for an acute asthma exacerbation (AAE) (defined as an ED visit, hospitalization or ICU admission).
Methods: This is a prospective cohort data linkage study of adults with asthma, linking high-dose methacholine challenge (MCH) data to administrative data. Dyspnea perception scores (PS) were calculated from MCH tests at standardized changes in FEV1 and inspiratory capacity (IC) of 20, 30 and 40% predicted, representing mild, moderate and severe BC and DH respectively. AAE in the 5 years following MCH were identified from administrative data and compared between groups. The relative risks comparing poor to normal perceivers were determined using zero-inflated Poisson regression.
Results: Forty-one AAEs were identified in 155 subjects (age: 34.6±11.2 years (mean±SD); 67.1% female; FEV_1=90.6±16.0 %pr; PC_{20}=2.7±3.4 mg/mL; BMI=28.2±6.6 kg/m^2). The relative risk of AAEs in poor compared to normal perceivers of mild, moderate and severe BC and DH are summarized in Figure 2.
Conclusion: After controlling for age and sex, poor perception of BC and DH increase the relative risk of acute asthma exacerbations.

Background

- Abnormal symptom perception may contribute to asthma morbidity and mortality.[1] Individuals with poor symptom perception may underestimate asthma severity, under-utilize preventive anti-inflammatory medication, delay seeking care, and thereby increase the risk of fatal or life-threatening asthma (LTA). Conversely, individuals with heightened perception of the symptoms of airway narrowing may over-utilize beta-agonists, a factor linked in epidemiologic studies to increased asthma mortality.
- Currently, there is no consensus as to what constitutes normal perception of asthma symptoms[2] and therefore the prevalence of abnormal perception and its relationship to asthma morbidity and mortality remain speculative.
- The sensation of dyspnea has previously been shown to be strongly related to DH.[3,4,5]
- Dyspnea intensity at standardized levels of mild[6] and moderate to severe[7] bronchoconstriction (BC) are normally distributed across a population. In contrast, dyspnea intensity at standardized levels of dynamic hyperinflation (DH) is skewed to the right.[7]
- Only one published prospective study compared health services utilization of individuals with poor perception of external resistive loading.[8] No previous studies have assessed whether individuals with impaired perception of *intrinsic* mechanical loads, such as BC and DH, are similarly at increased risk of asthma-related morbidity and mortality.

Objective

- To determine whether poor perception of bronchoconstriction (BC) and/or dynamic hyperinflation (DH) are independently significant risk factors for an acute asthma exacerbation (AAE) (defined as an ED visit, hospitalization or ICU admission).

Funded by: The Physicians' Services Incorporated Foundation, the Ontario Thoracic Society, and the William M. Spear Endowment/Start Memorial Fund of Queen's University

Methods

- 183 adults (age 18-65 years old) with asthma recruited from Kingston General Hospital (KGH) ambulatory clinics, the KGH asthma education centre, and the KGH Asthma Research Unit study database attended one study visit. This study was approved by the Queen's University and Affiliated Teaching Hospitals Research Ethics Board, Kingston, Canada, and Institutional Review Board at Sunnybrook Health Sciences Centre, Toronto, Canada.
- Subjects completed a detailed screening questionnaire, baseline spirometry and lung volume measurement, and a high-dose methacholine (MCh) challenge test.

Baseline Questionnaire
- Age
- Sex
- Smoking history
- Asthma medication use
- Comorbidities
- Self-reported healthcare utilization
- Occupation
- Education

→ **High-dose MCh Challenge Test**
- Maximum change (Δ) in FEV_1 of 50%
- At each dose of MCh:
  - Spirometry (FEV_1, IC, etc.)
  - Dyspnea (Modified Borg Scale)[9]

Perceptual Acuity Calculation:

- Perception Scores (PS) at standardized changes (20%, 30% and 40%) in FEV_1(%pr) and IC(%pr) were calculated using log interpolation. Subjects were classified into groups of poor, normal and over perceivers of BC and DH respectively, as previously described.[7]
  - Normal perception of BC was defined as a PS within 1 SD of the mean value. Poor- and over-perception of BC were defined as a PS less than or greater than 1 SD of the mean PS, respectively.
  - Normal perception of DH was defined as the interquartile range of PS. Poor and over perception of DH were defined as the first and last quartile of PS, respectively.

Data Linkage:

- Individuals with at least a measureable PS for *either* BC at 20% change in FEV_1(%pr) *or* DH at 20% change in IC(%pr) were identified.
  - Name, sex, and date of birth were used to perform a probabilistic linkage to identify subjects in Ontario's administrative health databases. These datasets were linked using unique encoded identifiers and analyzed at the Institute for Clinical Evaluative Sciences (ICES). Health services utilization (HSU) related to asthma were identified for each subject over a 5-year period starting at the study visit.

Asthma Research Unit Study Database

↓ Probabilistic linkage

Subjects identified in Registered Persons Database (RPDB)

↓ Identifiers removed, linked using encrypted Health Card Number (HCN)

Health services utilization data obtained from ICES databases:
- Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD)
- Canadian Institute for Health Information National Ambulatory Care Reporting System (CIHI-NACRS)
- Ontario Health Insurance Plan (OHIP)
- Ontario Asthma Surveillance Information System (OASIS)

Statistical Analysis:

- Zero-inflated Poisson regression was use used to determine the relative risk of AAE in poor perceivers compared to normal perceivers for each perceptual acuity classification.

Results

Subject Characteristics, n=183 (mean ± SD)		
	Matched (n=155)	**Unmatched (n=28)**
Age, yrs	34.6 ± 11.4	35.3 ± 13.2
Female, %	67.1%	57.1%
BMI, kg/m^2	28.2 ± 6.6	28.4 ± 7.6
PC_{20}, mg/mL	2.7 ± 3.4	3.2 ± 3.7
Life-long non-smoker, %	52.3%	*
Spirometry & Lung Volumes (mean ± SD)		
	Matched (n=155)	**Unmatched (n=28)**
FEV_1 (%pr)	90.6 ± 16	91.2 ± 14.6
FEF_{25-75} (%pr)	58.3 ± 23.3	56 ± 24.5
FEF_{50} (%pr)	67 ± 31.1	63.7 ± 32
FEF_{75} (%pr)	48.7 ± 21.3	51.8 ± 42.4
FVC (%pr)	96.2 ± 13.5	94.9 ± 9.4
IC (%pr)	107.1 ± 18.8	110.9 ± 19.4
TLC (%pr)	105.6 ± 12.3	102.7 ± 15.9
RV (%pr)	124.1 ± 38.5	103.8 ± 26.2

* Cell counts <6 have been suppressed to ensure patient confidentiality.

