10TH ANNUAL
Resident Research Fair

2025

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

TIME
TRANSLATIONAL INSTITUTE OF MEDICINE

Queen's UNIVERSITY

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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

- *Clinical Validation of Specialized Particulate Control Environmental Exposure Unit (SPaC-EEU) Cat Dander Exposure*
- *Serum biomarkers and bacterial carriage in allergen-induced allergic rhinitis models*
- *The Nasal Microbiome of Individuals with Allergic Rhinitis is Stable Following a Nasal Allergen Challenge with Ragweed*

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.*

Serum Immunoglobulin Levels are Associated with Altered Nasal Microbiomes after Nasal Allergen Challenge

Linton S[1,2], Hossenbaccus L[1,2], Greenlaw J[1,3], Sjaarda C[2,4], Thiele J[5], Steacy LM[2], Sheth P[2,3,4,5], and Ellis AK[1,2,5]

[1] *Department of Medicine, Queen's University*
[2] *KGH Research Institute, Kingston Health Sciences Centre – KGH Site*
[3] *Gastrointestinal Disease Research Unit, Queen's University*
[4] *Department of Pathology and Molecular Medicine, Queen's University*
[5] *Department of Biomedical and Molecular Sciences, Queen's University*

Introduction

Studies on the nasal microbiome in **allergic rhinitis (AR)** are limited by variations in design and sampling, preventing definitive conclusions.[1-4]

Elevated immunoglobulin-E (IgE) levels in AR have been shown to correlate with reduced diversity, increased *Staphylococcus aureus*, and decreased *Propionibacterium acnes*.[3] However, **past studies have not considered seasonality.**

The nasal allergen challenge (NAC) model developed by the Allergic Rhinitis Clinical Investigator Collaborative has been optimized and validated for several allergens.[5]

Recent work using this protocol demonstrated that the nasal microbiome of ragweed-allergic participants can be assessed using a NAC.[6] **We sought to assess the relationship between nasal microbiome and serum IgE outcomes using a validated out-of-season ragweed NAC.**

References

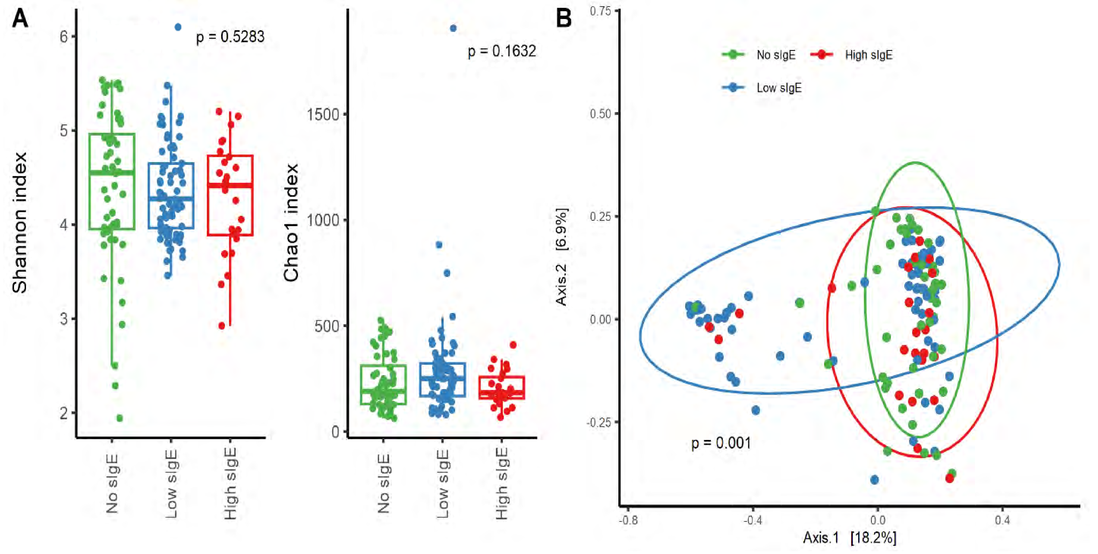


Figure 1. Stratifying participants by ragweed pollen sIgE revealed community-level differences in the middle meatus microbiome. K-means clustering stratified samples (31 participants, n=155) from Baseline-NAC, 6hr post-NAC, and 24hr post-NAC into three groups based on Ragweed sIgE levels: No sIgE (0.0016–0.046 kUA/L, n=60), Low sIgE (1.084–37 kUA/L, n=70), and High sIgE (58.68–91.42 kUA/L, n=25). **(A)** No significant differences in Alpha diversity (Shannon, Chao1) were found (Kruskal-Wallis: *P = 0.5283*, *P = 0.1632*). **(B)** Significant separation exists between sIgE groups (PERMANOVA: *P = 0.001*). Boxplots show quartiles and medians; ellipses indicate group separation.

There was a significant difference in the nasal microbial composition of NAC participants when stratified by sIgE.

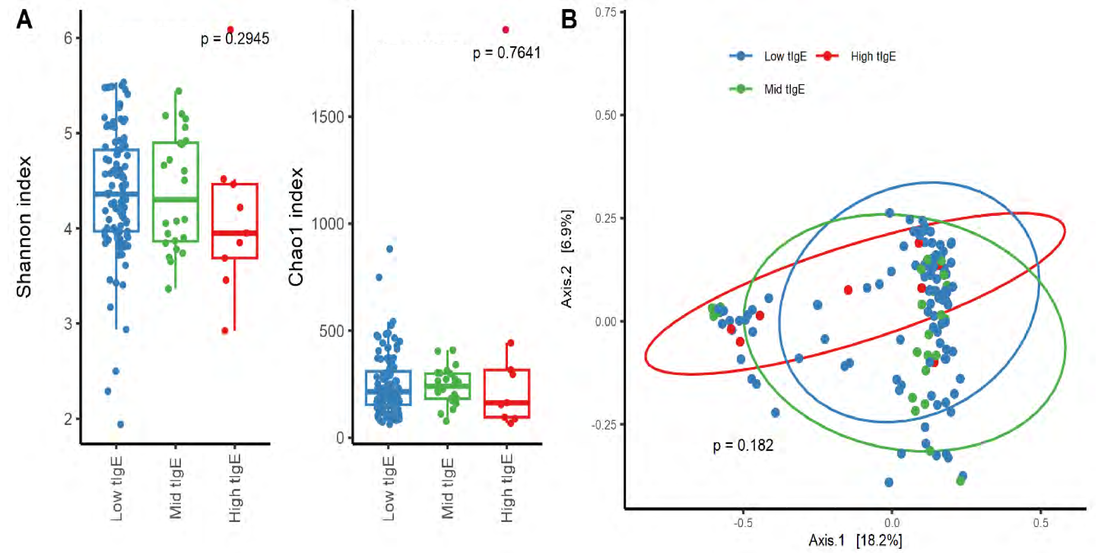


Figure 2. Stratifying participants by tIgE did not reveal community-level differences in the middle meatus microbiome. K-means clustering stratified samples (31 participants, n=155) from Baseline-NAC, 6hr post-NAC, 24hr post-NAC, and 48hr post-NAC into three groups based on tIgE levels: Low tIgE (2.178–211.8 kUA/L, n=120), Mid tIgE (293.8–545.8 kUA/L, n=25), and High tIgE (691.8–897.4 kUA/L, n=10). **(A)** No significant differences in Alpha diversity (Shannon, Chao1) were found (Kruskal-Wallis: *P = 0.2945*, *P = 0.7641*). **(B)** Non-significant separation exists between tIgE groups (PERMANOVA: *P = 0.182*). Boxplots show quartiles and medians; ellipses indicate group separation.

Poster #497

Methods

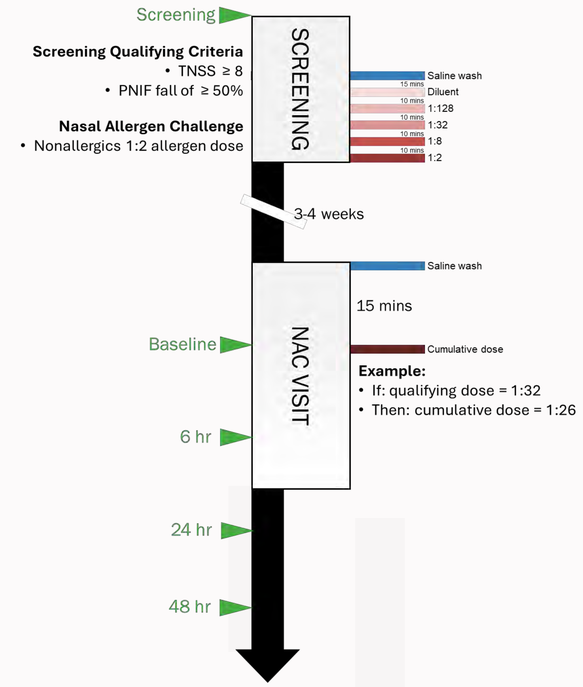


Figure 3. NAC Study Design. At screening, participants received incremental concentrations of ragweed allergen until they reached a qualifying symptom score. For the NAC visit (21–28 days later), participants were challenged with a single cumulative dose. Nasal sponges (green arrows) were used to sample the middle meatus microbiome at the screening and NAC visits.

Ragweed-specific serum IgE (sIgE) and total IgE (tIgE) levels were measured using **ImmunoCAP™ technology** on the **Phadia 100 system**.

Bacterial DNA was extracted, and the V3–V4 regions of the 16S rRNA gene were amplified and sequenced using the **Illumina MiSeq 2000.**

Quality control, taxonomic classification, and abundance estimation were performed using the DADA2 package in R.[7,8]

Microbial alpha diversity was quantified using the Shannon and Chao1 indices (phyloseq v1.42.0, vegan v2.6).

Beta diversity was assessed using principal coordinate analysis (PCoA) based on Bray-Curtis dissimilarity distances (ordinate function, phyloseq package).[9,10]

Summary and Discussion

This is the **first study to examine the nasal microbiome using a validated exposure model that controls for seasonality.**

These findings do not align with previous research by Hyun *et al.* who noted the inferior turbinate microbiota was significantly altered in AR patients with high tIgE levels.[3]

Future studies should seek to increase the sample size, incorporate longer pollen exposure periods, and perform broader microbiome and metabolomic analyses.

Clinical Validation of the Specialized Particulate Control Environmental Exposure Unit (SPaC-EEU) for Cat Dander Exposure

Lubnaa Hossenbaccus MSc[1,2], Sarah Garvey RPN, CAE[2], Terry Walker BA[2], Hannah Botting BA[2], Lisa Steacy BSc[2], and Anne K Ellis MD, MSc, FRCPC[1,2]

1 Department of Medicine, Queen's University, Kingston, ON, Canada 2 Allergy Research Unit, Kingston Health Sciences Centre – KGH Site, Kingston, ON, Canada

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 antigen responsible for cat allergy in humans[2]

The SPaC-EEU is a micro-controlled room within the established EEU in Kingston, ON Canada, used to study perennial AR[3,4,5]

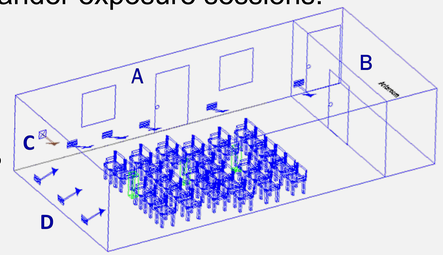
It has recently undergone a successful technical validation for cat dander delivery, specifically assessing Fel d 1 distribution

Here, we performed a clinical validation with cat-allergic and non-allergic participants.

Methods

Cat dander (Greer®, USA) was distributed in the SPaC-EEU for 3 hours in two cat dander exposure sessions.

Figure 1. 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). The influx of allergen is regulated through the feeder (C) located near the front. Fans (D) are distributed throughout the room to disperse the allergen.



Fel d 1 concentrations were assessed using a Fel d 1-specific ELISA (Indoor Biotechnologies, USA).

Forty-six participants were successfully enrolled in this study, consisting of 31 cat-allergics and 15 non-allergics.

Visit 1 Screening → **Visit 2** Allergen Exposure → **Visit 3** Follow Up

Symptom and safety scores were collected using diary cards at 18 timepoints during Visit 2 and 3.

Peak Nasal Inspiratory Flow was captured using a PNIF meter.

Statistical analyses were completed using GraphPad Prism.

Results

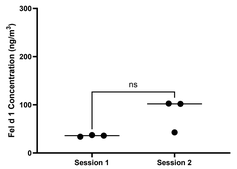


Figure 2. Fel d 1 concentrations following cat dander exposure sessions. Two cat dander exposure sessions were held in the SPaC-EEU. Air samples were collected using sampling cassettes and assessed using a Fel d 1-specific ELISA. Median Fel d 1 concentrations were 36.1 ng/m³ for Session 1 and 102.0 ng/m³ for Session 2.

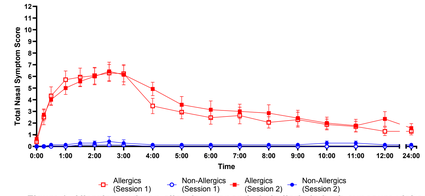


Figure 3. Allergics and non-allergics responded similarly in both exposure visits. Participants reported nasal symptoms of runny nose/post-nasal drip, nasal congestion/stuffiness, sneezing, and itchy nose, ranked from 0 to 3 increasing in severity. Symptoms were tallied as Total Nasal Symptom Score (TNSS) with a total score out of 12. No significant differences in TNSS were observed at any timepoint between allergics in Sessions 1 and 2.

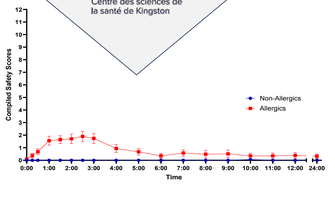


Figure 4. No clinically significant safety outcomes were reported during allergen exposure. Asthma-related symptoms, specifically coughing, wheezing, chest tightness, and shortness of breath, were ranked by participants from 0 to 3 and tallied as safety scores. Allergics experienced a non-clinically relevant increase in safety scores compared to non-allergic participants, likely associated with post-nasal drip.

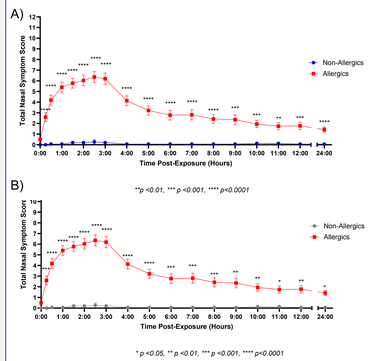
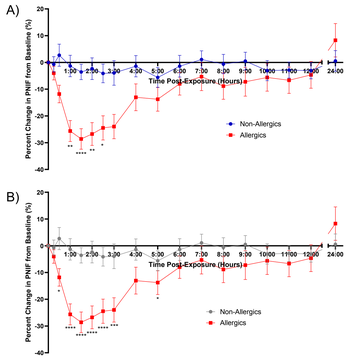


Figure 5. Allergics experienced significantly increased Total Nasal Symptom Scores. Allergic participants experienced significantly increased TNSS as early as 15 minutes until 24 hours post-onset of allergen compared to both non-allergic participants (A) and to their own baseline (B).

The SPaC-EEU can safely produce clinically relevant and meaningful nasal symptoms in cat-allergic participants.



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References

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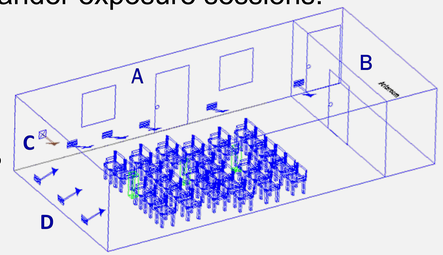

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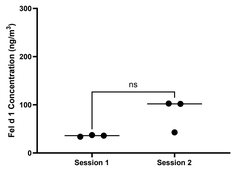

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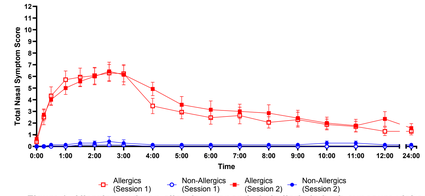

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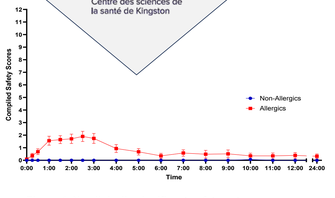

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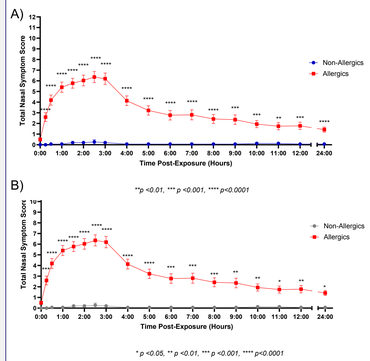

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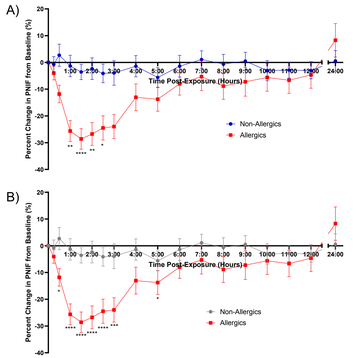

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The Nasal Microbiome of Individuals with Allergic Rhinitis is Stable Following a Nasal Allergen Challenge with Ragweed

Linton S BSc[1,2], Greenlaw J MSc[1,3], Sjaarda C PhD[2,4], Hossenbaccus L MSc[1,2], Thiele J MSc[5], Steacy LM BSc CCRP[2], Sheth P PhD[2,3,4,5], and Ellis AK MD MSc FRCPC [1,2,5]

[1] Department of Medicine, Queen's University [2] Kingston General Health Research Institute, Kingston Health Sciences Centre – KGH Site [3] Gastrointestinal Disease Research Unit, Queen's University [4] Department of Pathology and Molecular Medicine, Queen's University [5] Department of Biomedical and Molecular Sciences, Queen's University

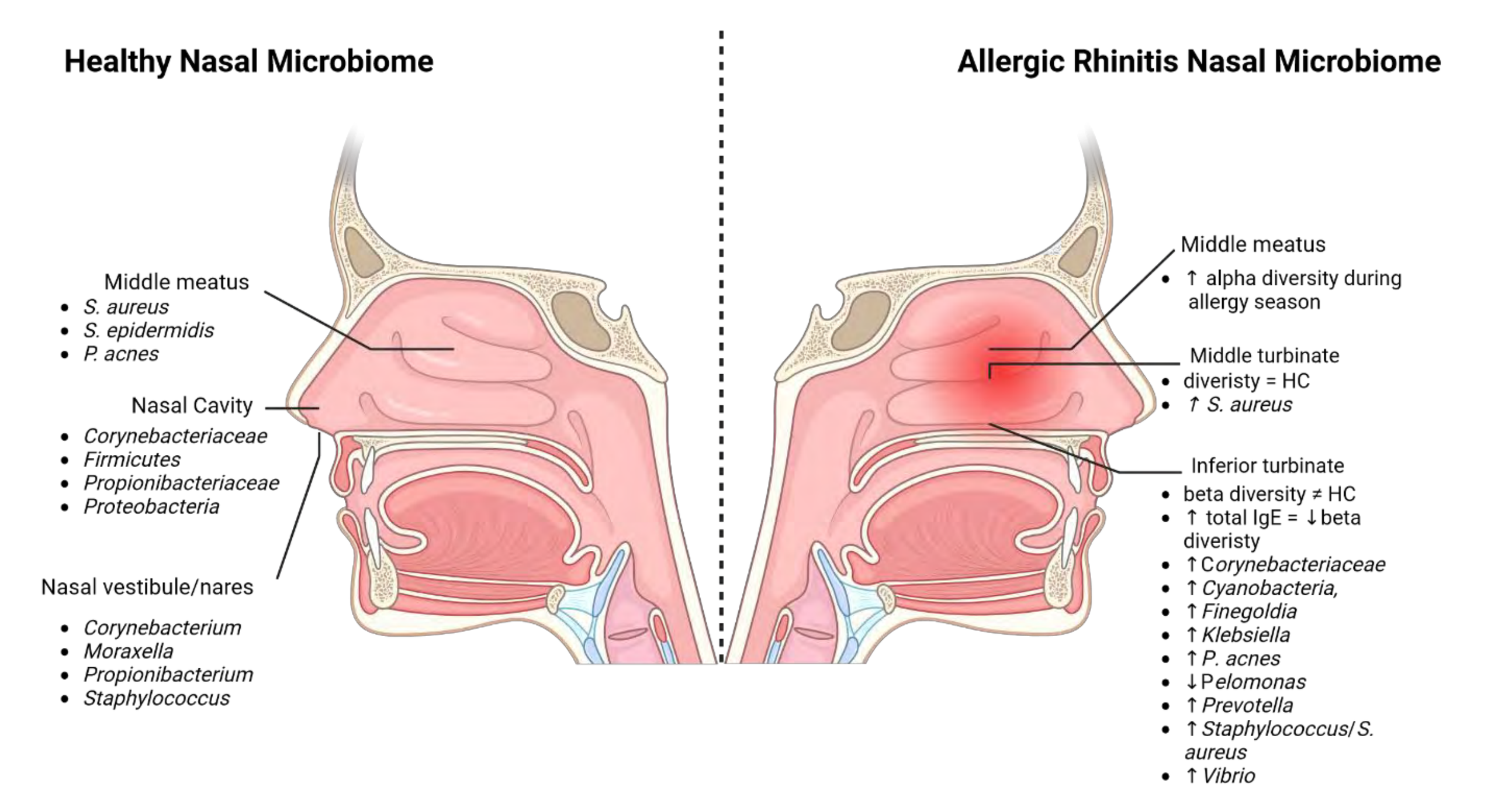
CSACI ANNUAL SCIENTIFIC MEETING

Poster #2

Background

- The microbiome has been implicated in the development of allergic rhinitis (AR): gut microbial diversity has been cited as a protective factor against atopy. (1)
- The healthy **nasal microbiome** is dominated by *Corynebacterium*, *Moraxella*, *Propionibacterium*, and *Staphylococcus*. (2)
- Studies characterizing the **nasal microbiome** in AR patients are limited, vary in study design, and sampling location. Thus, no conclusions can be drawn. (**Figure 1**). (2-7)
- The pollen season has been shown to impact the community profile of the nasal microbiota. (4) **Yet, no studies have examined the microbiome using a controlled model of AR out of pollen season.**