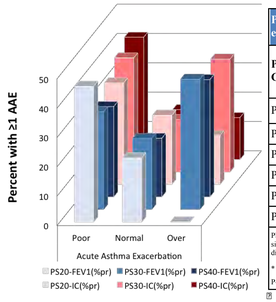
- 183 subjects completed MCh testing.
- Records for 155 subjects were successfully linked to ICES databases to obtain information on HSU.
- Demographic factors and baseline spirometry data are displayed on the left, comparing subjects from the cohort whose records were matched, with those who were not matched to ICES databases.

- The proportions of poor perceivers were similar at different levels of BC and DH.
- Moderate and severe BC and DH had higher proportions of over-perceivers.

Perceptual Acuity Groups for BC and DH			
Perceptual Acuity Classification	Poor Perceiver	Normal Perceiver	Over perceiver
PS_{20}-FEV_1(%pr)	17.6%	80.4%	2.0%
PS_{30}-FEV_1(%pr)	16.8%	74.2%	7.2%
PS_{40}-FEV_1(%pr)	14.8%	73.9%	11.4%
PS_{20}-IC(%pr)	21.4%	73.5%	5.0%
PS_{30}-IC(%pr)	18.4%	68.4%	13.2%
PS_{40}-IC(%pr)	18.2%	71.2%	10.6%

Please note that not all subjects have a measurable PS at the 20, 30, or 40% change in FEV_1 or IC and sample size for each perceptual acuity group will resultantly vary. The n for each perceptual acuity category is not displayed to reduce the risk of re-identifying individual subjects as per ICES guidelines.

Figure 1. Acute Asthma Exacerbations (AAEs) Stratified by Perceptual Acuity for Bronchoconstriction and Hyperinflation



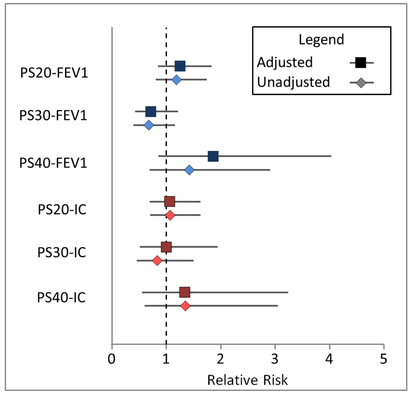
Percentage of subjects who experienced ≥ 1 acute asthma exacerbation*, stratified by perceptual acuity				
Perceptual Acuity Classification	Poor perceiver	Normal perceiver	Over perceiver	p-value
PS_{20}-FEV_1(%pr)	46.2%	21.8%	0%	0.0215
PS_{30}-FEV_1(%pr)	33.3%	24.2%	44.4%	0.3679
PS_{40}-FEV_1(%pr)	30.8%	20%	40%	0.3193
PS_{20}-IC(%pr)	34.6%	23.6%	16.7%	0.3682
PS_{30}-IC(%pr)	38.9%	17.9%	38.5%	0.0905
PS_{40}-IC(%pr)	41.7%	17%	14.3%	0.1363

Please note that not all subjects have a measurable PS at the 20, 30, or 40% change in FEV_1 or IC and sample size for each perceptual acuity group will resultantly vary. The n for each perceptual acuity category is not displayed to reduce the risk of re-identifying individual subjects as per ICES guidelines.

* Acute asthma exacerbation was defined as an ED visit, and/or hospitalization, and/or 1 ICU admission

P-values were calculated using the Kruskal-Wallis test.

Figure 2. Relative Risk of Acute Asthma Exacerbations (AAEs) for Poor vs. Normal Perceivers



- The adjusted and unadjusted relative risk and 95% CI of AAEs for poor compared to normal perceivers of mild, moderate, and severe BC and DH are displayed on the left.
- Adjusted relative risks control for age and sex.

Conclusions

- Poor perceivers of mild, moderate, and severe BC and DH had more acute asthma exacerbations than normal perceivers.
- After controlling for age and sex, poor perception of BC and DH increase the relative risk of acute asthma exacerbations.
- This study has demonstrated the clinical relevance of blunted and over-perception of BC and DH as measured by perceptual acuity scores, by linking bronchoprovocation data to administrative health services utilization databases.

Acknowledgements

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References

1. Rubinfeld AR, Pain MCF. Perception of asthma. *Lancet* 1976; 1:882-884.
2. Banzett RB, Dempsey JA, O'Donnell DE et al. Symptom perception and respiratory sensation in asthma. NHLBI Workshop Summary. *Am J Respir Crit Care Med* 2000; 162:1178-1182.
3. Lougheed MD, Lam M, Forkert L, Webb KA, O'Donnell DE. Breathlessness during acute bronchoconstriction in asthma: pathophysiologic mechanisms. *Am Rev Respir Dis.* 1993; 148:1452-1459.
4. Lougheed MD, Webb KA, O'Donnell DE. Breathlessness during induced lung hyperinflation in asthma: the role of the inspiratory threshold load. *Am J Respir Crit Care Med* 1995; 152:911-920.
5. Lougheed MD, O'Donnell DE. Dyspnea in Asthma. In: Mahler DA, O'Donnell DE, editors. Dyspnea: Mechanisms, Measurement and Management. Lung Biology in Health and Disease. Vol 208. Boca Ratan: Taylor and Francis Group, 2005: 59-86.
6. Boulet LP, Leblanc P, Turcotte H. Perception scoring of induced bronchoconstriction as an index of awareness of asthma symptoms. *Chest* 1994; 105(5):1430-1433.
7. Lougheed MD, Fisher T, O'Donnell DE. Symptom Perception in Asthma: Identification of Poor Perceivers of Dynamic Hyperinflation. *Proceedings of the American Thoracic Society* 2, 2005:A626.
8. Magadle R, Berar-Yanay N, Weiner P. The risk of hospitalization and near-fatal and fatal asthma in relation to the perception of dyspnea. *Chest* 2002; 121:329-333.
9. Borg GAV. Psychophysical basis of perceived exertion. *Med Sci Sports Exerc* 1982; 14:377-381.

Sleeping with the enemy:
Foam in bedding can cause Hypersensitivity Pneumonitis

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Rationale

Chronic Hypersensitivity Pneumonitis (HP) has a poor prognosis, similar to Idiopathic Pulmonary Fibrosis (IPF) when no antigen is identified.

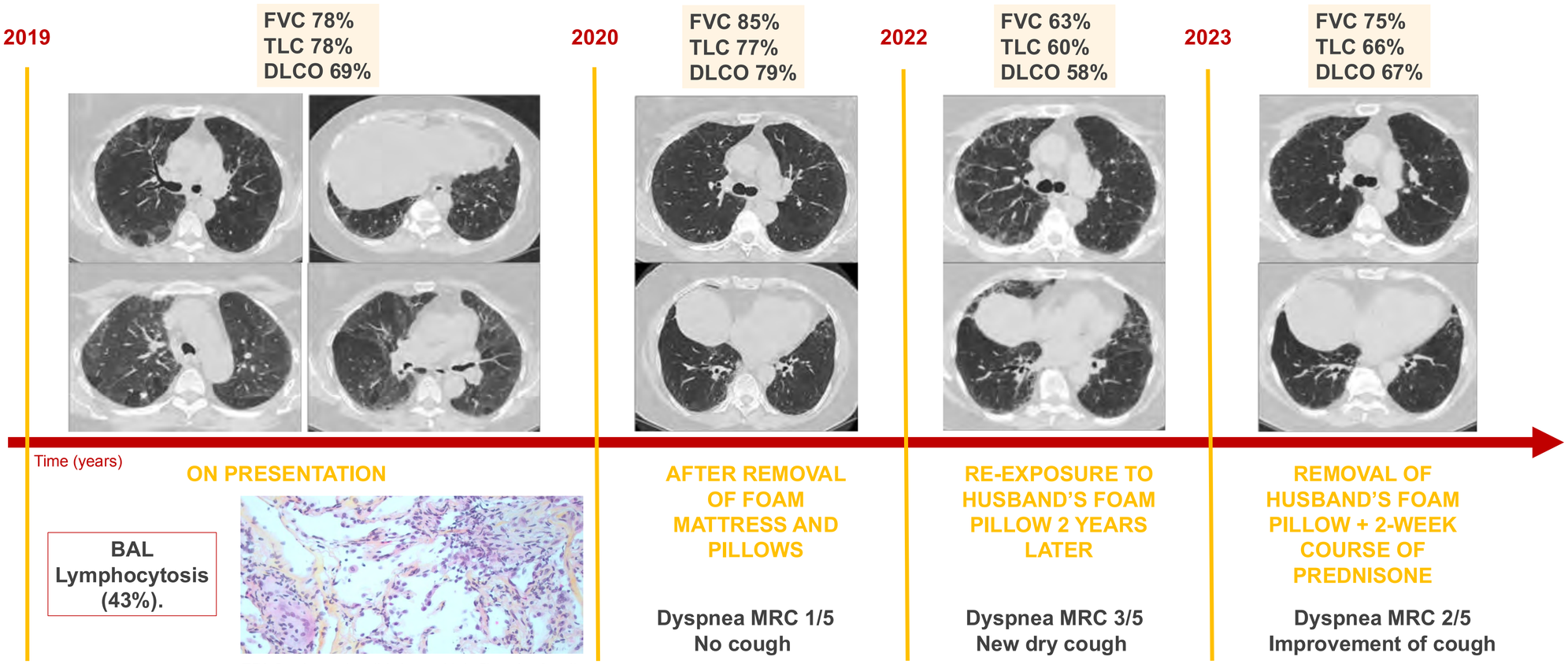
In up to 53% of HP cases, no antigen is identified.

Aim

We present a case of HP due to foam in bedding, an unrecognized cause of HP.

Case report

A 77-year-old woman was referred to our ILD clinic with MRC 2/5 dyspnea and dry cough. She denied infectious, constitutional, and CTD symptoms. She was **exposed only to foam in mattress and pillows.** She **had no exposures to chemicals, fumes, feathers, organic or inorganic dusts.**
On exam, her SpO2 was 94% and had bibasilar fine inspiratory crackles. Her CTD work up was negative/normal.



TBLC showed mild interstitial fibrosis focally suggestive of organizing pneumonia (top right) and rare multinucleated giant cells (bottom left) (hematoxylin phloxine saffron stain, X200).

Discussion

We present a case diagnosed with HP due to foam in bedding, with improvement after avoidance, worsening following foam pillow re-exposure.

We isolated *Penicillium sp* from the foam pillow, a known cause of HP.

Recognizing foam as a cause of HP could lead to early identification and avoidance of this exposure, preventing disease progression and death.

Exploring Factors Affecting Variability in Lung Cancer Outcomes across Southeastern Ontario, Canada

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BACKGROUND

- Lung cancer (LC) is the leading cause of cancer-related mortality.
- The five-year relative LC survival in Ontario ranges from 22 – 32% in 2014-2018, while in Southeastern (SE) Ontario, it was 22%.
- The Lung Diagnostic Assessment Program (LDAP) is a rapid assessment clinic that provides efficient and guideline recommended care for patients undergoing evaluation for suspected LC.

OBJECTIVES

- We sought to characterize patient, disease, and system factors, including the influence of Lung Diagnostic Assessment Program (LDAP) care on survival outcomes.

METHODS

- Population-based retrospective cohort study conducted using data from LDAP database (Jan 2017 - Dec 2019), linked to Ontario Cancer Registry to identify patients with newly diagnosed LC.
- Cox-model approach to compare 2-year survival for patients receiving care through LDAP versus non-LDAP pathways.

RESULTS

- A total of 1741 patients with LC identified; 818 (47.0%) managed through LDAP vs. 923 (53%) in non-LDAP pathways.