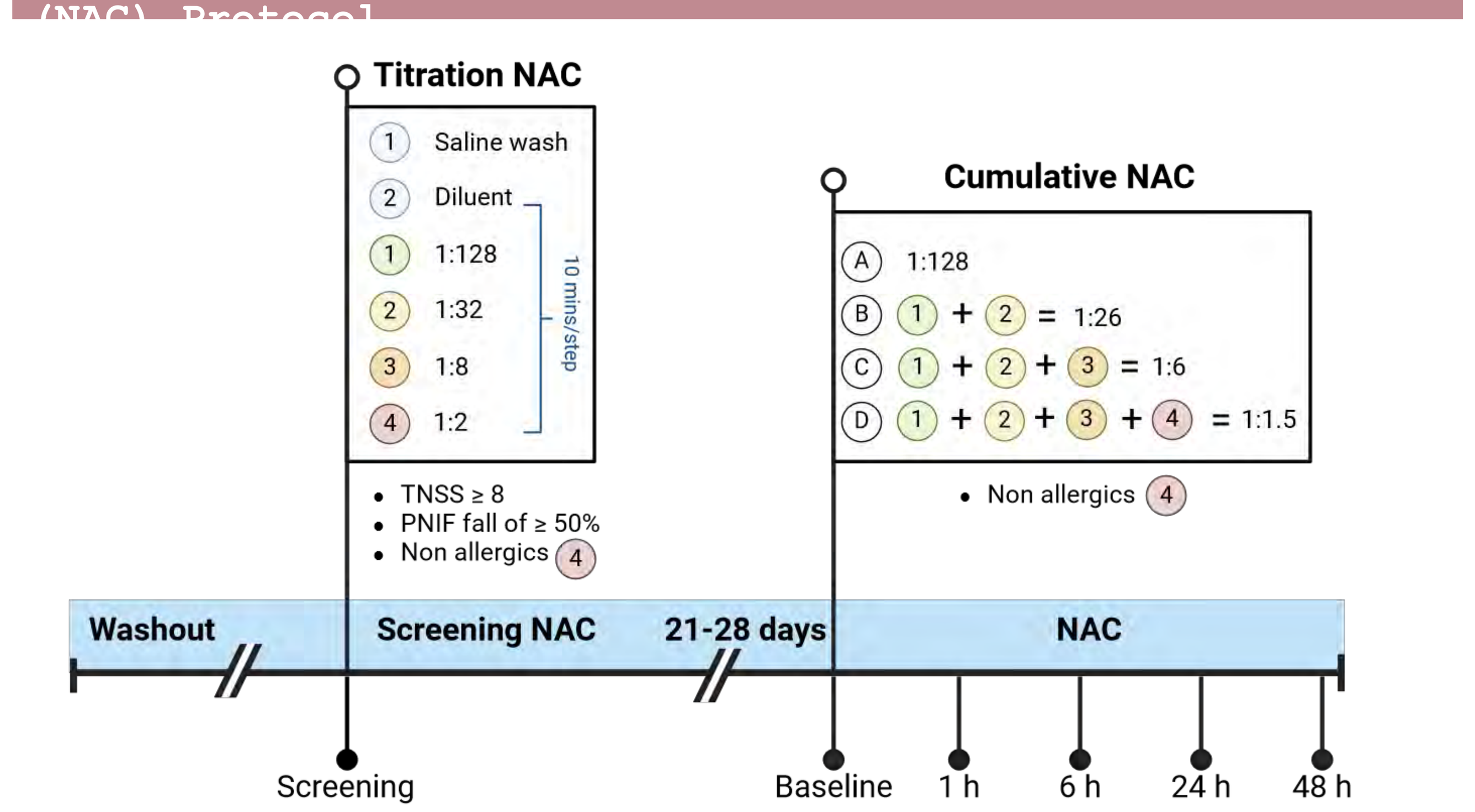
Figure 1. Allergic Rhinitis Nasal Microbiome: there is no consensus



- The nasal allergen challenge (NAC) model developed by the Allergic Rhinitis Clinical Investigator Collaborative (AR-CIC) has been optimized and validated for several allergens. (8-9)
- **Aim: To assess the microbiome of the middle meatus (an anatomical site of AR) of AR participants and healthy controls before and after controlled NAC exposure to ragweed, outside of the pollen season.**

Methodology

Figure 2. Optimized AR-CIC Nasal Allergen Challenge (NAC) Protocol



h = hours; NAC = nasal allergen challenge; PNIF = peak nasal inspiratory flow; TNSS = total nasal symptom score

- During a **screening visit**, incremental concentrations of ragweed allergen were administered until each participant achieved a qualifying symptom score. For the subsequent **NAC visit** (21-28 days later), participants were challenged with a single allergen dose cumulative to the amount administered at the screening visit (**Figure 2**).
- **Nasal sponges** were collected at screening and NAC visits (baseline, 6-, 24-, and 48-hours post-NAC) to capture the middle meatus microbiome. **Samples were collected from 19 AR participants and 12 healthy controls.**
- The variable regions V3-V4 of the bacterial 16S rRNA gene were sequenced using the **Illumina MiSeq 2000 platform.**
- Microbial abundance and taxonomic classification were determined using the DADA2 package in R. (10-12)
- Differences between groups and timepoints were quantified by alpha diversity (Shannon and Chao1 indices) and beta diversity (principal coordinate analysis on Bray-Curtis dissimilarity). (13-14)

Results

Figure 3. AR and non-AR participants have comparable alpha diversity

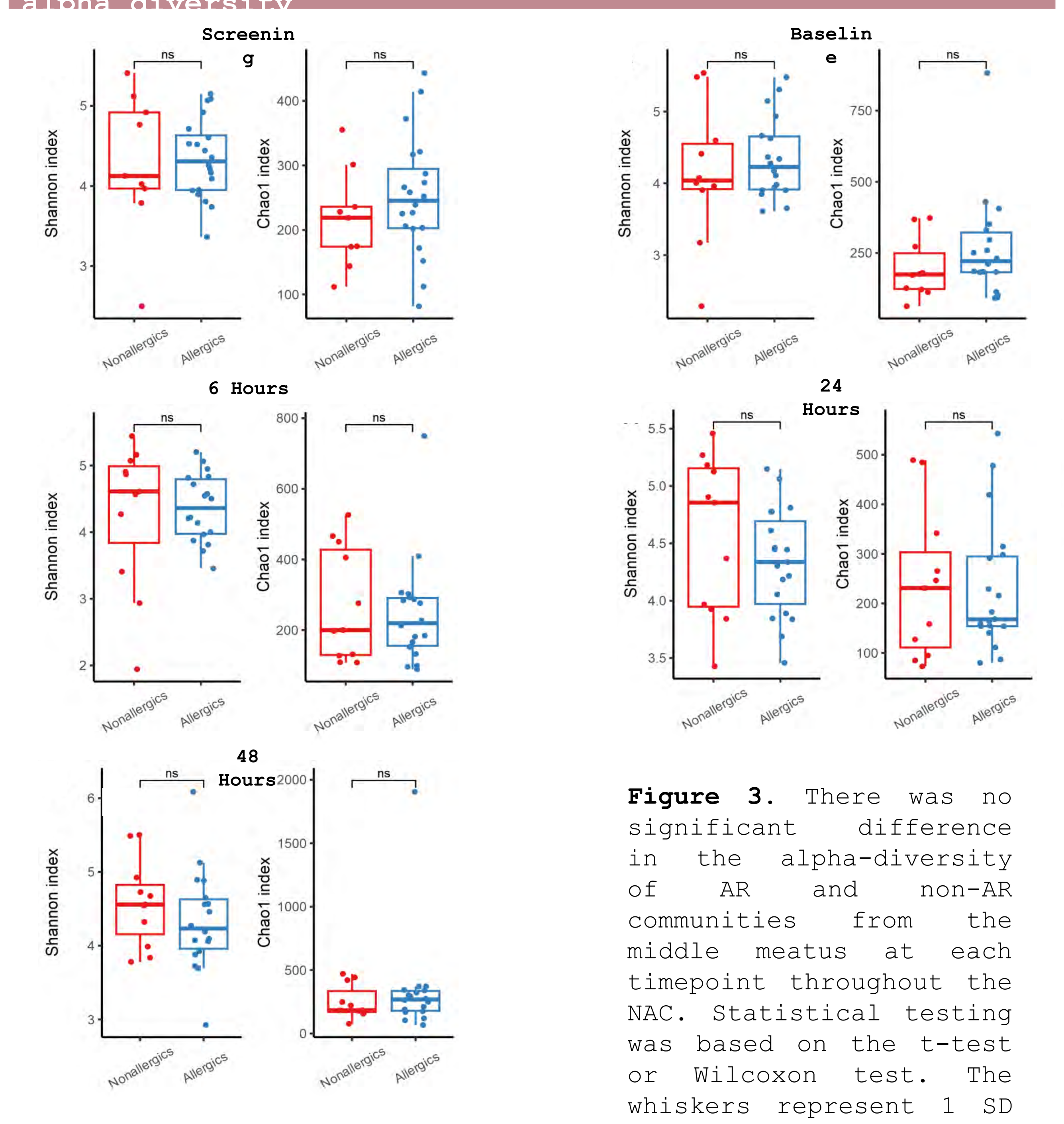


Figure 3. There was no significant difference in the alpha-diversity of AR and non-AR communities from the middle meatus at each timepoint throughout the NAC. Statistical testing was based on the t-test or Wilcoxon test. The whiskers represent 1 SD above and below the mean of the data. ns = not significant; P > 0.05.

Figure 4. AR and non-AR participants have comparable beta diversity

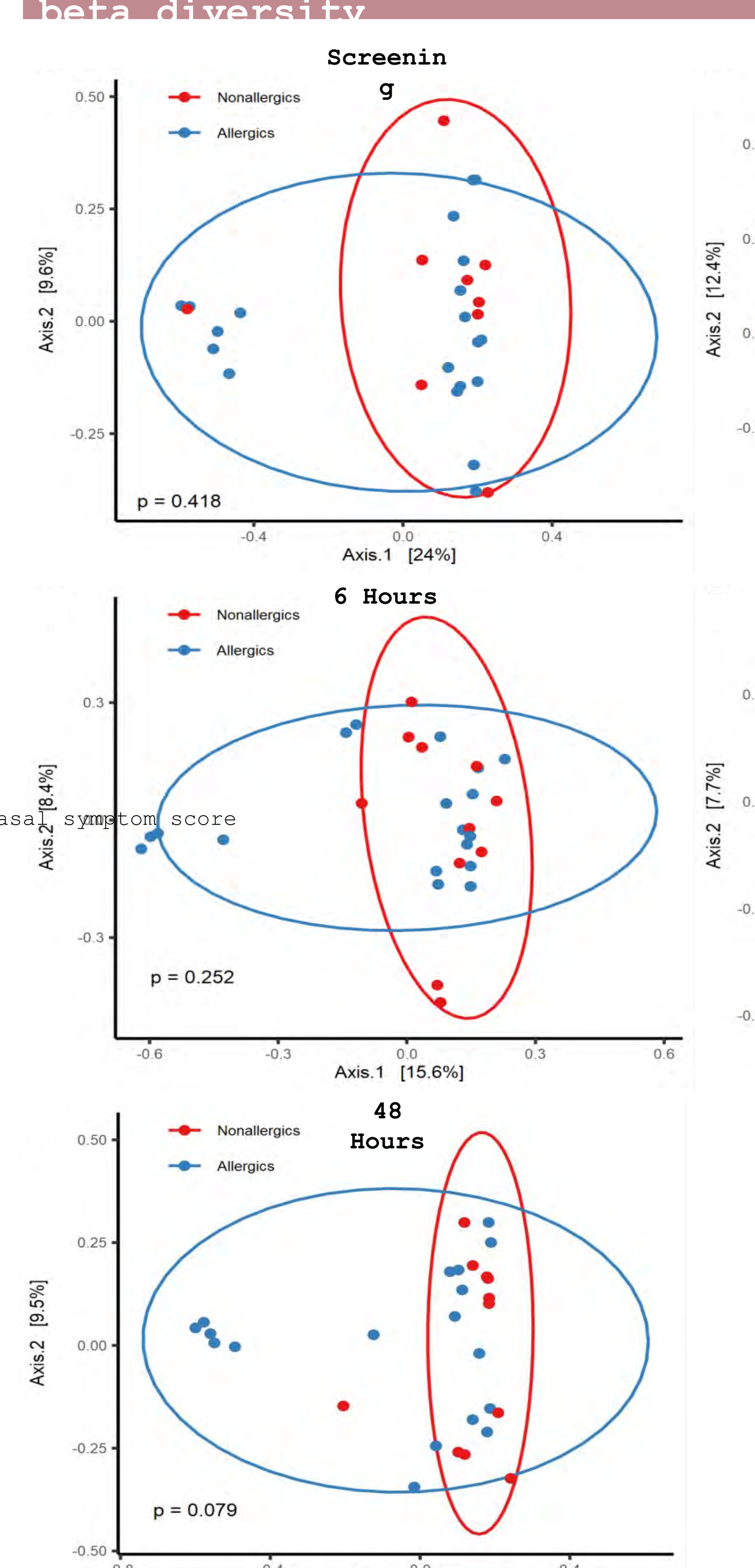


Figure 4. The ellipses reveal an almost complete overlap of the nasal microbial communities of AR and non-AR participants at all timepoints throughout the NAC. A non-significant cluster of AR participants is apparent at each timepoint. Statistical testing was based on PERMANOVA.

Figure 5. Genera legend for taxonomy plots

Actinomyces, Akkermansia, Alistipes, Anaerococcus, Bacillus, Bacteroides, Blautia, Capnocytophaga, Clostridium_sensu_stricto, Corynebacterium, Curvibacter, Cutibacterium, Delftia, Dolosigranulum, Dorea, Duncaniella, Elizabethkingia, Enterobacter, Enterocloster, Enterococcus, Escherichia/Shigella, Faecalibacterium, Finegoldia, Flintibacter, Fusobacterium, Haemophilus, Holdemanella, Kineothrix, Lactobacillus, Lawsonella, Moraxella, Muribaculum, Neisseria, Pelomonas, Phocaeicola, Porphyromonas, Prevotella, Pseudomonas, Ralstonia, Rothia, Schaalia, Serratia, Sphingomonas, Staphylococcus, Streptococcus, Veillonella, N/A

Figure 6. AR and non-AR participants' taxonomic profiles are alike pre-NAC

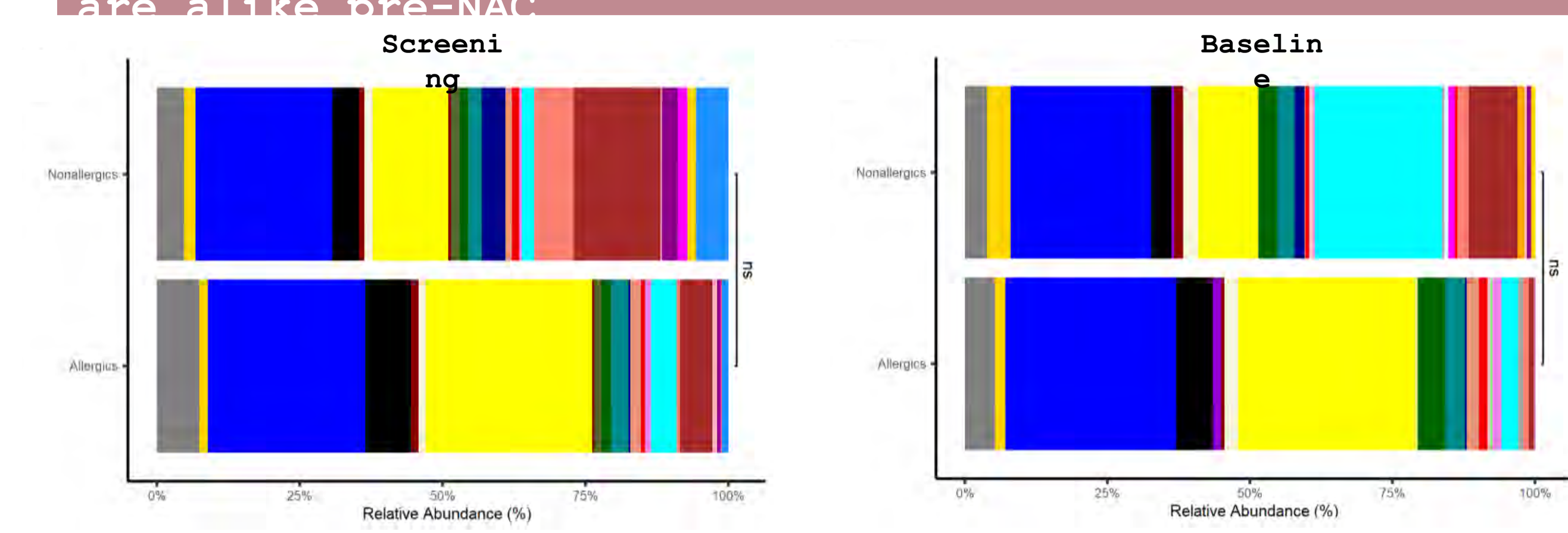


Figure 6. The mean relative abundances of bacterial genera in the middle meatus of AR and non-AR participants are not significantly different pre-NAC. No significant differences taxonomy were found between Screening and Baseline among either group. Statistical testing was based on the Wilcoxon test. ns = not significant; P > 0.05.

Figure 7. Taxonomic profiles of AR and non-AR participants differ post-NAC

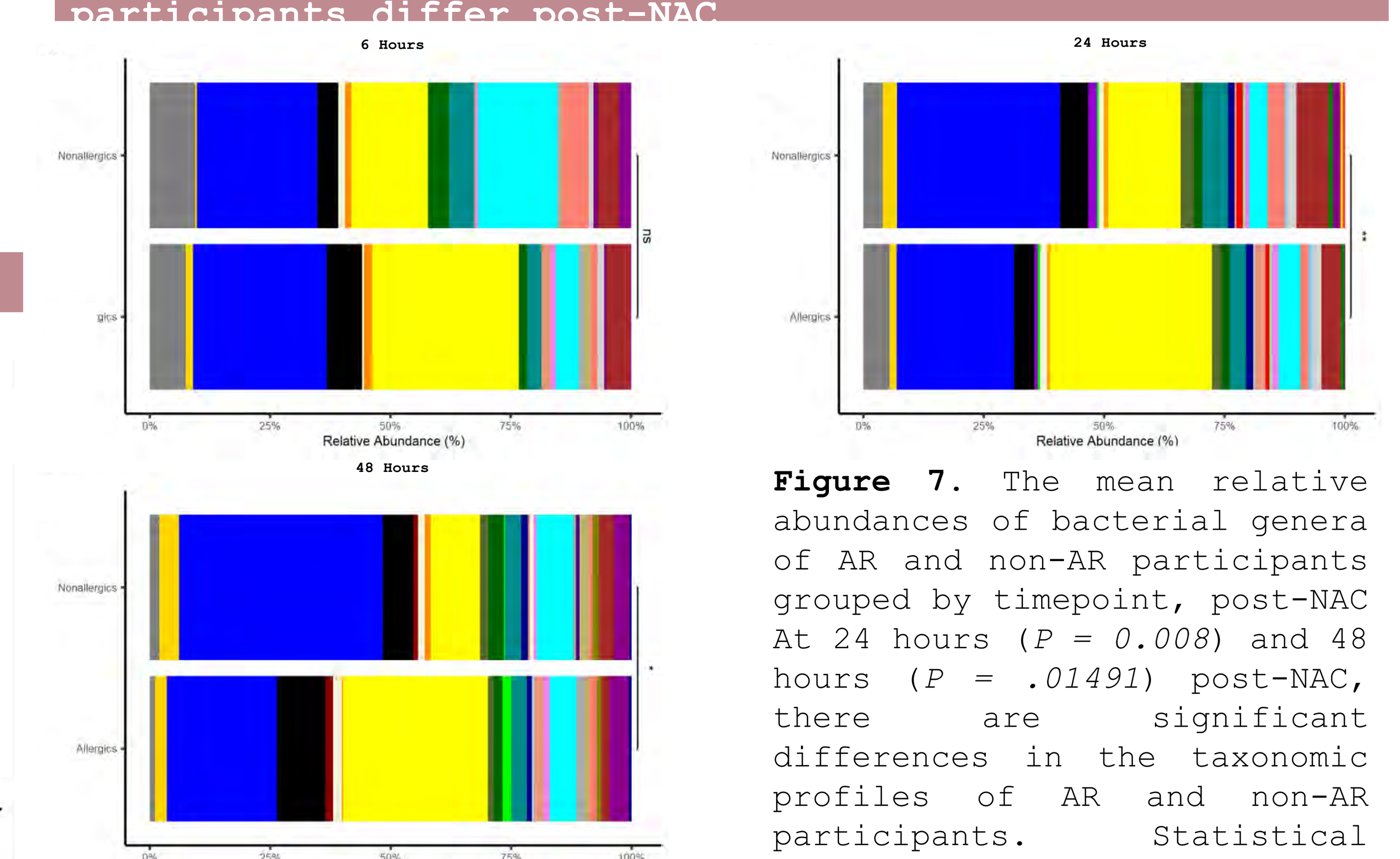


Figure 7. The mean relative abundances of bacterial genera of AR and non-AR participants grouped by timepoint, post-NAC. At 24 hours (*P = 0.008*) and 48 hours (*P = .01491*) post-NAC, there are significant differences in the taxonomic profiles of AR and non-AR participants. Statistical testing was based on the Wilcoxon test. ns = not significant; P > 0.05, * = P < 0.05, ** = P < 0.01.

Figure 8. AR nasal microbiota community profile is stable during NAC

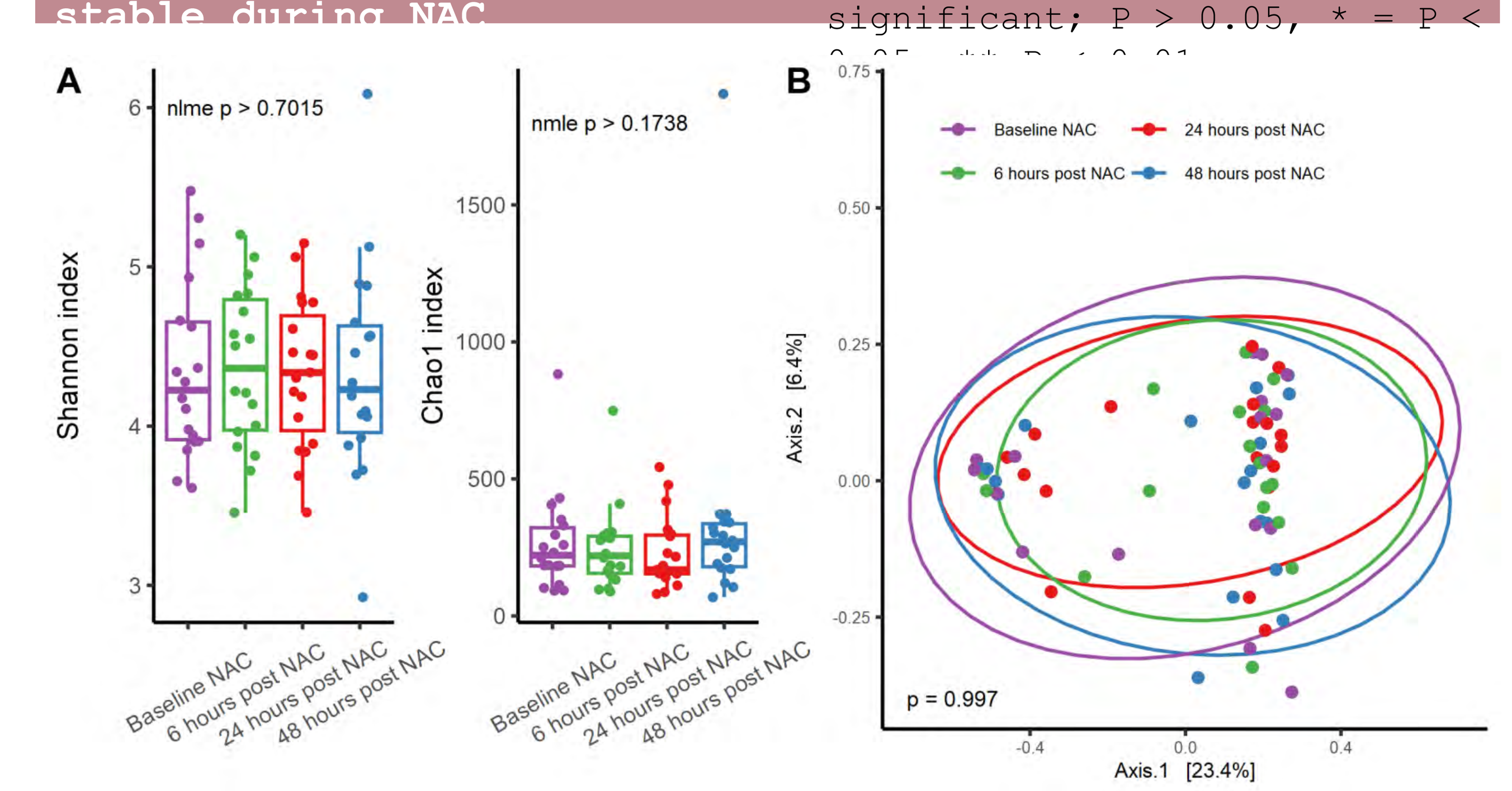


Figure 8. Among AR participants, there was no significant differences in the alpha diversity of the middle meatus over the NAC. Similarly, the beta diversity of the middle meatus microbiome is unchanged throughout the NAC as the ellipses are overlapping considerably. Statistical testing was based on **(A)** linear mixed effects model and **(B)** PERMANOVA test. (A) The whiskers represent 1 SD above and below the mean of the data.

Figure 8. Non-AR nasal microbiota community profile is stable during NAC

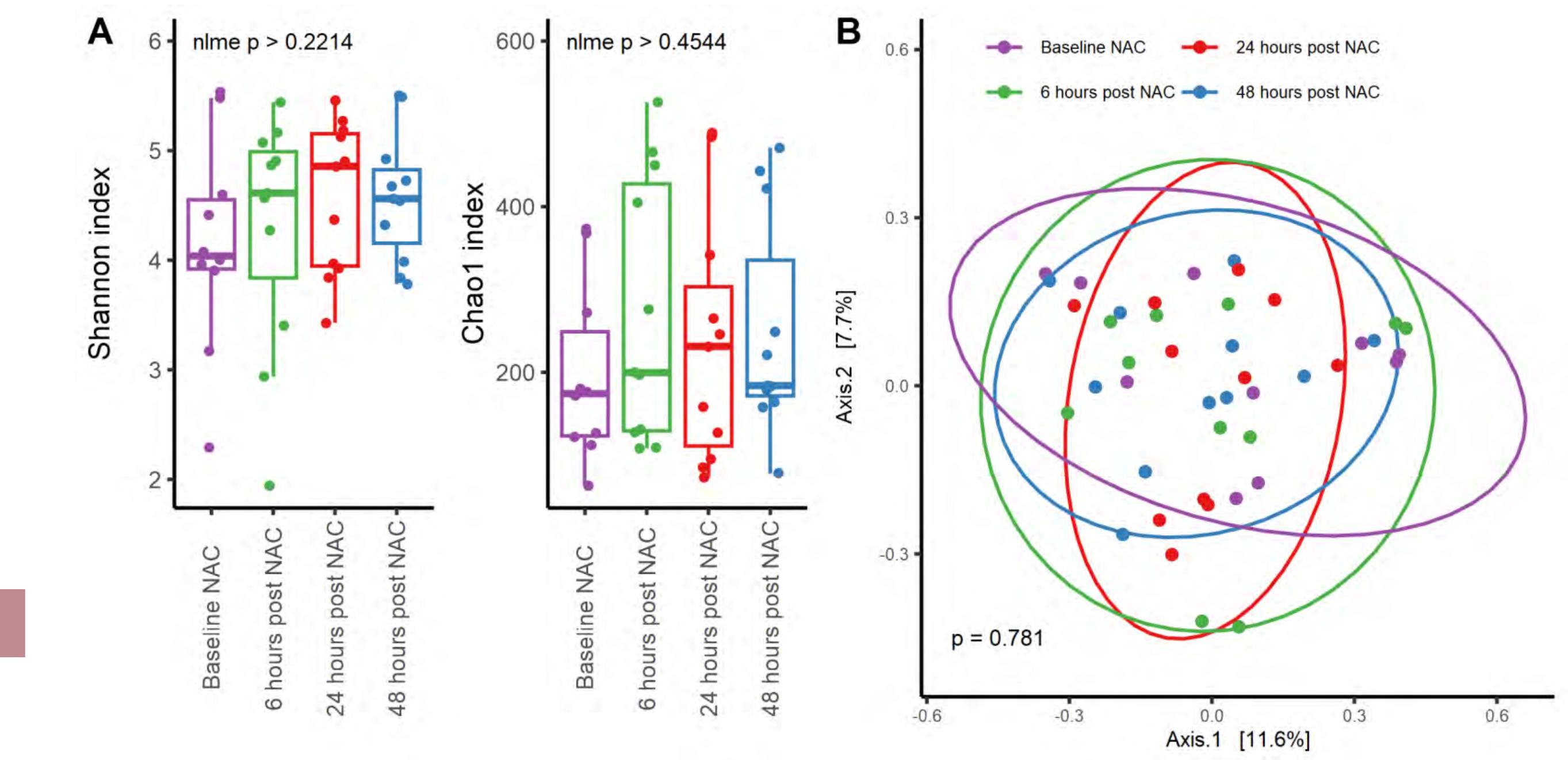


Figure 8. The alpha and beta diversity of non-AR participants did not vary significantly throughout the NAC. Statistical testing was based on **(A)** linear mixed effects model and **(B)** PERMANOVA test. The whiskers represent 1 SD above and below the mean of the data.

Figure 10. NAC does not impact taxonomic profile middle meatus

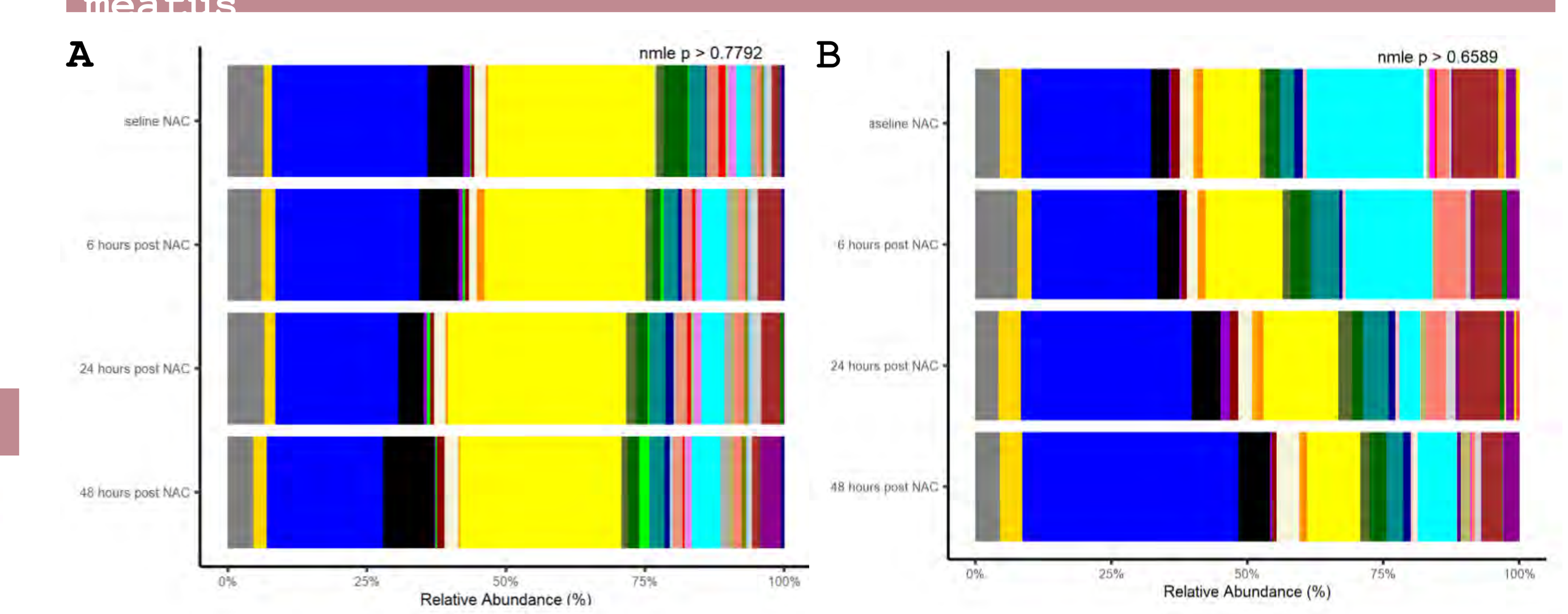


Figure 10. There was no significant difference in the taxonomic profiles of AR (A) or non-AR participants (B) throughout the NAC. Statistical testing was based on a linear mixed effect model.

Discussion/Conclusions

- This is the first study to employ the AR-CIC NAC protocol to investigate the nasal microbiome, out-of-season.
- The nasal microbiome of ragweed allergic participants is stable out-of-season, despite many participants being polysensitized to perennial allergens.
- According to this study, the NAC does not appear to influence the community profile dynamics of the middle meatus microbiome. However, significant differences in the relative abundance of genera present were found at 24 and 48 hours post-NAC. Future investigations will seek to identify the differences in specific genera between AR and non-AR participants.
- The current literature suggests that the abundance of certain bacterial taxa, such as Corynebacterium, Propionibacterium, and Staphyloccocus, may have a greater impact on the relationship between the microbiome and AR and, even more broadly, immunoglobulin-E (IgE). (2-7) As IgE was collected as a biomarker in this study, future investigations will assess the potential role of IgE on the microbiome.
- This pilot study is limited by sample size and participant compliance. A larger study with longer pollen exposure and more extensive nasal microbiome analysis is warranted.

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Acknowledgements: We collaborated with Dr. Prameet Sheth and Jill Greenlaw to perform the sample sequencing. We were fortunate to collaborate with Dr. Calvin P. Sjaarda to process the 16S rRNA sequence data and perform a detailed statistical analysis. This study would not have been possible without Kingston Allergy Research, with special thanks to Abigail Davis, Cortney Haird, Hannah Botting, and Sarah Garvey.

AR-CIC · Kingston Allergy Research · Kingston Health Sciences Centre / Centre des sciences de la santé de Kingston · Queen's University

Development of Nasal and Ocular Symptoms with Cat Dander Exposure in the Specialized Particulate Control Environmental Exposure Unit (SPaC-EEU)

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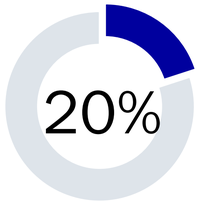
Poster #10

Introduction



of the world's population is affected by cat allergen-induced allergic rhinitis (AR)[1]

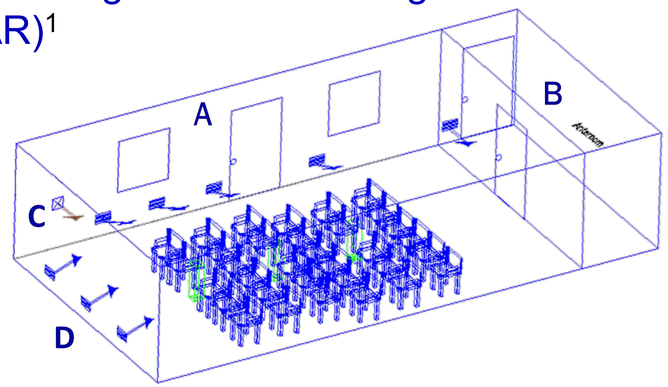


Figure 1. Rendering of the SPaC-EEU. The SPaC-EEU consists of a central room (A), which can seat up to 30 participants, and an anteroom (B). The influx of allergen is regulated through the feeder (C) located near the front. Fans (D) are distributed throughout the room to disperse the allergen.

The SPaC-EEU is a micro-controlled room in Kingston, ON that has recently undergone successful technical and clinical validations for use with cat dander.[2,3]

Here, we present ocular symptom outcomes and comparisons with nasal symptoms.

Methods

31 cat-allergics and 15 non-allergics completed this study.

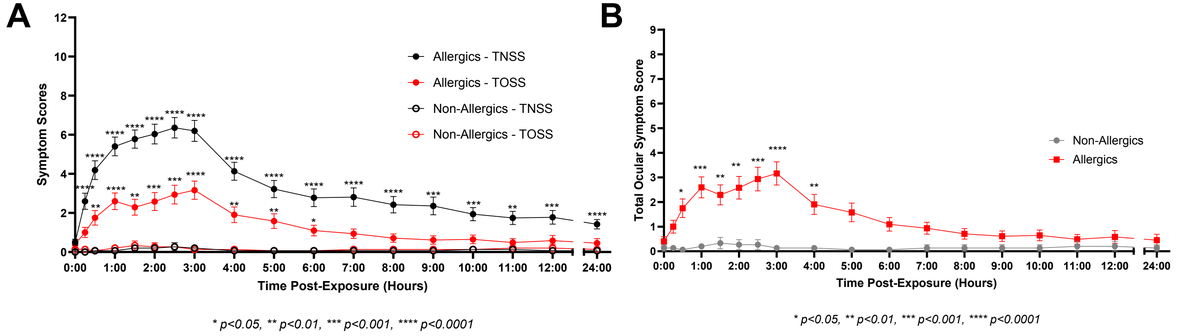
Visit 1 Screening → **Visit 2** Allergen Exposure → **Visit 3** Follow Up

Total Nasal Symptom Scores (TNSS) and Total Ocular Symptom Scores (TOSS) were collected using diary cards.

GraphPad Prism was used for statistical analyses.

Results

Total Ocular Symptom Scores were significantly increased for allergics compared to healthy controls and their own baseline.

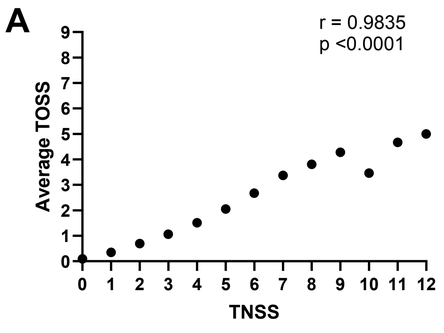


* p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001

* p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001

Figure 2. Allergic participants had significantly increased nasal and ocular symptoms. Cat-allergic participants experienced significantly increased (p<0.05) nasal and ocular symptom scores as early as 30 minutes into cat dander exposure in the SPaC-EEU compared to healthy controls (A) and their own baseline scores (B). Nasal symptoms were scored out of 12 whereas ocular symptoms were scored out of 9.

Nasal and ocular symptoms were significantly positively correlated, with a TNSS of 6 or higher often associated with a minimum TOSS of 3.



B

TNSS	Frequency of TOSS									
	0	1	2	3	4	5	6	7	8	9
0 (n=103)	92%	6%	2%	0%	0%	0%	0%	0%	0%	0%
1 (n=77)	78%	16%	3%	3%	0%	1%	0%	0%	0%	0%
2 (n=79)	59%	24%	8%	5%	4%	0%	0%	0%	0%	0%
3 (n=79)	48%	28%	8%	6%	8%	1%	1%	0%	0%	0%
4 (n=47)	43%	13%	17%	11%	15%	0%	2%	0%	0%	0%
5 (n=40)	28%	23%	15%	13%	10%	3%	8%	3%	0%	0%
6 (n=46)	24%	11%	11%	13%	26%	7%	4%	2%	2%	0%
7 (n=27)	19%	4%	11%	19%	22%	4%	15%	4%	0%	4%
8 (n=21)	14%	5%	5%	24%	10%	19%	14%	5%	0%	5%
9 (n=18)	22%	6%	6%	0%	6%	22%	17%	6%	11%	6%
10 (n=13)	31%	0%	8%	0%	31%	8%	8%	8%	0%	8%
11 (n=6)	17%	0%	17%	0%	17%	0%	0%	33%	17%	0%
12 (n=6)	0%	0%	17%	0%	17%	33%	17%	0%	17%	0%

Figure 3. There was a positive and significant correlation between nasal and ocular symptoms. Average nasal and ocular symptoms were significantly positively correlated (A) for allergic participants with cat dander exposure in the SPaC-EEU. Ocular symptoms were associated with higher nasal symptoms (B).

Allergic participants had more pronounced and longer-lasting nasal symptoms than ocular symptoms with cat dander exposure in the SPaC-EEU.

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Poster #3

Serum cytokine profiles following a cat allergen challenge in the Specialized Particulate Control Environmental Exposure Unit (SPaC-EEU)

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Background

7-25% of the global population has cat allergen-induced AR.[1]

Fel d 1 → the major cat allergen[1]

The Specialized Particulate Control Environmental Exposure Unit (**SPaC-EEU**) is an allergen exposure unit located at Kingston Health Sciences Centre – KGH Site. It has been previously validated for use with house dust mite, ragweed, and cat allergen as well has been used for one study with Diesel Exhaust Particulates.[2-6] It can serve as an **important tool for analyzing biologic outcomes of allergen exposure.**

Serum cytokine levels in response to Fel d 1 exposure in an EEU have been studied before, but not extensively.[7,8] **We aimed to assess biological outcomes of SPaC-EEU exposure to Fel d 1.**

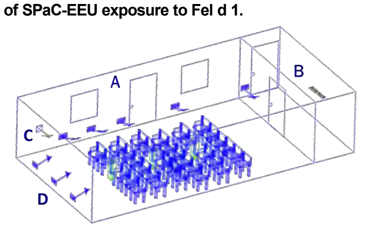

Figure 1. Visual Rendition of the SPaC-EEU. A central room (A) which seats up to 30 participants, and an anteroom (B) make up the SPaC-EEU. The feeder (C) located near the front regulates allergen influx. Fans (D) are located throughout the room to disperse the allergen.

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 from screening to baseline, and between baseline and 3 hours, 6 hours, and 24 hours-post onset of SPaC-EEU exposure to Fel d 1.