Table 1: Factors affecting 2-year Overall Survival in LC

FACTOR	UNADJUSTED HR (95% CI)	UNADJUSTED P-VALUE
AGE		
18 - 60	0.71 (0.57, 0.87)	0.0015
61 - 70	0.79 (0.66, 0.94)	
71 - 80	0.88 (0.74, 1.04)	
> 80	referent	
SEX		
FEMALE	0.68 (0.61, 0.77)	<.0001
MALE	referent	
DISTANCE FROM CCSEO (KMS)		
< 50	0.82 (0.72, 0.93)	0.0027
50 - 100	referent	
> 100	1.05 (0.86, 1.27)	
INCOME QUINTILE		
1 (LOWEST)	2.27 (1.53, 3.36)	0.0003
2	1.79 (1.21, 2.63)	
3	1.89 (1.28, 2.77)	
4	1.81 (1.22, 2.70)	
5 (HIGHEST)	referent	
HISTOLOGY TYPE		
ADENOCARCINOMA	referent	<.0001
SQUAMOUS CELL	1.44 (1.21, 1.73)	
POORLY DIFFERENTIATED	2.55 (2.20, 2.95)	
SMALL CELL	2.65 (2.18, 3.23)	
OTHER	1.27 (0.93, 1.73)	
STAGE		
I	0.16 (0.13, 0.20)	<.0001
II	0.24 (0.17, 0.32)	
III	0.50 (0.42, 0.59)	
IV	referent	
LDAP		
NO	1.64 (1.45, 1.85)	<.0001
YES	referent	

All variables including LDAP management remained significant in adjusted model for 2-year survival (HR 1.18 for non-LDAP vs. LDAP, p<0.016).

KEY FINDINGS

- Factors associated with a **lower probability of dying at 2 years** included **younger age**, **female sex, less distance from SE cancer center,** and **earlier stage**.
- Factors associated with a **higher probability of dying** were **lower income quintile, non-adenocarcinoma subtype** and **non-LDAP management.**

Patient and disease factors associated with LDAP management included: ages 61-70 (HR 1.36 vs. ages 71-80, p=0.012), income quintile (HR 1.52 for middle quintile vs. lowest quintile, p=0.023), and earlier stage (HR ≥2.20 for Stages I-III vs. IV, p<.0001).

Increasing distance from CCSEO lowered the probability of LDAP assessment (HR 0.76 for every 20km increase, p<.0001).

CONCLUSION

- While several patient and disease factors influence LC survival in SE Ontario, **LDAP management appears to be an independent factor influencing survival,** suggesting that system characteristics play a contributing role in survival.

Hypersensitivity Pneumonitis Due To Domestic Exposure to Foam And Bamboo In Bedding And Other Sources – Microbiologic Analyses

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[1]Queen's University, Kingston, ON, Canada. [2]Kingston Health Sciences Centre, Kingston, ON, Canada.

Rationale

Hypersensitivity pneumonitis (HP) results from an immune-mediated reaction induced by an inhaled antigen in susceptible people.

The prognosis in chronic HP with unidentified antigen is very poor and similar to patients with IPF.

In up to 53% of HP cases, no antigen is identified, suggesting a common but unrecognized exposure.

Aim

We report a variety of molds known to cause HP, isolated from foam and bamboo samples in bedding and other domestic exposures, not previously recognized.

Methods

HP is diagnosed in our ILD center based on identified exposures through a standardized questionnaire, chest high-resolution computed tomography (HRCT), bronchoalveolar lavage (BAL), +/- lung biopsy and multidisciplinary discussion (MDD).

We sent foam and bamboo samples from sources identified through our questionnaire for microbiological analyses to a certified environmental microbiological laboratory in Canada.

Results

N= 14 patients with HP and no other apparent exposure.
Female 57%, Male 43% **Mean age 72 years (min 50 – max 88)**

Molds recovered on direct microscopic examination and culture

Foam mattress	Foam Pillows	CPAP foam filter	Humidifier foam filter	Exposed foam in sofa
• *Aspergillus sp.* ¶ • *Alternaria sp.* ¶ • *Chaetomium sp.* • *Cladosporium sp.* ¶ • *Epicoccum sp.* • *Fusarium sp.* ¶ • *Mucor racemosus* ¶ • *Nigrospora sphaerica* • *Penicillium sp.* ¶ • *Pseudopithomyces chartarum* • *Syncephalastrum racemosum* • *Stachybotrys chartarum*¶	• *Aspergillus sp.* ¶ • *Alternaria sp.* ¶ • *Arthrinium phaoespermum* • *Aureobasidium pullulans* ¶ • *Cladosporium sp.* † ¶ • *Chaetomium sp.* • *Emericella nidulans* • *Epicoccum nigrum* • *Penicillium giabrum* ¶ • *Penicillium sp* ¶ • *Pithomyces chartarum* • *Stachybotrys sp.* ¶ • *Syncephalastrum racemosum* • *Scopulariopsis sp*	• *Aspergillus sp.* ¶ • *Alternaria sp.* ¶ • *Arthrinium phaoespermum* • *Cladosporium sp.* ¶ • *Curvularia sp.* • *Emericella nidulans* • *Eurotium sp.* • *Fusarium sp.* ¶ • *Mucor plumbeus* ¶ • *Penicillium sp.* ¶ • *Ulocladium chartarum*	• *Alternaria sp.* ¶ • *Cladosporium sp* ¶ • *Penicillium sp.* ¶ • *Trichoderma harzianum*¶	• *Aspergillus ustus*¶ • *Aspergillus sydowii* ¶ • *Chaetomium globossum* • *Cladosporium sphaerospermum*¶
Exposed water damaged ceiling insulation (foam)	**Bamboo filled duvet**	**Bamboo pillow**	**Bamboo pillow cover**	**Magic bag (organic seeds)**
• *Alternaria alternata* ¶ • *Aspergillus sp* ¶ • *Cladosporium sp and Cladosporium cladosporioides* ¶ • *Mucor plumbeus* ¶ • *Penicillium sp and penicillium decumbens* ¶ • *Rhizopus stolonifer* ¶ • *Trichoderma harzianum*¶	• *Alternaria alternata* ¶ • *Aspergillus flavum* ¶ • *Chaetonium sp* • *Cladosporium cladosporioides*¶ • *Epicoccum nigrum* • *Penicillium chrysogenum* ¶ • *Pithomyces chartarum*	• *Cladosporium herbarum* ¶ • *Penicillium glabrum* ¶	• *Alternaria alternata* ¶ • *chrysogenum* • *Cladosporium sp and Cladosporium cladosporioides* ¶ • *Fusarium sp.* ¶ • *Penicillium sp* ¶ • *Ulocladium chartarum*	• *Cladosporium sp.*¶ • *Rhizopus sp.* ¶

¶ Molds known to cause HP.