Methodology

Visit 1: Screening Visit
Screening sample collection

Visit 2: Exposure Visit
1. **Baseline sample collection**
2. 3-hour long Fel d 1 exposure in the SPaC-EEU
3. **3-hour timepoint sample collection**
4. **6-hour timepoint sample collection**

Visit 3: Follow-Up Visit
Follow-Up sample collection

Sample Processing

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-1 (Panel A); IL-33 (Panel B)

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

Statistical Analysis: GraphPad Software

Results

Cytokine Levels: Pre-Exposure Timepoints

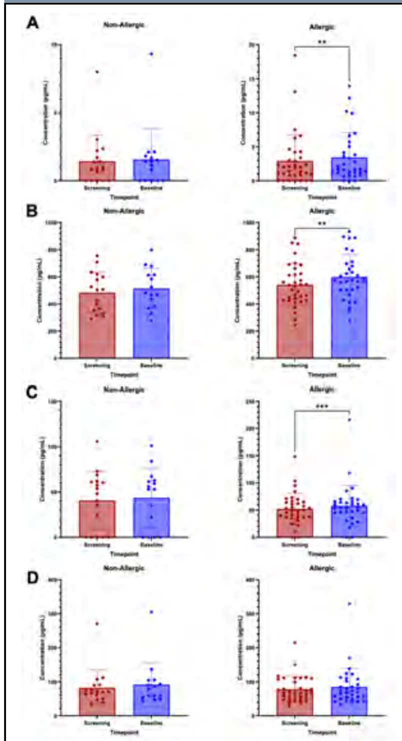

Figure 2. Inflammatory cytokine concentrations were significantly increased from screening to baseline timepoints. (A) IL-5, (B), MCP-1, (C) MIP-1ß, (D) Eotaxin-1. A Kruskal-Wallis test was used to determine significance. * = p<0.05, ** = p<0.01, *** = p< 0.001.

Cytokine Levels: Exposure Timepoints

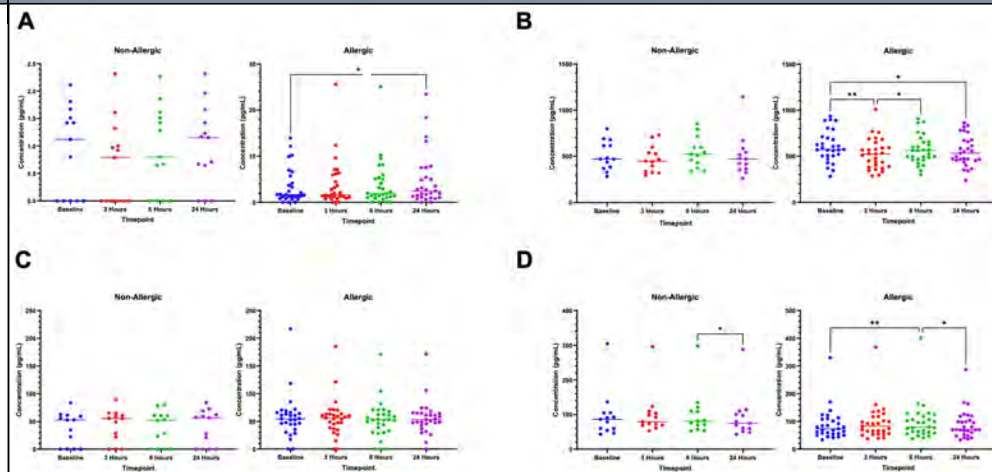

Figure 3. Chemoattractant and pro-inflammatory cytokine concentrations were significantly increased in allergic participants after cat allergen exposure in the SPaC-EEU exposure. (A) IL-5, (B), MCP-1, (C) MIP-1ß, (D) Eotaxin-1. Friedman tests with Dunn's multiple comparisons tests were performed to determine the significance. * = p<0.05, ** = p<0.01, *** = p< 0.001.

Discussion

- This study was a component of the clinical validation of the SPaC-EEU for the use of cat allergen.
- We found that between two pre-exposure timepoints (screening and baseline), cat allergic participants experienced significant increases in inflammatory cytokine levels. Previous studies have noted generally increased levels of these cytokines in the serum and nasal fluid of allergic cohorts, but no day-to-day fluctuation changes have been noted.[9-11]
- The allergic cohort was found to experience various significant increases in serum cytokine levels after SPaC-EEU exposure to cat allergen; this is supported by other research that has found increases in inflammatory cytokines in allergic participants.[8,12-13]
- Overall, non-allergic participants did not experience many significant changes in serum cytokine levels prior to or during Fel d 1 exposure in the SPaC-EEU; this generally parallels other studies.[13,14]
- The immune response may be impacted by uncontrollable confounding variables such as exposure to cats outside of the study visit.
- Between visits, participants were able to be exposed to cats as normal without restriction. This exposure may influence the results of the allergic cohort by leading participants to come on-site with elevated inflammatory cytokine levels.
  → Further analysis by comparing the biologic profiles of allergic participants who live with versus without a cat in this study are warranted.

Conclusions

Allergic participants experienced significant biologic changes in their inflammatory cytokine levels between the screening and baseline collection timepoints. This suggests significant day-to-day changes in some cytokine levels in the cat-allergic population.

Eotaxin-1 and MCP-1 (both chemoattractants) and IL-5 (a pro-inflammatory cytokine) levels changed significantly in allergic participants upon exposure to Fel d 1 in the EEU, supporting the involvement of these inflammatory molecules in the allergic response and suggesting that the SPaC-EEU was able to induce AR at a biologic level.

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Acknowledgements: We are grateful for the hard work of the Kingston Allergy Research Team, with special thanks to Cortney Haird and Dr. Anne K. Ellis. This study was self funded.

Nasal Cytokine Insights from Allergic and Non-Allergic Participants Following Cat Allergen Exposure in the Specialized Particulate Control Environmental Exposure Unit (SPaC-EEU)

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Poster #384

Introduction

- Cat allergies are estimated to affect ~20% of the population, with rates of sensitization on the rise.[1,2] There remains an unmet need for better therapies.
- Allergen exposure models are useful tools to investigate disease pathophysiology and potential therapies.[3]
- The Specialized Particulate Control Environmental Exposure Unit (SPaC-EEU) is an allergen exposure facility recently clinically validated for cat allergen.[4]

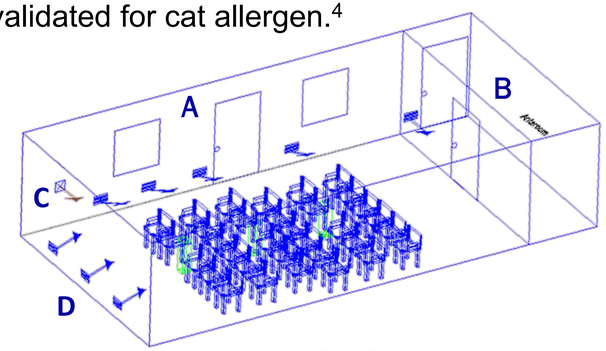


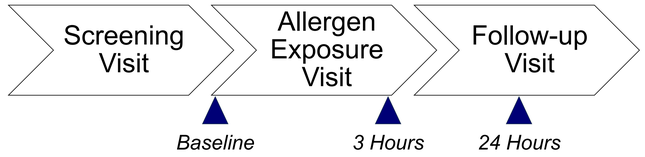
Figure 1. Rendering of the SPAC-EEU. The SPaC-EEU consists of a central room (A), an anteroom (B), an allergen feeder (C), and forced airflow (D) to distribute allergen throughout the room.

- We previously reported significant changes in serum cytokine concentrations following cat dander exposure in the SPaC-EEU.

Here, we characterize nasal cytokine profiles of allergic and non-allergic participants following cat dander exposure in the SPaC-EEU.

Methods

- Participants were exposed to cat dander for 3 hours in the SPaC-EEU:
  - 31 cat-allergic participants
  - 15 non-allergic controls



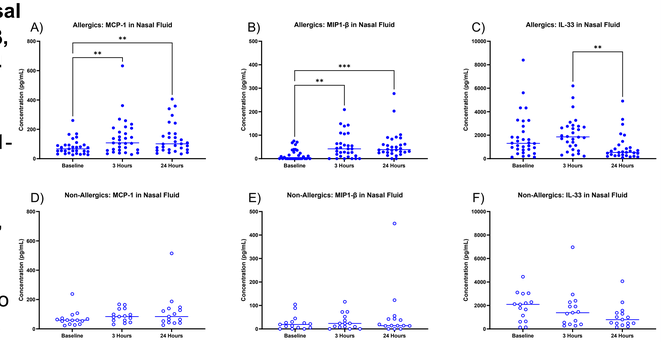
- Nasal samples were collected using Merocel® sponges inserted into the middle meatus for 5 minutes at 3 timepoints. They were placed in a 15 mL polypropylene tubes containing 1 mL of saline for one hour.

- Sponges were centrifuged at 1500g for 15 minutes at 4 ˚C prior to the eluent being aliquoted and frozen at -80 ˚C until analysis.
- Cytokine concentrations were measured using the MILLIPLEX® Human Cytokine/ Chemokine/ Growth Factor Panel A kit (MilliporeSigma) on a Bio-Plex™ 200 system (Bio-Rad Laboratories Ltd).
- The following targets were assessed: IL-4, IL-5, IL-10, IL-13, IL-25, IL-33, Eotaxin-1, MIP1-β, and MCP-1.
- A mixed-effects analysis with Tukey's multiple comparisons test was used for statistical testing using GraphPad Prism 10.4.1.

* p<0.05, ** p<0.01, *** p<0.001

Results

Figure 2. Significant shifts in nasal concentrations of MCP-1, MIP1-β, and IL-33 were captured up to 24 hours post-exposure in cat-allergic participants. Concentrations of MCP-1 (A), MIP1-β (B), and IL-33 (C) in the nose of allergic participants significantly increased from baseline to 3 hours, and subsequently decreased at 24 hours, remaining significantly elevated for MCP-1 and MIP1-β. No significant changes for non-allergic participants were observed (D-F).



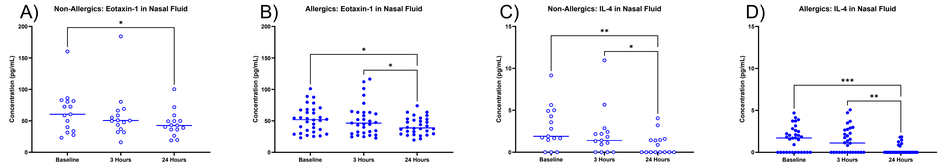


Figure 3. Changes in Eotaxin-1 and IL-4 were observed in both allergic and non-allergic participants. Nasal concentrations of Eotaxin-1 (A, B) and IL-4 (C, D) significantly decreased up to 24 hours post-onset of allergen exposure from baseline.

- No significant changes were observed for IL-5, IL-10, and IL-13.
- Nasal IL-25 concentrations were below the assay detection limit at all time points for both allergics and non-allergics.

Summary & Future Directions

- Cat allergic participants exhibit significant and differential nasal cytokine patterns following cat dander exposure in the SPaC-EEU.
- Epithelial alarmin IL-33 and chemoattractants MCP-1 and MIP1-β have distinct roles in mediating the local allergic response in the nose. These could potentially be therapeutic targets.
- Comparisons of serum and nasal cytokines could inform a kinetic understanding of biological changes.

References

[1] Evcen, Recep et al. "Increasing Prevalence of Sensitization to Cat/Dog Allergens in the COVID-19 Pandemic." International archives of allergy and immunology vol. 185,2 (2024): 133-141. doi:10.1159/000534173
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[3] Hossenbaccus, Lubnaa et al. "Study of Cat Allergy Using Controlled Methodology-A Review of the Literature and a Call to Action." Frontiers in allergy vol. 3 828091. 17 Mar. 2022, doi:10.3389/falgy.2022.828091
[4] Clinical Validation of The Specialized Particulate Control Environmental Exposure Unit (SPaC-EEU) For Cat Dander Exposure, Hossenbaccus, L. et al. Annals of Allergy, Asthma & Immunology, Volume 133, Issue 6, S17

Poster 18

Nasal gene expression of IL-4 is elevated in house dust mite-allergic participants after allergen exposure in the Environmental Exposure Unit

Rachel Lucyshyn BHSc[1], Lubnaa Hossenbaccus MSc[2,3], Cortney Haird MLA/T[3,4], and Anne K. Ellis MD, MSc, FRCPC[2,3,4]

[1]Department of Medicine, University of Ottawa, Ottawa, ON, Canada, [2]Department of Medicine, Queen's University, Kingston, ON, Canada, [3]Allergy Research Unit, Kingston Health Sciences Center - KGH Site, Kingston, ON, Canada, [4]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada

Background

Previously:

- Participants with and without house dust mite (HDM) allergic rhinitis (AR) [1,2].
- Exposed to modest or higher target concentrations of airborne HDM for 3 hours in the **Specialized Particulate Control Environmental Exposure Unit** [1,2].
- Allergic participants had significant differences in serum cytokine concentrations & significantly higher symptom scores compared to non-allergic participants [1,2].

Current study:

- IL-4 & IL-25 cytokines play essential roles in the AR response.

In nasal brushing samples from the same participants exposed to HDM, how do interleukin (*IL*)*-4* and *IL-25* relative gene expression vary between allergic status, timepoint, and dose? Are previous cytokine findings reflected transcriptionally?

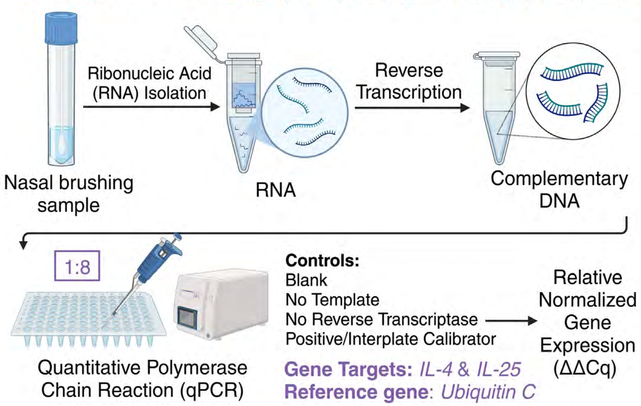
Objectives

1. Compare relative gene expression between HDM-allergic and non-allergic participants pre- and post-HDM exposure.
2. Compare relative gene expression between modest and higher HDM concentrations in allergic participants.
3. Assess correlations between gene expression and serum cytokine levels & symptoms scores.

Methodology

Nasal brushing samples collected at screening (1-2 weeks pre-allergen exposure) & immediately post-exposure.

101 samples: 41 HDM-allergic participants, 10 non-allergic participants



Results

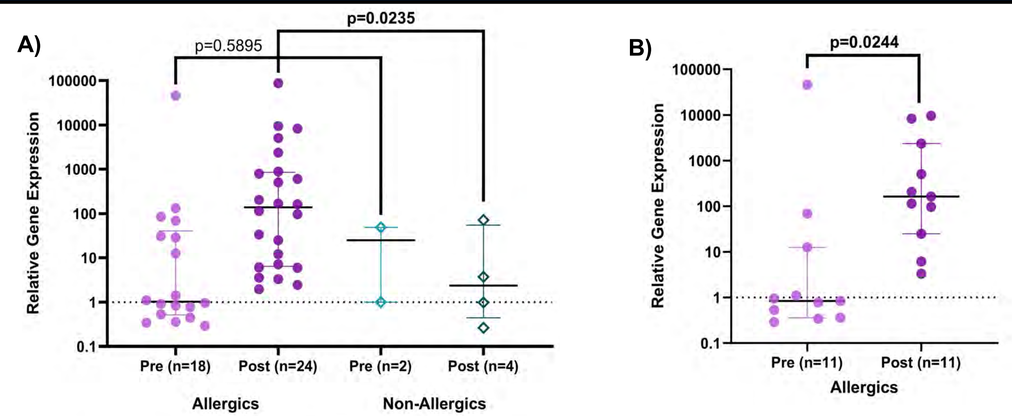


Figure 1. *IL-4* expression is significantly higher in allergic participants post-exposure. (A) Unpaired analyses using Mann Whitney tests showed allergic participants had significantly increased (p=0.0235) *IL-4* expression compared to non-allergic participants post-exposure. Pre-exposure *IL-4* expression was not significantly different (p=0.5895) between allergic and non-allergic participants. (B) Paired analyses using a Wilcoxon Matched Pairs Signed Rank test revealed that allergic participants had significantly increased (p=0.0244) *IL-4* expression post-exposure compared to pre-exposure. Relative gene expression displayed on log10 scale. Median and IQR shown.

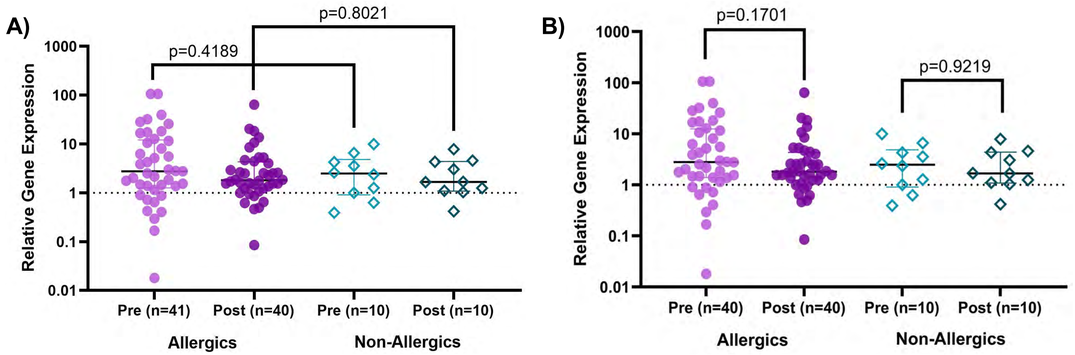


Figure 2. No significant differences in *IL-25* expression exist between allergic status and timepoints. (A) Unpaired analyses using Mann Whitney tests showed no significant differences between allergic and non-allergic participants at both pre-exposure (p=0.4189) and at post-exposure (p=0.8021). (B) Paired analyses using Wilcoxon Matched Pairs Signed Rank tests showed no significant differences in *IL-25* expression post-exposure compared to pre-exposure for both allergic (p=0.1701) and non-allergic participants (p=0.9219). Relative gene expression displayed on log10 scale. Median and IQR shown.

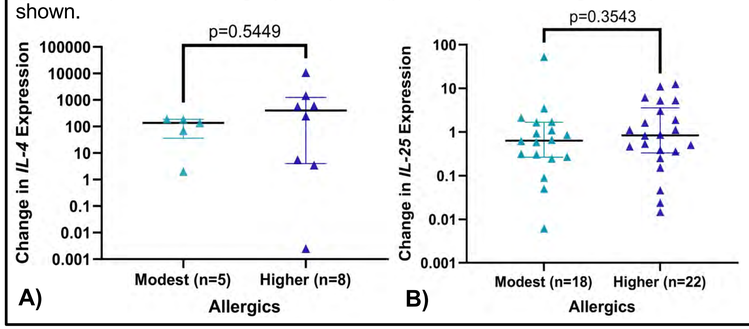


Figure 3. No dose-dependent response in expression of either gene target in allergic participants. Change in gene expression was not significantly different between modest HDM and higher HDM concentrations for *IL-4* (p=0.5449) (A) and *IL-25* (p=0.3543) (B). Change in gene expression displayed on log10 scale. Median and IQR shown. Statistical test: Mann Whitney.

Results

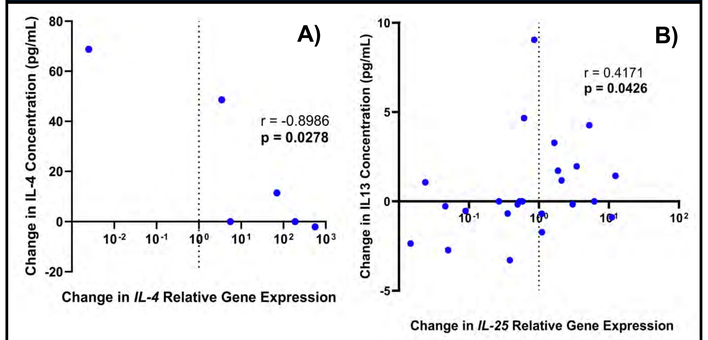


Figure 4. Gene expression correlated with certain serum cytokines. *IL-4* expression showed significant negative correlation (p=0.0278) with IL-4 cytokine serum concentration (A). *IL-25* expression showed significant positive correlation (p=0.0426) with IL-13 cytokine serum concentration (B).

IL-4 and *IL-25* gene expression did not show significant correlations with symptom scores (Total Nasal Symptom Score [TNSS], Peak Nasal Inspiratory Flow [PNIF]).

Conclusions

- *IL-4* nasal expression mirrors trends in literature where nasal expression of Th2 cytokines increased in participants with AR after allergen exposure [3,4]. This indicates IL-4 involvement in the nasal HDM-AR response.
- Lack of significant differences in *IL-25* nasal expression could be due to its role as an alarmin that is released earlier in AR response and was thus not detected at the measured timepoints [5,6].
- Lack of dose dependent responses and lack of correlation with symptom scores may be attributed to the complexity of pathways involved in the AR response [7,8].
- Negative correlation between *IL-4* expression and IL-4 serum cytokines could be due to tissue differences and timing of the AR response. Positive correlation between *IL-25* expression and IL-13 serum cytokines mirrors known trends given that IL-25 enhances Th2 cytokine production [9].

Acknowledgements

Sincerest thanks to the Ellis Lab and Kingston Allergy Research teams, Lubnaa Hossenbaccus and Cortney Haird for sharing their expertise, Dr. Anne K. Ellis for her support throughout this project, and the CSACI for their generous support through the Summer Studentship.

References

Cardiology

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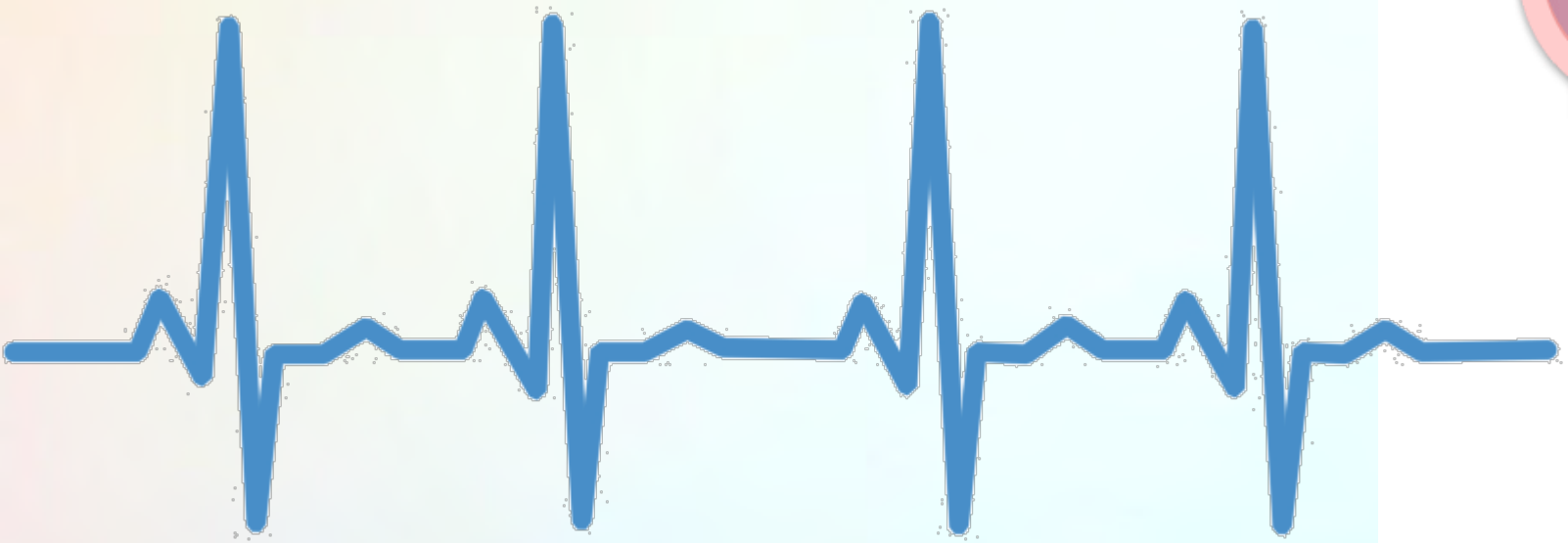
Research Lead

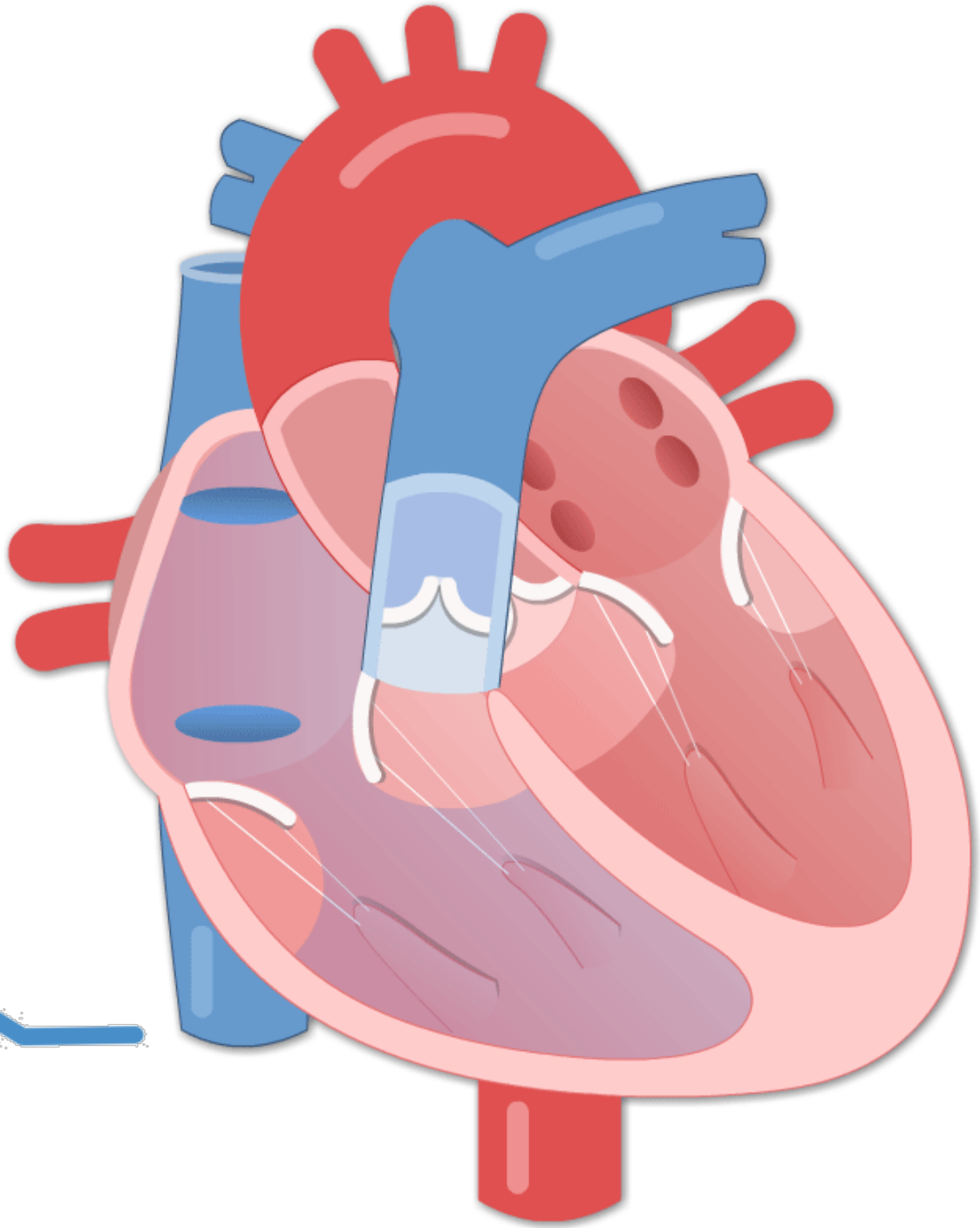
Summary

- *Outcomes in Heart Failure Patient Management by Primary Care Providers Compared With Cardiologists*
- *Streamlining Cardiac Amyloidosis Diagnosis and Treatment*
- *Coordinated Multidisciplinary Care for Cardiac Amyloidosis*
- *Linking COPD & HF Emergency Patients to PCPs*
- *Gender-based differences in POCUS use in the Emergency Department*
- *Develop and deliver an echocardiography assessment tool to test competence in independent echocardiography performance and interpretation*

Division of Cardiology

Resident Research Fair





Introduction

- Research ideas and projects available across various subspecialties in Cardiology
  - Cardiovascular Imaging (CINQ)
  - Interventional Cardiology
  - Interventional Electrophysiology
  - Heart Failure

Introduction

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

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

Background: Limited cardiologist capacity results in many heart failure (HF) patients being treated solely by primary care providers (PCPs). The outcomes of these patients have not been well studied.

Aim: Evaluate outcome differences in HF patients managed by cardiologists vs PCPs

Results:

- studies | 35,528 patients | Age 67–75
- Higher NYHA class & lower EF → more likely followed by cardiologist
- **Cardiologist care:**

  ↓ All-cause death (RR 0.79, CI 0.73–0.86)

  ↑ Beta-blocker & MRA use

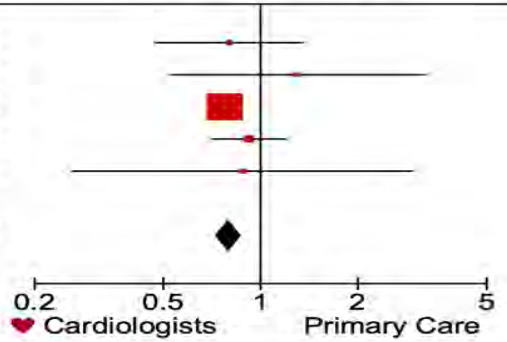
  No difference in: HF readmission & ACEi/ARB use

Conclusions: When continuous co-management by cardiologists is not feasible, systems should consider intermittent cardiology evaluations and pursuing medication optimization programs.

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]**

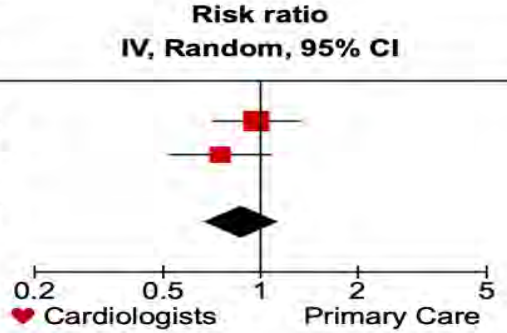
Heterogeneity: Tau² = 0.00; Chi² = 2.59, df = 4 (P = 0.63); I² = 0%
Test for overall effect: Z = 5.45 (P < 0.00001)
Test for subgroup differences: Not applicable



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]**

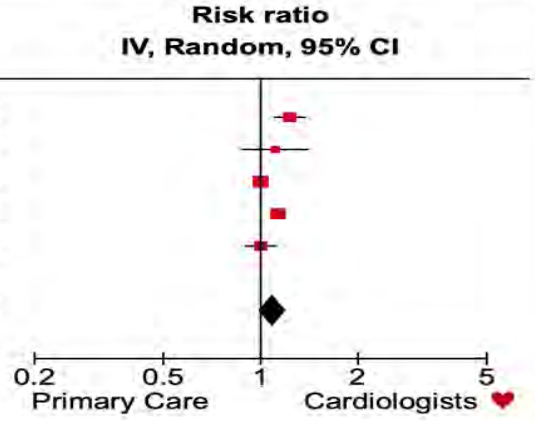
Heterogeneity: Tau² = 0.00; Chi² = 1.10, df = 1 (P = 0.30); I² = 9%
Test for overall effect: Z = 1.11 (P = 0.27)
Test for subgroup differences: Not applicable



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



Streamlining Cardiac Amyloidosis Diagnosis and Treatment

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

Background: Cardiac amyloidosis screening is done with transthoracic echocardiography (TTE), followed by pyrophosphate (PYP) scan or endomyocardial biopsy to confirm diagnosis.

Challenge: Significant delays in 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 diagnosis time and improve patient outcomes.

- **Key findings**: **190 patients** → 62 positive PYP scans

  PYP scans: ↑ from 31 (pre) → 145 (post) | Median scans/month: **2** → **5** *(p = .002)*

  Negative scan rate: 51.6% → 74.5% *(p = .011)*

  ECHOs per patient (5 yrs): 2 → 1 *(p = .038)*

  TTE → PYP time: 6.3 mo → 2.56 mo *(p < .001)*

- **Conclusions:**

  Intervention **improved diagnosis** via physician education & streamlined testing

  Increased negative PYP scans → ongoing need for education & quality assurance

Coordinated Multidisciplinary Care for Cardiac Amyloidosis

Background:

- Cardiac amyloidosis may present with early signs such as **carpal tunnel syndrome** and **spinal stenosis**
- **Early screening & treatment** can facilitate timely detection and improve disease progression management
- QI initiative: collaboration between cardiologists, neurologists, nurses, and other allied health professionals to ensure comprehensive and coordinated care for patients with cardiac amyloidosis

Aim: Improve **quality of life** and potentially alter **disease course** through early detection & optimal management of neurologic involvement

Project status: This project is pending initiation

HF Discharge Project

Rami Idris, Ansh Patel, and Dhruv Srikanth

Background:

- Most HF clinics cannot absorb their high volume of referrals.
- Effectiveness of clinic discharge protocols to offload stable patients is understudied.

Aim:

- Examine predictors and barriers of a **two-level discharge criterion** at our tertiary HF clinic
- Extract **patient- and provider-related characteristics** at initial and most recent visits
- Primary outcome: **successful discharge** | Study Period: Aug 1, 2023 – Mar 31, 2024

Results:

- 56/92 (60.9%) of the patients deemed suitable for discharge were discharged
- **Discharge failure** associated with
  - Atrial fibrillation (not-discharged 66.7% **vs** discharged 30.4%; $p<0.001$)
  - Ejection fraction <50% at the last visit (77.8% **vs** 51.8%; $p=0.012$)
  - More phone visits (12 **vs** 7, $p<0.001$)
  - Longer follow-up duration (30 **vs** 18 months; $p<0.001$)
  - Reduced kidney function at initial (101.0 **vs** 86.5 µmol/L; $p=0.036$) & final visit (106.5 **vs** 99.0 µmol/L; $p=0.048$)
- **Common reasons for not discharging:**
  - Waiting for an extra LV function assessment (48.6%)
  - Coordinating with other cardiac care teams (27.0%).

Conclusions:

- Several **patient- and provider-specific barriers** identified
- Further studies needed to optimize **HF clinic discharge protocols**

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 When Compared to Acute Care Settings: Insights from Linked Administrative Health Databases

Alex Van, Nilah Ahimsadasan, Hannah Willms

Background: HF is often diagnosed during acute decompensation, but earlier diagnosis in community settings may improve outcomes.

Aim:

- Population-based cohort of **597,025 Ontarians ≥40** (2010–2022)
- Compare **community vs acute care diagnosis**
- Assess characteristics, primary care models, and outcomes

Results:

36.9% diagnosed in acute care — more common in:

- **Age >85** (46.4% vs 28% in 40–61 yrs, *p<0.0001*)
- **Women** (38.2% vs 35.8% men, *p<0.0001*)
- **Lowest income quintile** (40.4% vs 33.3%, *p<0.0001*)
- **No PCP** (57.2% vs 35.4%, *p<0.0001*)

Acute care diagnosis → ↑ risk of:

- **1-year mortality**: RR 1.78 (95% CI 1.77–1.80)
- **HF hospitalizations**: RR 2.78 (95% CI 2.74–2.83)
- **ED visits: RR 2.58** (95% CI 2.51–2.65)

Conclusion: Earlier HF dx in the community could improve HF outcomes and reduce disparities.

IC/ES

HF & COPD Integrated Care Pathways (ICP)

PIs: Mike Fitzpatrick & Aws Almufleh
Longitudinal Research Course Students: Hasan Al-Hasani & Mehak Khangura

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:

- **Inpatient arm** → reduce readmissions & ED returns
- **Outpatient arm** → empower PCPs to manage HF & COPD
- **Data collection:** 2019-2024 HF admissions; March 2024-Feb 2025 ED visits

Impact

- Hired: Virtual Care HF NP, HF PA, COPD Nurse Navigator
- Launched: PCP lunch & learn sessions

Next Step:

- **Retrospective cohort study** to assess **effectiveness & cost-effectiveness** of ICP for HF in our region using population-based data

OUTPATIENT
HEART FAILURE **DIAGNOSIS** ALGORITHM

Kingston Health Sciences Centre
Centre des sciences de la santé de Kingston
Hôpital Hotel Dieu Hospital
KGH Hôpital Général de Kingston General Hospital

Heart Failure Suspected

Initial Clinic Visit

Please note:
Diagnosis and management can occur simultaneously in patients who are symptomatic with a high suspicion for HF. See management algorithm (click here to go to management algorithm).

Clinical Assessment

History

- Duration of symptoms.
- SOB/orthopnea/PND
- Fatigue/weakness
- Dependent edema
- Weight gain
- Abdominal distension
- Exercise intolerance
- Cough
- Cool extremities
- Chest pain
- Palpitations
- Syncope

Physical

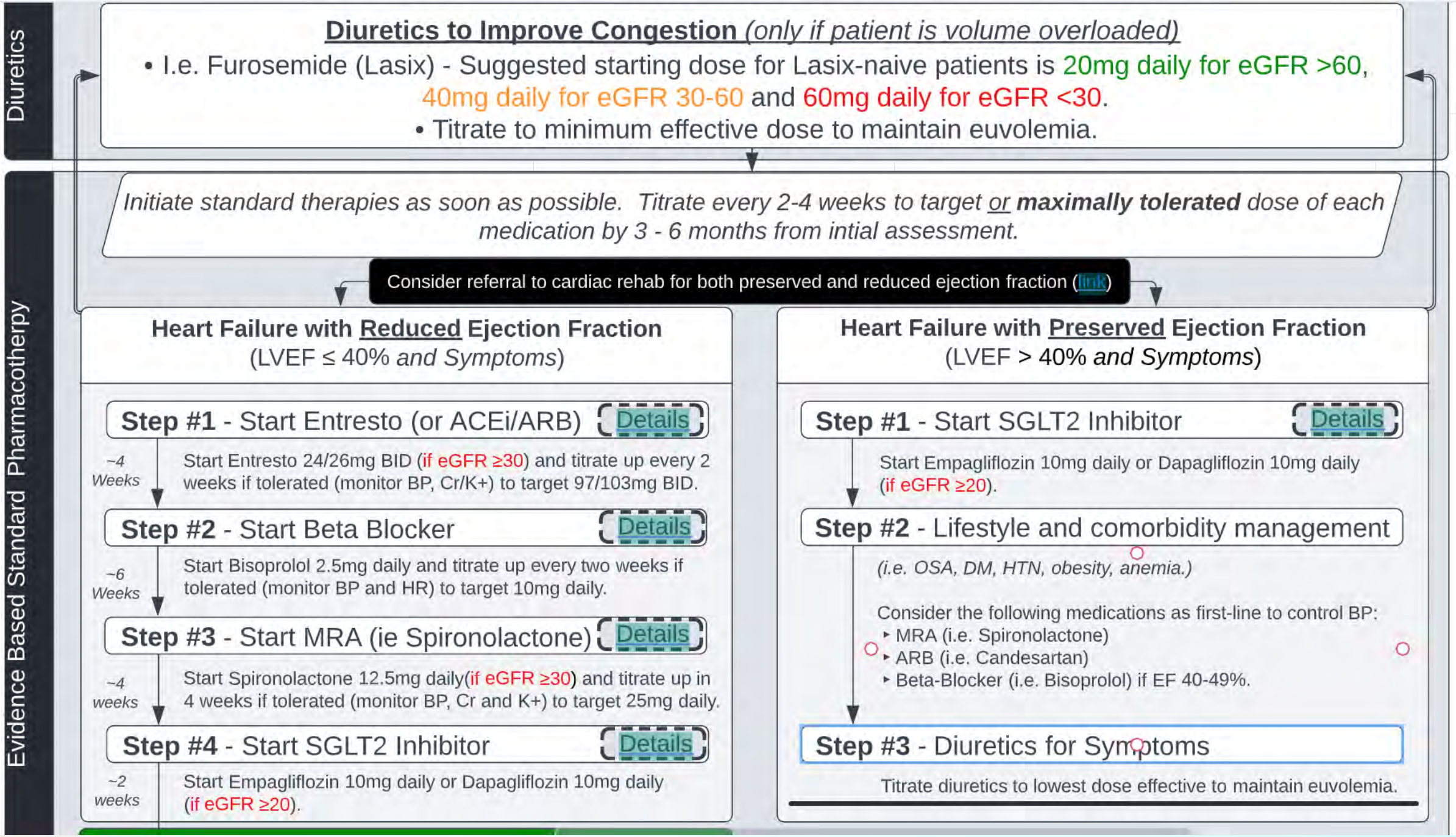
- Mental status
- Heart rate
- Heart rhythm
- Blood pressure
- SpO2
- Weight
- Heart sounds
- Murmurs?
- Elevated JVP?
- Crackles?
- Pitting edema?
- Abdominal distension?

Red Flags

- SOB at rest
- Hypoxia
- Signs of PE or MI
- Prolonged chest pain.
- Fainting
- Confusion

Emergency Treatment

Advise patient to attend the nearest Emergency Department for assessment. Please follow-up within one week of discharge to reassess suitability for pathway.


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.

Linking COPD & HF ED Patients to PCPs

Wendu Gebeyehu

Background:

- COPD & HF patients → high ED use, admissions, readmissions
- Impacts: **ED strain** + **reduced patient quality of life**

Aim:

- Retrospective chart review to identify **ED patients without a PCP**
- Link unattached patients to a PCP to:
  - Reduce ED returns & readmissions
  - Improve access for socially disadvantaged individuals

Project status: Ongoing data collection & patient attachment

Improving Clinic Attendance through Pre-Appointment Reminder Calls: A Quality Improvement Study

Rami Idris

Background: A high rate of missed clinic appointments increases the burden on waitlists and reduces overall clinic efficiency. While appointment reminders have traditionally been sent by mail and have demonstrated moderate effectiveness, there remains potential for improvement.

Aim: By providing two reminders calls —one during the week preceding the appointment and another on the day before—we aim to **improve attendance rates** and **enhance overall clinic efficiency**

Project status: Ongoing data collection and pending statistical analysis

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?