Diagnosis of HP

	Frequency	(%)
BAL Lymphocytosis (> 20%)	5	37
TBLC	3	21
VATS biopsy	3	21
3-density pattern on HRCT	3	21

Conclusions

Foam and bamboo in bedding and other domestic sources harbor molds known to cause HP that could explain a large percentage of HP cases with previously unrecognized antigens.

Early identification and avoidance of foam and bamboo at home may prevent HP progression and death.

Effects of Outdoor Particulate Air Pollution on Lung Function in Healthy Adults and Adults with Asthma: A Systematic Review and Meta-Analysis

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Abstract

PURPOSE: The short- and long-term effects of particulate air pollution on lung function of healthy adults and adults with asthma are not well established. The objective of this study was to review the evidence amongst these populations and to quantify the impact of air pollution on lung function by performing meta-analyses.

METHODS: We searched MEDLINE, EMBASE, and the Cochrane Library for English studies published from 1991 to 2016 that assessed the relationship of particulate air pollution and lung function. Additional studies were identified by inspecting references of the included studies and literature reviews. Studies that contained data on particulate matter levels (PM2.5 or PM10) and lung function (FEV1 or PEF) in healthy adults or adults with asthma were included in the quantitative analyses. Effect estimates for healthy adults and adults with asthma, grouped by study type, were examined separately using inverse variance methods assuming a random effects model.

RESULTS: Database searches yielded 245 studies, of which all the abstracts were reviewed. An additional 15 studies published between 1991 and October 2016 were identified through a manual search of references. After full text screening, 32 relevant studies were identified. 12 studies including 53,281 healthy adult subjects and 8 studies including 641 adults with asthma were included in the quantitative analyses. Of the studies including healthy subjects, 8 were panel studies with multiple spirometric measurements, for which 3 assessed long-term (2 months – 8 years) PM10 exposure and 5 assessed short-term (5 hours – 1 week) PM2.5 exposure. Four studies of healthy subjects only included one spirometric measurement and looked at the effect of long-term (1 – 20 years) PM10 exposure on FEV1. All 8 studies of adults with asthma assessed the relationship of short-term (daily) PM10 exposure on PEF with multiple spirometric measurements. A 10μg/m3 increase in long-term PM10 exposure was associated with a 4.76 mL (CI95: 2.40-7.12) greater decline in FEV1 amongst healthy individuals and with a 70.4 mL (CI95: 4.65-136.15) lower FEV1 amongst healthy individuals in cross-sectional studies. A 10μg/m3 increase in short-term PM2.5 exposure (days) was associated with a 14.15mL (CI95: 4.65-23.65) lower FEV1 amongst healthy individuals. Longitudinal studies in adults with asthma showed a 10μg/m3 increase in short-term PM10 exposure was associated with a 0.19L/min (CI95: 0.11- 0.26) decline in PEF. Longitudinal studies amongst healthy subjects and adults with asthma contained no heterogeneity, while cross-sectional studies of healthy subjects contained high heterogeneity.

CONCLUSIONS: Evidence from the identified studies revealed small but statistically significant negative associations between exposure to particulate air pollution and lung function in healthy adults and adults with asthma. More studies are needed to better quantify the long-term effects of particulate air pollution on lung function decline among these populations.

CLINICAL IMPLICATIONS: Overall, these results provide further support for health policies aimed at reducing ambient particulate air pollution.

Background

- In recent decades, PM_{10} and $PM_{2.5}$ (referring to particulate matter that is less than 10 and 2.5 micrometers respectively) have become the most common metrics used when analyzing particulate air pollution. The World Health Organization set the target PM_{10} level at 20μg/m^3, but levels exceed this target in most countries[1].
- High levels of PM_{10} and $PM_{2.5}$ are associated with adverse health outcomes, such as increases in all-cause mortality[2,3], lung cancer[3], and hospital admissions for COPD[2].
- Decreases in lung function (as measured by FEV_1 and PEF) have been associated with adverse health outcomes as well, including increased rates of lung cancer[4], and all-cause mortality[6].
- There are meta-analyses looking at air pollution and lung function in adults with COPD[6] and children with asthma[7], but there are no meta-analyses done examining the association between air pollution and lung function in healthy adults or adults with asthma.

Objective

- To assess the effect of particulate air pollution on lung function in healthy adults and adults with asthma by performing a systematic review and meta analysis of the literature.

Methods

Systematic Review

- Literature search of MEDLINE, EMBASE and Cochrane Library for records from 1991-2016 was performed by the primary reviewer. Search terms included "air pollution", "particulate matter", "lung function test", "forced expiratory volume in 1 second (FEV_1)" and "peak expiratory flow (PEF)". All records identified by abstract and title were examined by 2 reviewers for inclusion; additional studies were identified by examining bibliographies and literature reviews. Agreement between reviewers was quantified using % agreement and kappa statistics.
- Inclusion criteria: (1) original studies; (2) outdoor particulate air pollution as exposure; (3) $PM_{2.5}$ or PM_{10} as particulate air pollution metric; (4) lung function measured by spirometry; (5) populations with either a diagnosis of asthma or healthy population (defined as prevalence of lung disease <10%).
- Exclusion criteria: (1) diagnosis of COPD or other respiratory disease; (2) did not present an adequate effect estimate or one cannot be derived.

Meta-Analyses

- Data were extracted and effect estimates were converted to represent a 10μg/m^3 change in either $PM_{2.5}$ or PM_{10}. When different time lags were present for short-term exposures, the measure closest to 1-day lag was used.
- Estimates were combined to derive summary effect generic inverse variance method assuming a randor
- Heterogeneity between studies was reviewed using
- Publication bias among the studies was assessed us Egger's weighted linear regression and Begg's rank

Results

- 34 articles were identified, 20 of which pertained to 14 of which pertained to adults with asthma (see Fi 91.5% agreement among the reviewers with a kapp for inclusion in a meta-analysis.
- Characteristics of included studies are summarized i from 19 countries were included in the studies conta adults, and data from 12 countries were included in containing adults with asthma.