Barriers:

- 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, full-text review underway

ACCELERATE-HF

Robyn Jackson, Bryce Alexander

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

Aim:

- Compare a **resident-led QI initiative**
  - HF decision aid + POCUS use at admission **vs** routine care in admitted HF patients
- Outcomes: Readmission | 30-day mortality | GDMT use | Adverse events

Key findings:

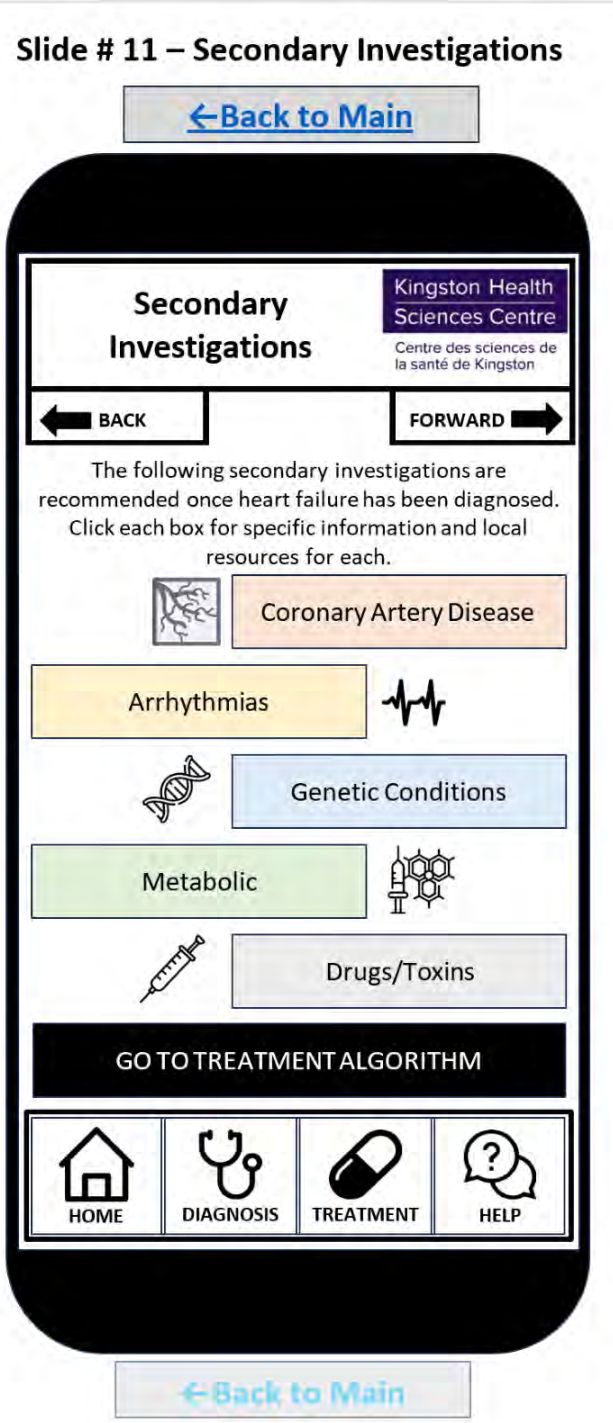
- Higher Renin-Angiotensin System (RAS) inhibitor use at discharge: 70.4% (QI) **vs** 51.4% (control), *p = .033*
- No significant difference in adverse events or 30-day outcomes
- More inpatient echos for patients with unknown EF in QI arm (71% **vs** 33%), not significant

Conclusions: This resident-led QI initiative proved feasible, and resulted in modest improvement in GDMT use and echocardiography utilization, but without effectively altering 30-day outcomes.

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

Hôpital Hotel Dieu Hospital

KGH Hôpital Général d Kingston Genera Hospital

Building a Point-of-Care Risk Communication Tool to Improve Perioperative Risk Estimation and Mitigation for Heart Failure Patients Undergoing Non-Cardiac Surgery

Drew McLean

Background: Even though patients with HF are at the greatest risk of surgical complications after surgery, there is no standardized way to provide accurate risk estimation and mitigation for these patients.

Aims: Develop and validate 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 into surgery.

Project plans:

- **Derivation & Internal Validation** → ICES
- **External Validation** → University of Alberta
- **Tool development** → Queen's U Center for Advanced Computing (CAC)
- **Tool refinement** → Patient Council (8-12 interested patient partners with lived experience of HF)

IC/ES

UNIVERSITY OF ALBERTA

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 SOCIETY OF ECHOCARDIOGRAPHY FUNDING OPPORTUNITY

CREATE GRANT

Canadian Cardiovascular Ultrasound Research Excellence Award for Technology and Education

Up to two awards of $50,000 over 2 years

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*
- *Chart Review: Use of ustekinumab in the management of pyoderma gangrenosum*
- *To investigate the demographics and time trends in melanoma incidence*
- *Overcoming retinoic acid catabolism as a treatment 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*

Dermatology Research Team Members

Dr. Yuka Asai

Dr. Lourdes Ramirez Hobak

Dr. Gaby Rodriguez Herrera

Dr. Erin Dahlke

Dr. Yuanshen Huang

Current Studies (As of AUG2025)

Case Reports & Chart Reviews	Summary
***Cryptococcus uniguttulatus* of the nails in a patient on secukinumab: A case report** **Team:** Dr. Yuka Asai (Dermatology), Dr. Lewis Tomalty (Clinical Microbiology), Arya Rahmani (MD Student), Chao Xue, Brie Fraser (Research coordinators)	This case report describes a rare fungus cryptococcus uniguttulatus in an individual on an IL-17 blocking biologic, which are known to suppress the fungal-fighting pathway. The case report will contribute to the existing level of knowledge and scientific evidence in the field of skin disorder.
Pseudoxanthoma elasticum with sarcoidosis: A case report **Team:** Dr. Yuka Asai (Dermatology), Reya Hanspal (MD Student), Brie Fraser, Chao Xue (Research Coordinators)	This case report describes a patient with pseudoxanthoma elasticum, with biopsy-proven cutaneous sarcoidosis. Few cases have been reported of this concomitant disease presentation.
Tralokinumab associated development of psoriasis	This case report describes a patient who developed psoriasis after being treated with an interleukin 13 blocking medication (Tralokinumab). The

Team: Dr. Yuka Asai (Dermatology), Joshua Lowe (Resident), Brie Fraser (Research Coordinators)	resulting publications will aid healthcare providers in diagnosing and managing immune mediating conditions of the skin.
Erythematous and boggy nodular eruption on right shin **Team:** Dr. Yuka Asai (Dermatology), Nicholas Lao (Resident), Brie Fraser, Chao Xue (Research Coordinators)	This case report describes a patient diagnosed with lichen planus follicularis tumidus, a rare subtype of lichen planus with less than 30 cases having been reported worldwide.
Combined use of dupilumab and ustekinumab for the treatment of atopic dermatitis, psoriasis, and ulcerative colitis **Team:** Dr. Yuka Asai (Dermatology), Jasmin Khela (Master's Student), Brie Fraser, Chao Xue (Research Coordinators)	This case report describes the use of combined interleukin 12 and 23 blocking medication with interleukin 4 and 13 blocking medication for the treatment of multiple conditions (eczema, psoriasis and ulcerative colitis) in the same patient.
"Islands of sparing": diagnosis and management of pityriasis rubra pilaris **Team:** Dr. Yuka Asai (Dermatology), Hibo Rijal (MD Student), Chao Xue, Brie Fraser (Research Coordinators)	This case report describes the treatment and management of a patient with a rare diagnosis of pityriasis rubra pilaris.
Use of ustekinumab in the management of pyoderma gangrenosum: A chart review **Team:** Dr. Yuka Asai (Dermatology), Anna Rzepka (MD Student), Chao Xue, Brie Fraser (Research Coordinators)	**Primary Objective:** to describe the clinical course of patients with pyoderma gangrenosum treated with ustekinumab at the Kingston Health Sciences Centre Dermatology clinic. **Secondary Objectives:** 1) To outline comorbidities found in patients presenting with pyoderma gangrenosum 2) To provide insights on treatment course and management of pyoderma gangrenosum 3) To outline practical challenges in management of refractory pyoderma gangrenosum, including access to medications
Hive and Go Seek: A Schnitzler Syndrome Case Report **Team:** Dr. Yuka Asai (Dermatology), Kristina Nazzicone (MD Student), Chao Xue, Brie Fraser (Research Coordinators)	This case report describes a patient with Schnitzler Syndrome, highlighting the diagnostic challenge and importance of biopsy in chronic urticaria with systemic features.
Pemphigus Vulgaris Post COVID Vaccine **Team:** Yuka Asai (Dermatology), Dr. Kaitlin Vanderbeck (Pathology), Bethany Wilken (MD Student), Chao Xue, Brie Fraser (Research Coordinators)	This case report describes a rare and unexpected clinical presentation of pemphigus vulgaris post COVID vaccination.

Association between perianal beta hemolytic streptococci infections and psoriasis in adults: A retrospective chart review (PAPSI) **Team:** Dr. Yuka Asai (Dermatology), Dr. Lewis Tomalty (Clinical Microbiology), Simryn Atwal (MD Student), Chao Xue, Brie Fraser (Research Coordinators)	**Primary Objective:** To characterize the clinical presentation of patients with concurrent perianal psoriasis and beta hemolytic streptococci infections at the Kingston Health Sciences Centre Dermatology clinic. **Secondary Objectives:** 1) To assess the effectiveness of various treatment approaches and management for concurrent perianal psoriasis and beta hemolytic streptococcal infections 2) To investigate potential risk factors or predisposing conditions associated with concurrent perianal psoriasis and beta hemolytic streptococcal infections 3) To identify and characterize the different strains of beta hemolytic streptococci present in affected patients

Investigator-Initiated Studies	Summary
Melanoma, In Situ melanoma and Pandemic Lockdown Adverse Consequences (MiSPLACE) **Team:** Dr. Yuka Asai (Dermatology), Dr. Timothy Hanna (Radiation Oncology), Dr. Ami Wang (Pathology), Jessica Ho (Resident), Nicholas Phillipow (Resident), Brie Fraser, Chao Xue (Research Coordinators)	**Rationale**: The COVID-19 pandemic has resulted in delayed cancer care due to postponement of non-urgent medical visits. Melanoma particularly may be subjected to diagnostic delay, leading to significant worse prognosis for patients. There have been dramatic reductions in skin biopsy during the pandemic, a key step in the diagnosis of melanoma. Our previous study shows that there was more than a five-fold drop in skin biopsies across the province during the first lockdown. Moreover, the numbers of biopsies have never returned to expected figures. **Objectives:** 1) To investigate the demographics and time trends in melanoma incidence (MIS, invasive melanoma, metastatic melanoma) at KHSC using pathology-confirmed diagnosis at baseline (January 2018- December 2019), during the pandemic period (March-December 2020), and post-pandemic period (December 2020 – December 2024). 2) To compare the proportion of MIS, invasive melanoma and metastatic melanoma cases at KHSC among all melanoma cases, during the baseline period compared to the pandemic period, and compare stage at presentation from baseline, to the pandemic period, and to the post-pandemic period. 3) To examine time trends in the histologic characteristics associated with the melanoma, including Breslow depth, ulceration, mitoses, as well as location.
Making resistance futile: Overcoming retinoic acid catabolism as a treatment for basal cell carcinoma **Team:** Dr. Yuka Asai, Dr Erin Dahlke (Dermatology), Dr. Martin Petkovich, Dr. Tracie Pennimpede, Dr. Donald Cameron (DBMS), Dr. Ami Wang, Dr. Kaitlin Vanderbeck, Dr. Kevin Ren	**Rationale**: Basal cell carcinoma (BCC) is the most commonly diagnosed cancer. Most BCC have mutations in the hedgehog (Hh) signaling pathway, and can be treated by suppressing Hh signaling using drugs (e.g vismodegib) which have side effects.This study will contribute to novel therapy on BCC. The experiments in this proposal could allow us to develop a rationale for retinoid therapy in BCC, and may provide interest in expansion and refinement of their use. Additionally, The CYP26 enzyme inhibitors used in the outlined project are protected by composition-of-matter patents, and if the studies are successful, we expect to continue to build on this intellectual property.

(Pathology), Jacob Rullo (Ophthalmology), Brie Fraser, Chao Xue (Research coordinators)	This impact may not be restricted to BCC or skin cancer alone: there is evidence that medulloblastoma and a variety of other human cancers, including brain, gastrointestinal, lung, breast and prostate cancers, also demonstrate inappropriate activation of Hh signaling. It is possible that the outcome of our skin cancer studies may also be applicable to treatment of these other cancers.
Effects of Establishment of a dermatology division on hospital admissions, emergency visits and outpatient appointments **Team:** Dr. Yuka Asai (Dermatology), Chao Xue, Brie Fraser (Research Coordinators)	**Rationale**: Hospital records of patients seen by dermatologists at Queen's University Division of Dermatology will be examined. All individuals seen by the dermatologists since the practice's inception will be included, with the exception of those who have indicated they do not wish to participate in research in their hospital file. Admission rates to hospital, admission duration, mortality will be investigated in the 5 years prior to the initial dermatology visit as well as the years after. Additionally, number of emergency visits will be investigated in the years preceding and following the initial dermatology visit, as well as hospital outpatient appointments. Analysis will take into account if individuals continue to be followed by dermatology. Demographic data and data relevant to the dermatology diagnosis and treatment will be collected from the initial dermatology visit and any following visits. Type of referring practitioner, wait times between referral and clinic visit, and geographic location (urban/rural, within-LHIN vs outside of LHIN) will be documented. Diagnoses, procedures and visit dates from emergency and urgent care visits and hospital visits will be collected. Additional data from other outpatient visits to KHSC will also be collected to determine health care utilization before and after contact with the dermatology service. The purpose of the project is to compare the pattern of use of emergent or inpatient hospital services in individuals who have been seen at the division of dermatology at Queen's University before and after their visit. Knowing the effectiveness and demographics of dermatology patients in the Kingston area will aid in a better allocation of resources and care to populations at higher risk to conditions. There are approximately 8000 participants enrolled to date.
Development and Validation of an Atopic Dermatitis Knowledge Assessment Tool (AD-KAT) **Team:** Dr. Yuka Asai, Dr. Sonja Molin, Dr. Thomas Herzinger, Dr. Lourdes Ramirez Hobak (Dermatology), Dr. Anne K Ellis (Allergy), Dr. Eleftherios Soleas (Lifelong Learning & Innovation), Jasmin Khela (Master's Student), Brie Fraser, Chao Xue (Research Coordinators)	**Rationale:** Patient education in AD improves the information available to patients, so that they can better manage their disease. We have designed a two-page, low-cost, photocopy-friendly graphic called "Eczema is a Wildfire" that includes key messages of patient education for AD. This patient education tool/intervention has undergone pilot testing to see whether it has improved patients' clinical scores and self-efficacy. We now want to determine whether the patient education tool can improve the knowledge of AD patients. **Primary Objectives:** **Objective 1:** To develop and validate an objective knowledge assessment tool for AD patients in the dermatology specialist clinic at Kingston Health Sciences

	Centre (KHSC), known as the atopic dermatitis knowledge assessment tool (AD-KAT). **Aim 1:** To determine whether the AD-KAT can measure AD knowledge, and successfully distinguish between the knowledge of patients with AD and those without. **Objective 2:** Use the AD-KAT as an outcome measure for the "Eczema is a Wildfire" patient education intervention. **Aim 2:** To evaluate the effectiveness of the "Eczema is a Wildfire" patient education intervention for improving AD patients' knowledge. **Objective 3:** To correlate AD patients' knowledge scores with changes in clinical scores and self-efficacy. **Aim 3:** To determine whether AD patients' objective knowledge is associated with improvements in self-efficacy and clinical scores. **Secondary Objectives:** **Objective 1:** To assess the effectiveness of the AD patient education intervention, "Eczema is a Wildfire", on AD patients' clinical scores (i.e., EASI, DLQI). **Aim 1:** To determine whether the "Eczema is a Wildfire" patient education intervention achieves similar improvements in AD patients' clinical scores, as previously observed during the pilot study. **Objective 2:** To assess the effectiveness of the AD patient education intervention, "Eczema is a Wildfire", on AD patients' self-efficacy. **Aim 2:** To determine whether the "Eczema is a Wildfire" patient education intervention achieves similar improvements in AD patients' self-efficacy, as previously observed during the pilot study. **Objective 3:** To seek feedback from AD patients on the recent changes (i.e., page 2 addition) that have been made to the "Eczema is a Wildfire" patient education tool. **Aim 3:** To evaluate the utility and quality of page 2 of the "Eczema is a Wildfire" patient education tool for AD patients.
Pictorial Intervention for Patient Education in the Real World: Qualitative Study of Atopic Dermatitis and Expert Care Providers (PIPER-QSAD ECP) **Team:** Dr. Yuka Asai (Dermatology), Dr. Nancy Dalgarno, Dr. Heather Braund, Celine Bruce-Lepage, Oluwatoyosi Kuforiji (Educational Scholarship), Brie Fraser, Chao Xue (Research Coordinators)	**Rationale:** There is a growing need for the development and utilization of patient education tools, such as pictorials, in doctors' offices and clinics to address the educational gaps faced by patients with AD and other chronic illnesses. AD is a complex condition that requires patients to have a deep understanding of triggers, treatment options, and self-management strategies. **Objective:** To evaluate the "Eczema as a wildfire" patient education tool for clinical use by specialists who provide care to people with AD.

Dermatology Clinical Trials	Summary
PURE: A registry of Patients with moderate to severe chronic plaqUe psoRiasis in Canada and Latin AmErica (LACan) **Team:** Dr. Yuka Asai, Dr. Lourdes Ramirez Hobak (Dermatology), Chao Xue (Research Coordinator)	**Rationale**: Psoriasis is a chronic, immunologically-mediated dermatosis, estimated to affect 2-3% of Canadians. Chronic plaque psoriasis (CPP) is the most common type, making up 90% of clinical cases. Plaques are red, thick and silver grey scaly and can be present on different parts of the body. In the past 3 years, new systemic and biologic therapies were approved around the world for CPP treatment. Secukinumab is one of these biologic agents. Although secukinumab has been approved to treat moderate to severe CPP patients, its safety and efficacy has been only evaluated in two international phase III clinical trials, and is yet to be described in a real-world clinical setting. The purpose of this observational registry study will be to describe the safety, long term effectiveness, and impact on quality of life of secukinumab and other indicated therapies administered to patients with moderate to severe CPP in a real-life setting. This will be a multi-national, prospective, observational, two-cohort study of patients with moderate to severe psoriasis, one treated with secukinumab and the other with other indicated therapies. The therapies used for treatment are decided independently by the patients' treating physicians and prior to the study enrolment. Each site will recruit approximately the same number of patients in each treatment arm. 2,500 patients will be followed for a total of 5 years from the Baseline assessment. The study involves assessments and questionnaires. **Objective:** To describe the long term safety profile of patients with moderate to severe chronic plaque psoriasis treated with secukinumab and other indicated therapies (systemic, phototherapy, or biologic therapy alone or in combination with a topical therapy).
A double-blind, randomized, placebo-controlled multicenter study to evaluate the efficacy and safety of deuruxolitinib in adolescent patients with severe alopecia areata with an open-label extension period **Team:** Dr. Yuka Asai, Dr. Lourdes Ramirez Hobak, Dr. Gaby Rodriguez Herrera (Dermatology), Chao Xue (Research Coordinator)	**Objectives:** The overall objectives of the study are to assess the efficacy and safety following administration of deuruxolitinib in adolescent subjects (12 to <18 years of age) with severe alopecia areata.

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Dr. Yuka Asai

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Dr. Lourdes Ramirez Hobak

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Dr. Erin Dahlke

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Dr. Yuanshen Huang

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Do you Have Questions?

Reach us at 

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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]

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[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

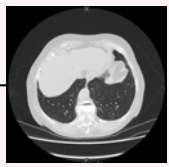
Cough mainly during day, occasional shortness of breath

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.

November 2021
Mold discovered in patient's foam pillows

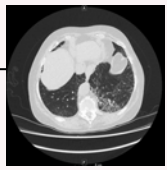
- Mold in foam pillows has been associated with ILD (2).
- Patient switches pillows from foam to polyester
- Incased pillows and mattress with anti-allergic waterproof casings.

Expect resolution of symptoms almost immediately (2).

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

Differential diagnosis: Drug induced interstitial lung disease

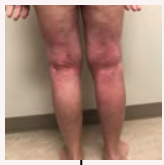
January 2022
Differential diagnosis of drug induced interstitial lung disease



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

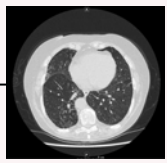
Worsening dyspnea and cough - productive of clear septum (50 mL/day).

March 2022
Patient discontinues dupilumab



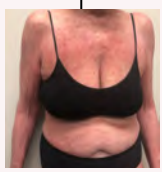
- **BSA - 97%**
- **EASI - 61**

April 2022
Patient erythrodermic

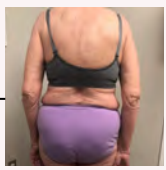


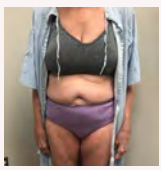
Significant improvements in the ground glass appearance and reticulations in the left lower lobe yet, the right middle lobe had progressive fibrosis.

Decline in pulmonary function



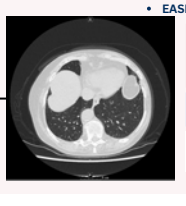
June 2022
Patient started tralokinumab





- **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

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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

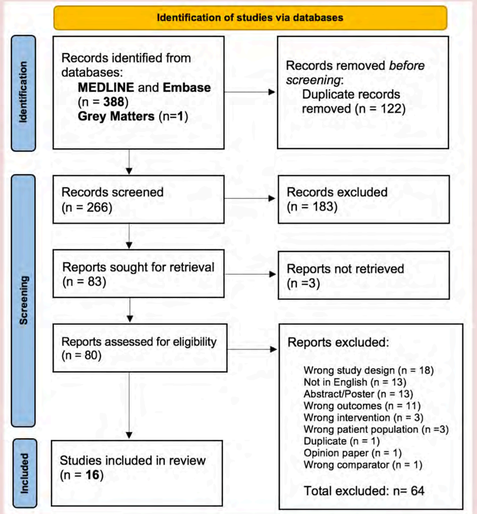


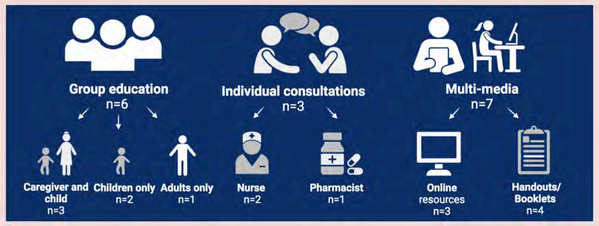
Figure 1. PRISMA flow chart of the screening process. **16** studies were included in the review.

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.***

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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*

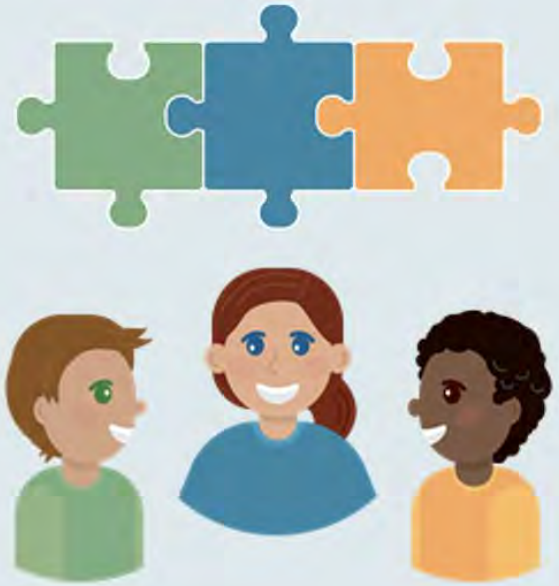
Division of Endocrinology Research Activities

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
  - Systematic Reviews
  - Quality improvement projects related to endocrine disease management (typically inpatient or other specialized diabetes populations)
  - Retrospective Cohort Studies

Current Research Opportunities

Topic	Rationale	Primary Contact
Thyroid Cancer	Access our thyroid cancer database (RedCAP) to help design various projects relating to thyroid cancer care	Josh Lakoff: JML7@queensu.ca
Thyroid Nodules	A Quality Improvement Initiative to Reduce AUS in Thyroid Biopsies	Josh Lakoff: JML7@queensu.ca
Diabetes	Interspecialty Collaboration: Bringing Care to the Patient in the Dialysis Unit Focussed project to close diabetes care gap in hemodialysis patients by bringing multidisciplinary diabetes clinic to the dialysis unit.	Bikram Sidhu: bss5@queensu.ca
QI project	Characterization of diabetes eConsult question type in Southeastern Ontario and outcome in our region	Bikram Sidhu: bss5@queensu.ca
Type 1 DM	Various projects using Type 1 Diabetes database	Bikram Sidhu: bss5@queensu.ca



Collaborative Learning in Postgraduate Medical Education

Karl Vantomme, MD FRCPC
PGY-5 Endocrinology and Metabolism, Queen's University

ICRE 2025

SAT-4299

ENDO TOPICAL CATEGORY
THYROID BIOLOGY AND DISEASE

Predictors and Prognostic Significance of Post-operative Anti-thyroglobulin Antibody Positivity in Patients With Differentiated Thyroid Cancer: A Retrospective Cohort Study

Matthew Leeder, MD, BSc[1], Aishwarya Rajesh Krishnan[2], Andrew Day[1], Sara F.M. Awad, MBBS[1], Josh Matthew Lakoff, MD BSc MHPE[1]
[1]Queen's University, Kingston, ON, Canada, [2]University of Toronto, Toronto, ON, Canada
*We declare no potential conflicts of interest related to this research

Introduction

Serum thyroglobulin (Tg) is a key prognostic marker in differentiated thyroid cancer (DTC). Twenty-five percent of DTC patients have positive serum anti-thyroglobulin antibodies (TgAb), which directly interfere with Tg measurement, thus impacting prognostication. Growing evidence suggests that TgAb-positivity is associated with an increased risk of persistent/recurrent disease (PRD). Little is known about what risk factors are associated with TgAb-positivity in DTC patients.

Table 1: Baseline Patient Characteristics

		n=329
Age at diagnosis		[328] 51.3±15.5 (19-85)
Sex	Male	101 (31.0%)
	Female	226 (68.7%)
	Missing	1 (0.3%)
Family History of Thyroid Cancer		
	Yes	16 (4.9%)
	No	310 (94.2%)
	Unknown	3 (0.9%)
History of Autoimmune disease		
	Yes	28 (8.5%)
	No	297 (90.3%)
	Unknown	3 (0.9%)
Radiation exposure		
	Yes	16 (4.9%)
	No	289 (87.8%)
	Unknown	1 (0.3%)
Aggressive features		
	Yes	136 (41.3%)
	No	190 (57.8%)
	Unknown	3 (0.9%)
Evidence of Lymphocytic Thyroiditis		
	Yes	78 (23.7%)
	No	241 (73.3%)
	Unknown	8 (2.4%)
Primary histology type		
	Papillary	298 (90.6%)
	Follicular	31 (9.4%)
Stage		
	1	246 (74.8%)
	2	44 (13.4%)
	3	11 (3.3%)
	4	18 (5.5%)

Methods

We retrospectively studied 329 DTC patients aged ≥18 who underwent total thyroidectomy and had at least one documented TgAb on follow-up seen at Kingston Health Sciences Centre between January 1, 2000, and September 1, 2023. Using a proportional hazards model, we examined the association between nine potential risk factors and TgAb-positivity. Using the Cox model for time-dependent covariates, we examined the association between "current" TgAb status and risk of PRD. We investigated TgAb status alone and in combination with Tg status.

Results

Of 329 DTC patients aged ≥ 18 who underwent total thyroidectomy with documented TgAb on follow-up, 38.9% had at least one positive TgAb. Lymphocytic thyroiditis (LT) was the strongest predictor of TgAb-positivity (HR=2.28, 95% CI 1.55-3.33, p<0.0001). Other associated risk factors were stage > 1 (p=0.009), family history of thyroid cancer (HR = 2.27, 95% CI, 1.02-5.05, p=0.044), and age at diagnosis (HR = 0.98, 95% CI 0.97-1.00, p = 0.028). TgAb-positivity was associated with increased PRD risk (HR=2.8, 95% CI, 1.5-5.3, p=0.0015). Combined positive TgAb and detectable Tg were associated with increased PRD risk compared to combined TgAb-negativity and undetectable Tg (HR = 29.6, 95% CI, 6.3-138.1). LT was associated with decreased PRD risk (HR = 0.39, 95% CI, 0.17 to 0.92, p=0.031).

Table 2: Risk Factors for Positive TgAb

		Hazard Ratio	Lower CL	Upper CL	P-value
Age at diagnosis (per year)		0.98	0.97	1.00	0.028
Male vs. female		1.19	0.79	1.77	0.403
Family history		2.27	1.02	5.05	0.044
Personal history of autoimmune disease		1.26	0.66	2.39	0.491
Radiation Exposure		1.48	0.74	2.99	0.270
Papillary vs. Follicular Histology		0.77	0.37	1.60	0.485
Aggressive Features		1.00	0.67	1.48	0.994
Evidence of Lymphocytic Thyroiditis		2.28	1.55	3.33	<.0001
Stage			Stage 1 vs. stage >1 p=0.009		
	2 vs 1	2.08	1.18	3.67	0.0112
	3 vs 1	1.48	0.47	4.72	0.5046
	4 vs 1	2.14	0.92	4.98	0.0766

Table 3: Association of Combined Tg- and TgAb-Positivity with PRD

Tg	TgAb	Follow-ups Prior to Event	Pys Follow-up Prior to Event	Number of Events	Events per 1000 pys	Relative Risk (95% CI)	Hazard Ratio (95% CI)
(+)	(+)	136	311	9	28.9	46.3 (10.0-214.4)	29.6 (6.3-138.1)
(+)	(-)	526	2626	24	9.1	14.6 (3.5-61.9)	11.8 (2.8-50.2)
(-)	(+)	232	679	6	8.8	14.2 (2.9-70.1)	11.9 (2.4-58.8)
(-)	(-)	633	3203	2	0.6	Referent	Referent
Overall		1527	6819	41			

Pys = patient years
(+) = Tg detectable or TgAb above ULN; (-) = Tg undetectable or TgAb below ULN

Conclusions

Longer follow-up periods and high-sensitivity assays may account for an increased prevalence of TgAb-positivity among DTC patients. LT was the most significant predictor of TgAb-positivity. Higher cancer stage, family history of thyroid cancer, and younger age at diagnosis were also associated with TgAb-positivity. TgAb-positivity is associated with increased PRD risk. This risk may be higher in patients with combined positive TgAb and detectable Tg. While LT is associated with TgAb-positivity, these patients have a lower risk of PRD.

Acknowledgements

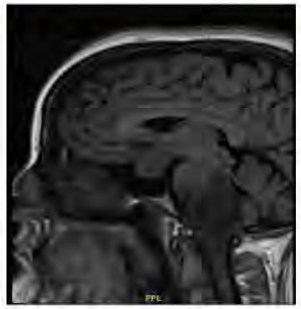
I would like to express my sincerest gratitude to Dr. Joshua Lakoff and Dr. Sara Awad for their guidance and support in completing this project. Their knowledge and experience were instrumental in enhancing the quality of this study. Additionally, I would like to thank the Clinical Teachers' Association of Queen's University for assisting in funding our project.

Case report: A rare case of Ollier's Disease with Coexistence Brainstem Glioma and Pituitary Macroadenoma

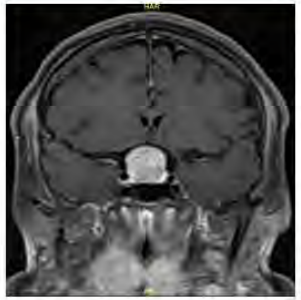
Raghad Mallesho[1] , MD , Joshua Lakoff [2], MD
[1]Internal Medicine Department, Queen's University
[2]Division of Endocrinology and Metabolism, Queen's University.

Background

Ollier's disease is a rare, non-inherited bone dysplasia characterized by multiple enchondromas [1,2]. It occurs in approximately 1 in 100,000 individuals [2]. Unlike Maffucci syndrome, Ollier's disease lacks associated hemangiomas and vascular anomalies [3]. The pathogenesis is linked to somatic heterozygous mutations in the IDH1 or IDH2 genes [4]. Patients with Ollier's disease are at increased risk for malignancies, particularly chondrosarcomas, which develop in about 30% of cases [3, 5]. Associations with central nervous system tumors are exceedingly rare. We present a unique case of Ollier's disease associated with both a brainstem glioma and a pituitary macroadenoma, highlighting the diagnostic complexities of the case.



Sagittal MRI shows an expansile T2 hyperintense lesion involving the brainstem and upper cervical spinal cord, with punctate enhancement. Findings are most consistent with a diffuse midline glioma.



Coronal T1-weighted post-contrast MRI shows a 2.1 x 1.8 x 2.4 cm sellar/suprasellar mass with heterogeneous signal intensity. The lesion demonstrates superior displacement and stretching of the optic chiasm without evidence of cavernous sinus invasion.

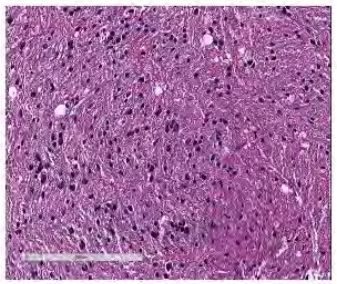
Case Presentation

A 32-year-old female with a history of Ollier's disease since childhood, depression, and migraines treated with topiramate presented to the emergency department with acute tonsillitis and altered level of consciousness. A non-contrast CT head scan revealed two incidental intracranial lesions: an expansile brainstem mass and a sellar/suprasellar lesion. Physical examination revealed central obesity and a dorsocervical fat pad, without other signs of Cushing's syndrome or neurological deficits. MRI and MR spectroscopy confirmed a diffuse midline glioma and a pituitary macroadenoma compressing the optic chiasm. Ophthalmologic evaluation revealed intact visual fields.

Initial endocrine workup showed elevated 24-hour urinary cortisol, normal ACTH, and inadequate suppression following a 1 mg overnight dexamethasone suppression test (DST). Repeat testing post-acute illness showed normal 24-hour urine cortisol, midnight salivary cortisol, and ACTH levels, though the DST remained unsuppressed. However, in the literature topiramate has been reported as a potential cause of false-positive DST results [6].

Biopsy of the brainstem lesion confirmed a WHO Grade 2 astrocytoma with an IDH1 R132C mutation. The patient underwent concurrent chemoradiation with temozolomide and 54 Gy of radiation. She subsequently developed polyuria and polydipsia. Empirical DDAVP therapy yielded no improvement, and copeptin was within normal limits. A water deprivation test confirmed primary polydipsia. Follow-up MRI showed a mild interval reduction in the pituitary lesion and stable glioma.

IHC staining for Ki-67 demonstrates scattered nuclear positivity within tumor cells, indicating a low-to-moderate proliferative index.



H&E staining shows a moderately cellular, diffusely infiltrative astrocytic glioma. Features are consistent with a diffuse glioma, WHO grade 2.

Adrenal Function Summary

Test	Result	Value(s)	Interpretation
Day 1	24h Urine Cortisol	161 (↑)	Elevated
08:00	ACTH	3 (Low)	Suppressed ACTH
	1 mg DST (AM Cortisol)	145 (↑)	Failed suppression
	DHEAS	1.7 (↓)	Suppressed androgen
Day 2	1 mg DST (AM Cortisol)	118 (↑)	Persistent cortisol excess
08:00	ACTH	3.8 (Low)	Consistently low ACTH
	24h Urine Cortisol	50	Within normal range
Any	DHEAS	1.9 (↓)	Low DHEAS
08:00	AM Cortisol	310 (↑)	Elevated basal cortisol
Day 3, 23:00	Low-dose DST (AM Cortisol)	118 (↑)	Failed suppression
Home	Midnight Salivary Cortisol	1.4 (<2.8)	Normal circadian rhythm
Any	Copeptin	9.8	Normal

Water Deprivation Test

	0 am	4 am	8 am	1st am	12 am
Na+	141	140	141	139	140
S Osm	292	292	302	294	302
U Osm	576	604	573	549	526

Conclusions

To our knowledge, there are no previously documented cases of this specific combination occurring in Ollier's disease but few cases were reported with Maffucci syndrome. The diagnostic process was further complicated by confounding hormonal test results, likely influenced by certain medication use. Additionally midline gliomas have been reported in Ollier's disease, particularly in the presence of IDH1 mutations. This case underscores the importance of considering atypical tumor associations in Ollier's disease.

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

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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[6]
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	130 (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[19]	CCT	99 (14/85)	VAS, NRS, VRS

Results

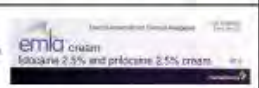
Patient Related Factors

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

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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)

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Case Presentation

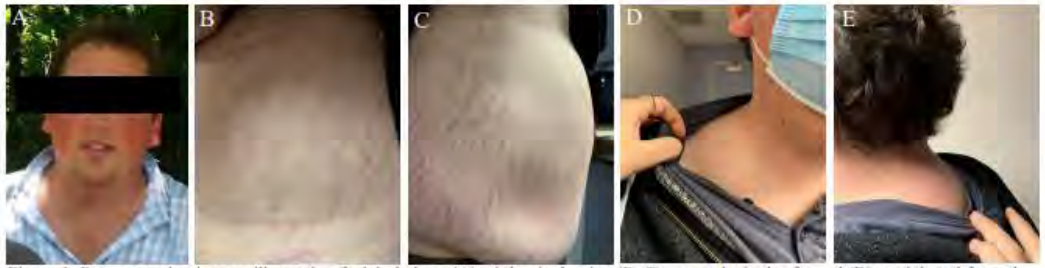

Figure 1. Representative images illustrating facial plethora (A); abdominal striae (B, C); supraclavicular fat pad (D); and dorsal fat pad (E)

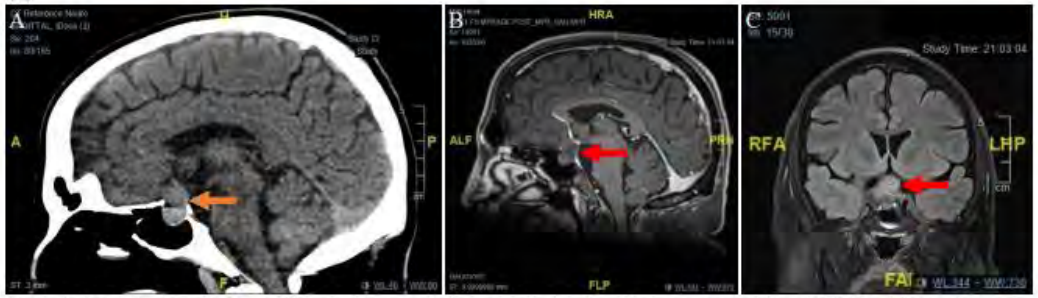

Figure 2. Hyperattenuating 2.0 cm x 2.8 cm x 1.5 cm mass (orange arrow) at the sella turcica on unenhanced CT (A); 1.9 cm x 3.2 cm x 2.4 cm heterogeneous mass (red arrow) on T1 (B); and T2-weighted imaging with flattening of the optic chiasm, remodeling/dehiscence of the floor of the sella and extending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

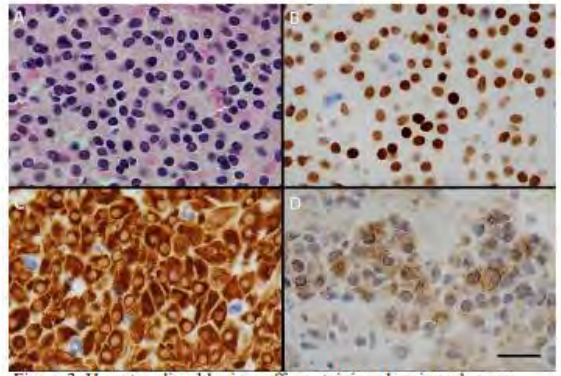

Figure 3. Hematoxylin phloxine saffron staining showing adenoma with solid growth pattern (Figure 3A); immunohistochemical staining showing T-pit reactivity of tumor nuclei (Figure 3B); diffuse cytoplasmic staining for cytokeratin CAM5.2 (Figure 3C); and regional moderately intense granular cytoplasmic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

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.

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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

PMID: 33046401 DOI: 10.1016/j.jcjd.2020.08.100

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

Shirley Shuster MD[1,2], Zeyana Al-Hadhrami MD[1,2], Sarah Moore MN NP[2], Sara Awad MBBS FRCPC[1,2], M. Khaled Shamseddin MD MSc FRCPC[1,2]
[1]Queen's University, Kingston, ON, Canada, [2]Kingston Health Sciences Centre, Kingston, ON, Canada

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)

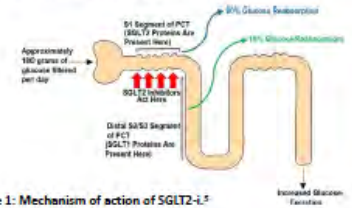

Figure 1: Mechanism of action of SGLT2-i.[5]

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	9	10	20	8	60	14	1	25	10
Mean Age (yr)	56.8±13.9	66 (56-73)	53.8±7.1	45.9±7.1	63 (31-72):59 (21-75)	56.5±9.9	58	-	KT: 61.6±12.6, PKT: 49.4±8.9
Gender (M:F)	6:2	8:2	23:1	4:4	17:5, 37:5	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: 15:15	-	-	-	KT: 6, PKT: 4
Type of Diabetes	DM II:2	DM II: 6	DM II: 20	DM II: 4	DM II: 0	DM II: 0	DM II: 1	DM I: 3, DM II: 19	DM II: 2
	NODAT: 6	NODAT: 4	NODAT: 5	NODAT: 4	NODAT: 60	NODAT: 14	-	NODAT: 7	NODAT: 8
eGFR	75.75±13.38	37 (47-73) (> 45)	86±20 (> 60)	NR	66 (57-68):59 (53-72)	54±21.8 (> 30)	93	71±20	KT: 78±18.2, PKT: 60±14
A1c (%)	9.34±1.36	7.3 (6.4-7.8)	8.5±1.5	8.1±0.2	8.9 (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	↓↓↓	↓	↓↓↓	↓↓	↓↓↓	↓↓ Decrease 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 4wks)	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 -Dizziness: 2 -Facial swelling: 1 -Hematuria: 1	-UTI: 3	NR	-Cystitis: 2	-Low BS: 1
		-AKI stage 1: 1 -Small lower limb ulcer: 1				-Balanitis: 1 -Paro-mania: 1 -HypoNa: 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

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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.

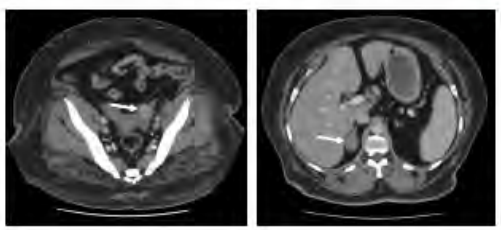

Figure 1: 2.1-cm left ovarian tumour (left, see arrow); 3.2-cm right adrenal tumour (right, see arrow).

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.

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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

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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

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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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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	64.98 ± 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.

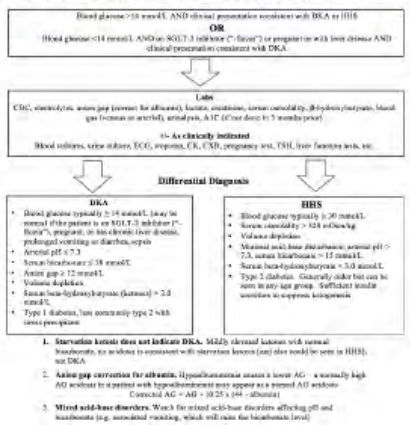
Our Strategy

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.