Figure 1 – Flow diagram of systematic search and selection

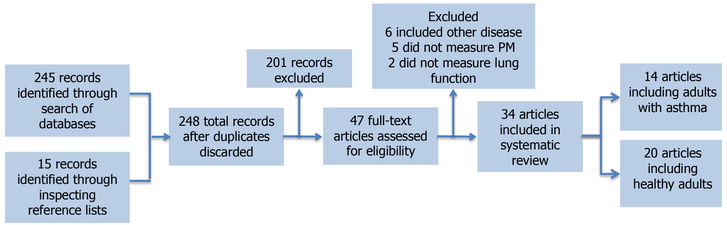


Table 1 – Characteristics of studies included in meta-analyses

#	Studies included (sample size)	Population	Design	Exposure	Spirometric measurement
1	4 (n=1,018)	Healthy adults	Longitudinal	Short-term $PM_{2.5}$ (days)	FEV_1
2	9 (n=779)	Adults with asthma	Longitudinal	Short-term PM_{10} (days)	PEF
3	4 (n=6,052)	Healthy adults	Longitudinal	Long-term PM_{10} (2 months – 8 years)	FEV_1
4	4 (n=46,589)	Healthy adults	Cross-sectional	Long-term PM_{10} (1 – 20 years)	FEV_1

- There was considerable variation between studies in terms of study design (longitudinal vs. cross-sectional), exposure duration (short vs. long), pollution parameter ($PM_{2.5}$ vs. PM_{10}), and spirometric outcome (FEV_1 vs. PEF). Groups of studies (>3) with similar clinical characteristics were combined in meta-analyses (see Table 1).

Figure 2A: Longitudinal studies of healthy adults: s

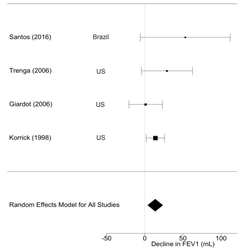


Figure 2B: Longitudinal studies of adults with asthma: short-term PM_{10} and PEF

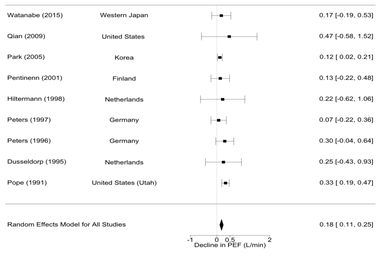
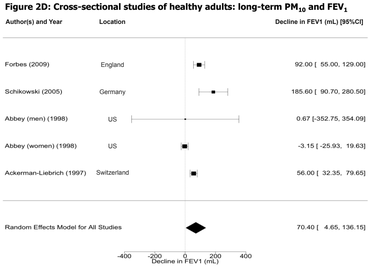
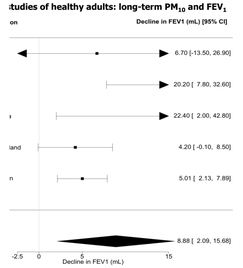


Figure 2D: Cross-sectional studies of healthy adults: long-term PM_{10} and FEV_1



tudies of healthy adults: long-term PM_{10} and FEV_1



Conclusions

- These meta-analyes identified small but statistically significant negative associations between particulate air pollution and lung function in both healthy adults and adults with asthma.
- The small effect sizes seen for a 10μg/m^3 change in $PM_{2.5}$ or PM_{10} could be much greater in individuals moving from areas of low to high pollution.

eview failed to identify studies looking at the long-term effects of air pollution on lung ults with asthma

; are needed to better quantify these effects, especially the effects of long-term exposures asthma.

References

nbient Air Pollution Database - Update 2016.

Hao B, et al. Short-term exposure to ambient fine particulate matter increases hospitalizations and mortality in COPD: A systematic a-analysis. *Chest.* 2016;149(2):447-458

tt RT, Thun MJ, *et al.* Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *JAMA.* 32-1141

irways Obstruction and the Risk for Lung Cancer. *Ann Intern Med.* 1987;106(4):512

ins R, Eaton TE. Forced expiratory volume in one second: Not just a lung function test but a marker of premature death from all *pir J.* 2007;30(4):616-622.

loek G, Smit LAM. Panel studies of air pollution in patients with COPD: Systematic review and meta-analysis. *Environ Res.* 68.

omeo E, Sario M De, Weiland SK, Forastiere F. Review Short-Term Effects of PM 10 and NO 2 on Respiratory Health among Children Asthma-like Symptoms : A Systematic Review. *Environ Health Perspect.* 2010;118(4):449-457.

Experience of the First 35 Transbronchial Lung Cryobiopsies At An Interstitial Lung Diseases Referral Center in Canada

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Rationale

- Interstitial Lung Diseases (ILD) remain undiagnosed in up to 30% of cases, requiring lung biopsy.
- The diagnostic yield of Transbronchial Lung Cryobiopsy (TBLC) is ~80%, compared to ~95% of Surgical Lung Biopsy (SLB), but with lower risk of death (0.3 – 0.7%) vs (~2%).
- Current IPF guidelines conditionally recommended TBLC as an alternative to SLB in the diagnosis of ILD in expert centers.

Objectives

- Analyze the diagnostic yield and complications of TBLC in our center.
- Compare the sample sizes obtained by two different cryoprobes (1.9mm and 2.4mm).

Methods

- Retrospective analysis of the first 35 consecutive patients who underwent TBLC in KHSC, between 2018 - 2023.
- All patients were assessed in ILD Clinic following current Guidelines.
- If diagnosis was not achieved, we offered patients lung biopsy.
- The lung pathologist was blinded to the TBLC cryoprobe used.
- The final diagnosis was based on MDD.

Results

Mean age 74 years (min 60 - max 87)
49% females, 51% males

Chest HRCT pattern before TBLC

HRCT Pattern	Frequency	%
UIP	0	0
Probable UIP	2	6
Indeterminate UIP	19	54
Alternative UIP	14	40

TBLC diagnostic yield

In 54% a single diagnosis was established:

- ✓ 9 IPF (26 %)
- ✓ 7 Hypersensitivity Pneumonitis (20%)
- ✓ 1 Sarcoidosis (3%)
- ✓ 1 Post-Infectious fibrosis (3%)
- ✓ 1 Smoking-related ILD (3%)

46% had Unclassifiable ILD after MDD

Mode and median differential diagnoses before vs after TBLC in patients with Unclassifiable ILD

Before TBLC: 3 (min 2 - max 4)

After TBLC: 2 (min 1 - max 3)

p-value <0.001.

TBLC complications

	Frequency	%
Bleeding*	24	68
Mild†	22	62
Moderate‡	2	6
Severe**	0	0
Pneumothorax	8	23
Bronchospasm	3	9
Death/Intubation/ICU admission	0	0

*Bleeding was controlled with Arndt blocker balloon tamponade and/or topical hemostatic. † Expected bleeding for procedure. ‡ Procedure was stopped. **There were no severe bleedings requiring hospital admission or blood transfusion.

Biopsy sample sizes according to Cryoprobe used

Cryoprobe size	Mean Sample size (mm)	Minimum – Maximum (mm)
1.9 mm	4.8	3 - 8
2.4 mm	5.7	4 - 11

Paired t-test p-value <0.001

Conclusions

- TBLC was useful to achieve a specific diagnosis in 54% of ILD cases; in the remaining 46% it significantly narrowed the differential diagnosis.
- There were no severe complications or deaths.
- The 2.4mm cryoprobe provided significantly larger biopsies.

Rheumatology



Dr. Mala Jonaja
Division Chair



Dr. Tanveer Towheed
Research Lead

Summary

- *Case studies may including documenting rare cases and rare presentations of disease*
- *Systematic reviews of therapeutics uses for osteoarthritis and osteoporosis*
- *Educations training on professionalism and postgraduate learning*
- *Use of a derivative of hyaluronic acid and glucuronic acid's pro-inflammatory properties in gout (through MatrixBiology)*
- *Investigation into mental illness's affect on lupus*
- *Identification of barriers for vaccination for patients with rheumatoid arthritis*
- *Therapeutics use associated with increased risk of infection for patients with low bone mineral density*
- *Risk assessment of fractures in rheumatoid arthritis patients*

Current and Upcoming Research Opportunities

The main areas of local expertise include: Osteoarthritis, Osteoporosis, Vasculitis, Inflammatory arthritis (including ultrasound), Education, and Matrix Biolog

(See Arthritis Research Centre Team Description for individual Staff contacts)
Research Ideas by Residents are strongly encouraged

1. Clinical Cases and Review of Literature.
These tend to be unusual cases encountered during clinical exposure to Rheumatology, leading to a review of the literature.

2. Systematic Reviews.
There is expertise in specific areas of Osteoarthrtis, Osteoporosis, and nutraceuticals such as glucosamine.

3. Educational Research.
The foci are in professionalism and post-graduate learning.

4. Canadian Multicenter Osteoporosis Data base.
This very large, 20 year data base can be used to address a variety of research questions, both locally and nationally. Collaborative projects with Dr. Rachel Holden (Nephrology) may be also offered nationally. Collaborative projects with Dr. Rachel Holden Nephrology) may be also offered.TOLOGY

5. Short Clinical Studies.

There are several clinical studies that Staff members are interested in, in where Residents can participate. These Studies generally require attendance at Rheumatology outpatient clinics, either in one long block, several shorter rotations, or in collaboration with another Center. Some of the studies are in areas of interest of Rheumatology Fellows. Many can be done without outside financial support. The Arthritis Society, Physicians Services Inc., or SEAMO, provides support on a competitive basis. However, the Resident would need sufficient lead time to write and submit the Application and obtain approval from the Queen's/Kingston Hospital Research Ethics Board.

Examples include: (i) The relation of skin thickness to osteoporosis (BMD) and collagen markers; (ii) Nailfold video capilaroscopy in inflammatory myopathies.

6. Basic Science Research.

Laboratory work is on matrix biology. The current focus is on hyaluronic acid (HA), a linear polymer of N-acetyl glucosamine and glucuronic acid. HA has essential structural and rheological properties when an intact huge polymer is generally pro-inflammatory when degraded to low molecular weights (LMW HA). We have IP with Queen's on how the pro-inflammatory effects of LMW HA can be abolished by substituting the N-acetyl group with other N-acyl groups, e.g. N-butyryl. There is also an ongoing collaboration with China on a gout animal mode and the use of N-butyryl LMW HA derivative that a Resident could participate in. An interested Resident would need a significant time commitment for the Laboratory work.

The Arthritis Research Centre (ARC) provides various opportunities for research in rheumatic diseases and in connective tissue biology.

ARC Research Fields and Academic Staff contacts:

- ***Osteoarthritis*** *(epidemiology, basic science):*

Dr. Towheed (TT) tt5@queensu.ca , Dr. Anastassiades (TA) anastass@queensu.ca

- ***Osteoporosis*** *(Clinical, CaMos data base):* TT, TA
- ***Vasculitis*** *(clinical):*

  Dr. Clements-Baker (C-B) marie.clements-baker@medportal.ca
- ***Inflammatory Arthritis*** *(Clinical, basic*):*

  MJ, C-B, TT, TK, TA.
- ***Ultrasound of inflamed joints*** *(Clinical):*

  Dr. Kung (TK) tabitha.kung@queensu.ca
- ***Matrix Biology*** *(*hyaluronic acid derivatives, Gout, a collaborative project in China is possible):* TA
- ***Education*** *(professionalism, post grad):*

  Dr. Joneja (MJ) mj6@queensu.ca

Selected Rheumatology Fellows, considering Academic careers, are encouraged to also explore the Clinical Investigation Program at Queen's (CIP),
https://meds.queensu.ca/academics/cip
and/ or the Translational Medicine Graduate Program of the Department of Medicine,
http://deptmed.queensu.ca/translational_medicine_graduate_program

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ORIGINAL ARTICLE

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WILEY

Identifying perceptions and barriers regarding vaccination in patients with rheumatoid arthritis: A Canadian perspective

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Abstract

Aim: Canadian guidelines recommend that patients with rheumatoid arthritis (RA) receive pneumococcal, influenza and shingles vaccinations. The aim of this study was to identify and understand vaccination rates in Canadian patients with RA.

Methods: We conducted an observational study to evaluate uptake of herpes zoster (HZ), influenza and pneumonia vaccination in a cross-section of patients with RA in Kingston, Ontario, Canada. Data were collected using a self-administered questionnaire in patients attending at an academic rheumatology clinic. If vaccination was not received, the reason was established.

Results: Ninety-eight out of a total of 103 patients surveyed met the inclusion criteria and were evaluated: 72.4% had received the influenza vaccination in the past year encompassing a period of 2017-2019. Of the 27.6% who did not, the most common chosen reason was personal preference not to get vaccinated (55.6%). Regarding HZ, 18.4% had received vaccination. Of the 2 available types of vaccines, more participants received Zostavax (66.7%) as compared to Shringrix (33.3%). For those not vaccinated (81.6%), "Other" was the most chosen option (37.5%) with the reasons subsequently specified as cost, concern over interaction with treatment and waiting until age ≥65 years. In terms of pneumococcal vaccination, 36.7% were vaccinated, with the majority being vaccinated with Pneumovax-23 (63.9%) compared to Prevnar-13 (16.7%) or both (19.4%). Of the 63.3% of the participants who did not receive vaccination, the most cited reason was they did not know they should receive pneumococcal vaccination (48.4%).

Conclusions: Vaccination rates among Canadian patients with RA are suboptimal.

KEYWORDS

herpes zoster, influenza, pneumoccocal, rheumatoid arthritis, vaccination rates

1 | INTRODUCTION

Rheumatoid arthritis (RA) is an insidious autoimmune inflammatory condition that typically presents as a polyarticular process. This chronic systemic condition is 2 to 3 times more prevalent in women and can present at any age; however, there is a predilection for the 6th decade of life.[1] It is estimated that 1% of Canadians are currently affected by RA and with an aging population there is evidence of an increasing incidence rate.[2] Given the nature of the disease and the immunosuppressive treatment modalities available including conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and biologics, there is higher propensity for

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REVIEW ARTICLE

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Is denosumab associated with an increased risk for infection in patients with low bone mineral density? A systematic review and meta-analysis of randomized controlled trials

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Abstract

Aim: Denosumab increases bone mineral density through inhibition of the receptor activator of nuclear factor κ-B ligand (RANKL). RANKL has known immunomodulatory effect. The largest study to date that reviewed denosumab efficacy in osteoporosis demonstrated an increased incidence of serious adverse events of infection (SAEI). We aimed to further evaluate risk of infection and SAEI in denosumab-treated patients.

Method: PubMed, Embase, Cochrane Central Register of Controlled Trials, and Web of Science were searched for randomized controlled trials. Studies comparing denosumab 60 mg every 6 months with placebo or bisphosphonate for treatment of low bone mineral density were included. Trials were excluded for use of denosumab in cancer patients treated for skeletal-related events, immunosuppressed patient populations, or for comparison to teriparatide. Risk ratios (RR) with a 95% confidence interval (CI) were pooled using a fixed effects model, or a random effects model if heterogeneity occurred.

Results: Twenty-four randomized controlled trials (20 470 patients) were analyzed. An increased incidence of any infection (RR 1.11; 95% CI 1.02-1.20; $P = 0.02$) was observed in denosumab-treated patients compared with bisphosphonates, but not when compared with placebo. In contrast, a higher incidence of SAEI (RR 1.21; 95% CI 1.03-1.43; $P = 0.02$) was seen with denosumab when compared with placebo, but not compared with bisphosphonates.

Conclusion: Denosumab-treated patients with low bone mineral density have slightly increased incidence of SAEI compared with placebo, but not when compared with bisphosphonates. Application of these results requires consideration of the entire body of data available regarding denosumab safety.

KEYWORDS

bone diseases, denosumab, infections, meta-analysis, metabolic, osteoporosis

Is Rheumatoid Arthritis a Risk Factor for Fractures: A Systematic Review of Observational Studies

A Gupta, MD, S Pipe, BSc, T Towheed, MD, Anastassiades T, MD, PhD

Background: Rheumatoid Arthritis (RA) is a risk factor for osteoporosis. There are many factors that contribute to this increased risk, including the use of glucocorticoids, systemic inflammation due to the disease and relative physical inactivity. Only a few studies have assessed the risk of fractures in RA. The objective of this systematic review was to assess the risk of fractures in adults with RA compared with controls from the general population.

Methods: Two authors screened citations from the following electronic databases: MEDLINE, EMBASE, Cochrane Database of Systematic Reviews and CINAHL. Included citations were written in English, included patients greater than or equal to 18 years of age and compared fracture incidence/prevalence between RA patients and a control group. Case control, cohort and cross-sectional studies were included. Abstracts and conference proceedings were not searched. The primary outcome was fracture incidence and/or prevalence. Two authors extracted data using a standardized data extraction form. The quality of the studies was assessed using the Newcastle-Ottawa Scale (NOS).

Results: The searches resulted in 3451 citations, and after applying the inclusion criteria, we selected seventeen observational studies. The risk of fracture was elevated in RA compared to controls in 14 of the 17 studies. Thirteen studies adjusted for glucocorticoid use and there was an increased risk of fracture with glucocorticoid use in 4/13 of these studies. Seven studies analyzed RA severity or functional impairment as a risk factor for fracture and the risk of fracture was elevated in 2/7 of these studies

racture ascertainment was performed by searching medical records in seven studies, analyzing spine radiographs in six studies, self-reported history in two studies and by multiple methods in two studies. Eight studies evaluated fractures at multiple sites, whereas nine studies evaluated fractures only at a single site. Only two studies reported specific data on fragility fractures, whereas in the remaining studies, the fracture mechanisms were not defined. Assessment using the NOS revealed that the studies were of high quality.

Limitations of the studies included: studies enrolled a diverse range of patient and control group populations, and generally included all types of fractures determined by various methods and involving multiple sites. These differences between the studies made it difficult to directly compare them. Due to the marked study heterogeneity, a meta-analysis was not performed.

Conclusion: The risk of fracture in RA is elevated compared to the general population.