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

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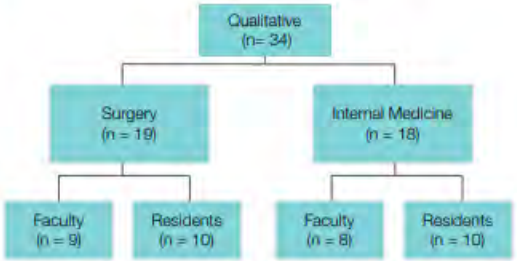
Introduction

- 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

Gastroenterology

Dr. Lawrence Hookey
Division Chair

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

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

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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

Summary

- *Understanding cardiovascular disease in cancer survivors, and also on patient-reported quality of life outcomes in patients with chronic disease*
- *Using large biological and clinical datasets to understand biological differences in critical illness states with a view to optimizing treatment strategies.*
- *Association of Omega-3 Status With Long-Term Risk of Hospitalization for Sepsis*
- *POCUS Characteristics to Differentiate Transudative and Exudative Pleural Effusions*
- *A deep learning model for the classification of atrial fibrillation in critically ill patients*

Maslove is Rep

1. Dr. Wijeratne's research focuses on understanding cardiovascular disease in cancer survivors, and also on patient-reported quality of life outcomes in patients with chronic disease. Methods include systematic reviews, narrative reviews, meta-analysis, and others.
(thiwankawijeratne@yahoo.ca)
2. Dr. Maslove's research focuses on two main areas:
i. Precision critical care — using large biological and clinical datasets to understand biological differences in critical illness states with a view to optimizing treatment strategies. Collaboration with School of Computing.
ii. Medical publishing and peer review
(david.maslove@queensu.ca)
3. Dr. Montague and Dr. Ames work in PoCUS and have supervised trainees doing projects in this area. (jba5@queensu.ca, sjm23@queensu.ca)
4. Dr. Marosi is looking at optimizing wait times for GIM clinics using data collected over the past year (kfm@queensu.ca)
4. Residents interested in Quality Improvement should contact Dr. Wilkinson (a.h.wilkinson@queensu.ca)
5. Residents interested in Medical Education should contact Dr. Leung (mjl18@queensu.ca)

CHEST

Is Mortality a Useful Primary End Point for Critical Care Trials?

Richard A. Veldhoen, MD; Daniel Howes, MD; and David M. Maslove, MD

Mortality has long been used as a primary end point for randomized controlled trials in critical care. Recently, a plurality of trials targeting mortality end points as their primary outcome has failed to detect a difference between study arms. While there are a number of reasons for the preponderance of such neutral trials, the use of mortality as an outcome is one important consideration. We explore some of the reasons why such trials may be biased toward a neutral result, as well as reasons to consider alternative end points that are better coupled to the expected therapeutic effect. We also discuss to what extent mortality as a binary outcome is patient-important in the ICU.

CHEST 2020; 158(1):206-211

KEY WORDS: critical care; mortality outcomes; neutral trials; patient-important outcomes; randomized controlled trials

Each year, the pantheon of critical care research expands with the publication of new, randomized controlled trials (RCTs) that use a mortality end point as their primary outcome. Several contemporary examples include TARGET,[1] SCARLET,[2] SUP-ICU,[3] EUPHRATES,[4] ANDROMEDA-SHOCK,[5] IDEAL-ICU,[6] HIGH,[7] REDUCE,[8] ROSE,[9] SPICE III,[10] ADRENAL,[11] and EOLIA[12] (to name but a few). This cohort spanned a range of issues from ventilation in ARDS, to sepsis, to GI stress ulcer prophylaxis. Their combined enrollment exceeded 21,000 patients, and the longest study spanned 6 years of recruitment. These trials represent significant achievements in clinical research and collaboration. They also represent the expenditure of considerable amounts of research funding, the commitment of time and effort on the part of investigators, and the generosity of thousands of patients and families who were willing to participate. Unfortunately, they are also united by the fact that they are what we call *neutral trials*, meaning that in each of these cases, there was no statistically significant difference detected in the primary outcome between study arms.[13,14] This offers a stark reminder of the lineage of neutral critical care trials[15] with over 100 observed in sepsis alone.[16]

There are many proffered reasons for the preponderance of neutral trials in critical care, and they have been considered previously.[17-19] In some cases the heterogeneity in critical illness syndromes, including sepsis, ARDS, acute kidney injury, delirium, and others, may lead to

ABBREVIATIONS: RCT = randomized controlled trial; TTM = targeted temperature management

AFFILIATIONS: From the Department of Medicine (Drs Veldhoen and Maslove), and the Department of Critical Care Medicine (Drs Veldhoen, Howes, and Maslove), Queen's University, Kingston, ON, Canada.

FUNDING/SUPPORT: D. M. M. is supported by a Clinician Scientist award from the Southeastern Ontario Academic Medical Organization (SEAMO).

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DOI: https://doi.org/10.1016/j.chest.2019.11.019

Can J Diabetes 48 (2024) 66–72

Contents lists available at ScienceDirect

Canadian Journal of Diabetes

journal homepage: www.canadianjournalofdiabetes.com

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.

ARTICLE INFO

Article history:
Received 28 April 2022
Received in revised form
26 May 2023
Accepted 12 July 2023

Keywords:
breast cancer
diabetes
pharmacotherapy
screening

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.

Mots clés:
cancer du sein
diabète
pharmacothérapie
dépistage

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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1499-2671/
https://doi.org/10.1016/j.jcjd.2023.07.008

Association of Omega-3 Status With Long-Term Risk of Hospitalization for Sepsis

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Andrew G. Day, MSc[3]
Patrick Norman, MSc[3]
Michael J. Rauh, MD, PhD[4]
David M. Maslove, MD, MS[1,2,3]

OBJECTIVES: Sepsis is a life-threatening condition characterized by a dysregulated host response to infection. Despite decades of clinical trials, there are no specific treatments; care of the nearly 50 million annual cases worldwide is limited to antimicrobials and supportive measures. A primary prevention strategy may therefore be of value. We hypothesized that higher premorbid omega-3 fatty acid levels would be associated with a reduced incidence of sepsis.

DESIGN: Population-based cohort study.

SETTING: Retrospective data from the United Kingdom (U.K. Biobank).

PATIENTS: Two hundred seventy-three thousand three hundred twenty-five participants from the U.K. Biobank.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: Our exposure was baseline estimated omega-3 index (eO3I), modeled both categorically in quartiles, and continuously with restricted cubic splines. Our outcome measure was hospital admission with an *International Classification of Diseases*, 10th Edition code consistent with sepsis. The median (interquartile range) baseline eO3I was 6.0% (4.8–7.3%). Over a mean follow-up period of 13 years, 9241 participants experienced hospitalization with sepsis. In our adjusted model, compared with the lowest eO3I quartile, participants had lower risks of sepsis incidence in the second quartile (hazard ratio [HR], 0.88; 95% CI, 0.86–0.91; $p < 0.001$), third quartile (HR, 0.80; 95% CI, 0.78–0.83; $p < 0.001$), and fourth quartile (HR, 0.75; 95% CI, 0.73–0.77; $p < 0.001$). When analyzed as a continuous variable, increasing eO3I was associated with a decreasing risk of sepsis ($p < 0.001$).

CONCLUSIONS: In this population-based cohort study, baseline eO3I was inversely associated with subsequent sepsis incidence. Given that omega-3 levels can be increased with dietary supplementation, primary prevention should be explored to mitigate the burden of sepsis.

KEYWORDS: cohort studies; fatty acids; omega-3; sepsis; survival analysis

With an estimated 48.9 million incident cases in 2017 and a 30-day mortality rate of approximately 24% despite treatment, sepsis carries a substantial global burden of disease (1, 2). From a public health perspective, this burden highlights the potential impact of preventative therapy to decrease sepsis incidence. Nutritional status is thought to be a critical factor modulating sepsis risk and prognosis. Specifi ally, omega-3 polyunsaturated fatty acids (PUFAs) have been proposed to be protective by modulating inflammatory signaling through several putative mechanisms (3). Th s includes downregulating pro-inflammatory pathways, such as nuclear factor kappa B signaling, as well as upregulating anti-inflammatory mediators, such as maresins, protectins, and resolvins, known collectively as specialized pro-resolving mediators (4, 5).

While biochemical evidence suggests omega-3 fatty acids may mitigate the dysregulated inflammatory response characteristic of sepsis, clinical evidence

DOI: 10.1097/CCM.0000000000006593

Duloxetine Induced Interstitial Lung Disease - A Novel Case Report

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[1]Division of Respiratory and Sleep Medicine, [2]Department of Pathology and Molecular Medicine, [3]Department of Diagnostic Radiology, Queen's University and Kingston Health Sciences Center

INTRODUCTION

Duloxetine is a commonly prescribed antidepressant and has been associated with eosinophilic pneumonia (EP) in one case report*.
We report here the first case of duloxetine-induced Interstitial lung disease (ILD) other than EP.

CASE REPORT

A 71-year-old female presented with a 1-month history of cough, yellow sputum, fever, vomiting, hyporexia, and 15-pound weight loss. A computed tomography pulmonary angiogram ruled out pulmonary embolism but revealed right upper lobe (RUL) consolidation and patchy consolidations/nodules in the right middle (RML) and lower lobes (RLL) (Figure 1-A). The respiratory virus panel, sputum and blood cultures, and legionella urinary antigen were negative. She was hospitalized, treated with antibiotics, and referred to Respirology.

At her clinic visit, she had dyspnea (Medical Research Council grade 2/5) and dry cough, with resolution of other symptoms.
She reported exposure to foam and bamboo in her pillow and mattress, but no exposure to chemicals, fumes, molds, or dusts.
Her medications included duloxetine (started one-year prior), simvastatin, omeprazole, levothyroxine, and bisoprolol. She had no clinical or serologic evidence of connective tissue diseases. On exam had 97% SpO_2 on room air and bibasilar fine/coarse inspiratory crackles.

INVESTIGATIONS

Laboratory tests revealed leukocytosis (12.3 x10^9/L), elevated CRP (114 mg/L), and ESR (73 mm/hr).
Pulmonary function tests showed restriction (FVC 72%, TLC 56%) and reduced diffusing capacity (DLCO 48%).

Follow-up chest CT showed resolution of RUL and RML consolidations and new consolidations in both lower lobes (Figure 1-B).
Migratory consolidations suggested organizing pneumonia (OP), from hypersensitivity pneumonitis (foam exposure), or drug-induced EP.

Bronchoalveolar lavage (BAL) from the LLL was negative for infections but showed neutrophilia (53%), eosinophilia (23%), and lymphocytosis (20%), suggesting EP or OP related to drug-induced ILD (DI-ILD).

A second BAL showed mild neutrophilia (7%) and eosinophilia (4%); transbronchial lung biopsies showed intra-alveolar foamy macrophages and mild interstitial inflammation including lymphocytes and few eosinophils. Findings were not supportive of EP.

MANAGEMENT & OUTCOME

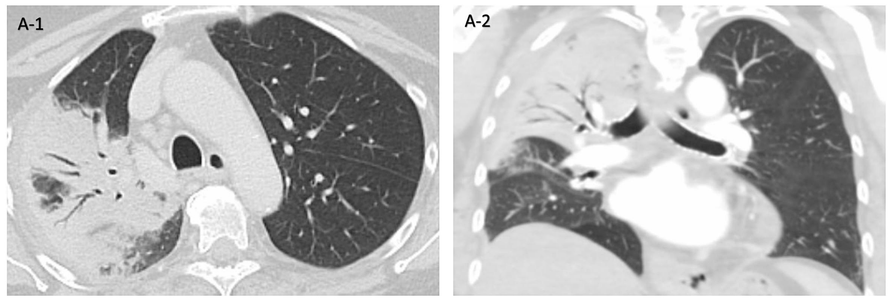
She was diagnosed with possible DI-ILD due to duloxetine that had been started a year prior.

Duloxetine was discontinued based. No immunosuppressive treatment was initiated.

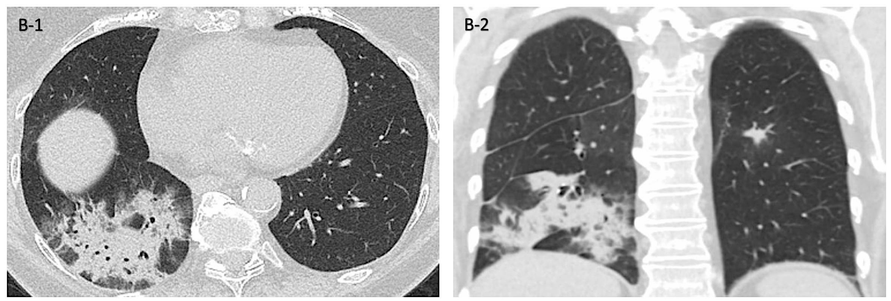
Following duloxetine discontinuation, she had complete resolution of symptoms and of the chest CT abnormalities (Figure 1-C).

IMAGES

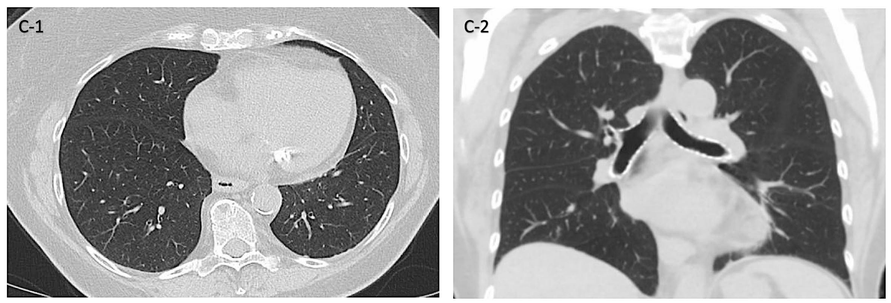
Figure 1



A (1-2): Axial and coronal images of CTPA demonstrate right upper lobe consolidation.



B (1-2): Axial and coronal images of follow up Chest CT scan demonstrate resolution of right upper lobe consolidation and new consolidations in right and left lower lobes.



C (1-2): Axial and coronal images of Chest CT scan demonstrate complete resolution of previously seen abnormalities after discontinuation of duloxetine.

DISCUSSION

We report here the first case of non-eosinophilic DI-ILD due to duloxetine, which fully resolved after drug discontinuation.

*Espeleta VJ, Moore WH, Kane PB, Baram D. Eosinophilic pneumonia due to duloxetine. Chest. 2007;131(3):901–903. doi:10.1378/chest.06-1659

Disclosures: None to declare.

Point of care ultrasound (POCUS) changes the needle insertion location from an anatomically landmarked site during bedside paracentesis

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Background and Aims

- Paracentesis is a procedure in which a needle is inserted into a patient's peritoneum to obtain ascitic fluid, either for diagnostic or therapeutic purposes.
- Historically, the method for performing this bedside procedure utilizes physical exam and anatomic landmarking to select a safe site to insert the needle, the most common approach being superiomedially to the anterior superior iliac spine.
- Point of care ultrasound (POCUS) technology has developed rapidly as a bedside aide to improve safety of procedures, with strong data in central line insertion and thoracentesis.
- Despite its widespread acceptance in clinical practice and medical education, the literature describing the safety benefit of ultrasound in paracentesis is limited.
- To date, there is no randomized controlled trial assessing POCUS vs. conventional anatomic landmarking and percussion for safety and efficacy of bedside paracentesis. This may be because paracentesis is safe in most circumstances and the number of patients required to show a safety difference, if any, would be exceedingly large.
- In this practical clinical trial, we aimed to assess if the use of POCUS yielded a preferred location for needle insertion compared to conventional anatomic landmarking, measured by user-perceived safety, depth of fluid pocket, proximity to nearby organs, or other anatomic considerations.

Methods

- This was a prospective, non-randomized trial comparing a POCUS-guided site to the conventional anatomic site in the same patient.
- Adult patients at Kingston Health Sciences Centre undergoing paracentesis were included.
- Physicians landmarked using conventional technique and compared this to a POCUS-guided site. The paracentesis was performed at whatever site was deemed optimal, if safe to do so.
- The primary outcome was whether POCUS yielded a change in needle insertion site of ≥ 5cm from the anatomic site. Secondary outcomes included depth of fluid pocket, and the reasons for which one site was chosen over another (i.e. abdominal wall considerations, nearby organs, optimizing fluid pocket, etc).
- Consent was obtained from all patients and physicians participating in the study, and the study was approved by the Queen's University Research Ethics Board.

Results

In total, 45 procedures featuring a unique combination of a physician and patient were included.

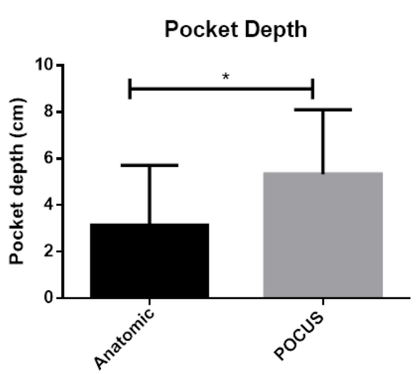
Table 1: Characteristics of physicians per procedure.

Training	
PGY 1	15 (33%)
PGY 2	14 (31%)
PGY 3	1 (2%)
PGY 4	4 (9%)
PGY 5	9 (20%)
Staff	2 (4%)
Training Program	
Internal medicine	30 (67%)
Gastroenterology	11 (24%)
Other	4 (9%)
Prior Paracentesis with POCUS	
<10	26 (58%)
≥10	19 (42%)
Prior experience of paracentesis without use of POCUS (y)	17 (38%)

Table 2: Characteristics of patients per procedure

Total patients	**30**
Paracenteses per patient (median, IQR)	1 (IQR 1,1); max number per patient = 5
Age (mean,SD)	61 (+/- 9)
Sex (F)	16 (36%)
Etiology of ascites per procedure	
Cirrhosis (primarily EtOH and NAFLD)	38 (84%)
Malignancy	4 (9%)
Cardiac	1 (2%)
Other	2 (4%)
Indication for procedure	
Therapeutic	24 (53%)
Diagnostic	13 (29%)
Both	8 (18%)
Suspicion of ascites prior to enrollment	
Clinical exam alone	6 (13%)
Radiologic findings alone	5 (11%)
Both	34 (76%)

Overall, POCUS resulted in a change in position of ≥5cm from the anatomic site in a 32 of 39 performed procedures (82%), within the 45 total cases.
The POCUS site was an average of 8.3cm +/- 4.7cm from the anatomic site, and superiolateral to the conventional site



Results

Table 3: Procedural results

Mean Volume of ascites (L) per indication	
Therapeutic (n = 24)	6.8L (+/- 2.7)
Diagnostic (n = 13)	0.14 (+/- 0.1)
Both (n = 8)	3.6 (+/-1.5)
Site preference	
POCUS	33 (73%)
Anatomic	1 (2%)
No preference	11 (24%)
Average depth of fluid (cm)	
Anatomic site	3.1 (+/-2.5)
POCUS site	5.4 (+/-2.8)
Reason(s) for choosing POCUS site over anatomic location	
Optimizing fluid pocket	24 (61%)
Abdominal wall consideration	
Adipose tissue	5 (11.5%)
Other	5 (11.5%)
Adjacent organ or vascular structure	15 (38%)
Cases aborted due to lack of sufficient ascites‡	6 (13 %)
Failed cases β	1 (3%)

‡ Case 1&2: Diagnostic procedure, with only clinical suspicion of ascites but no evidence by POCUS. Case 3: Therapeutic procedure with clinical suspicion and radiologic evidence, but minimal ascites on POCUS. Case 4&5: Diagnostic procedure, with clinical suspicion and radiologic evidence of ascites, but not safely accessible using POCUS. Case 6: Diagnostic procedure, with only radiologic evidence of ascites but not safely accessible using POCUS. β Fluid pocket was large and easily identified but needle was not long enough to traverse pannus.

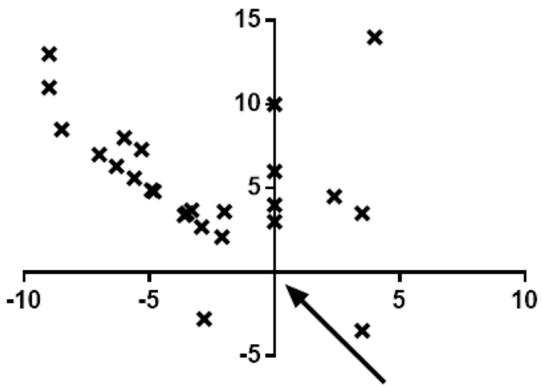


Figure 2 (above image):Schematic depicting the POCUS-guided needle puncture sites in relation to the conventional anatomic site, located at x,y=0cm (arrow).The y-axis is oriented vertically along the patient's midline (sagittal) with positive deflection being cephalad, whereas the x-axis lies horizontally (transverse) with positive deflections being medial. The POCUS-guided needle inerstion site was predominantly superiolateral to the anatomically landmarked site, away from vital structures (i.e. bladder, inferior epigastric artery)

Figure 1 (right image): The mean depth of ascites pocket at the conventional anatomic site (3.1cm +/- 2.5cm) compared to the POCUS-guided site (5.3cm +/- 2.8cm; *p<0.005). There was a significant increase in the depth of fluid at the POCUS site.

Conclusions

- Physicians overwhelmingly preferred the site obtained by POCUS over a conventionally-landmarked site
- POCUS gave physicians the ability to optimize the size of an ascitic fluid pocket, minimize proximity to adjacent organs and navigate around abdominal wall issues such as scarring, infection, or adipose tissue
- The latter is of particular importance given the increasing prevalence of NAFLD-associated cirrhosis in North America in which abdominal pannus may impair the ability to blindly perform paracentesis
- POCUS helped avoid 6 procedures where insufficient ascites was present despite clinical and/or previous radiologic suspicion of ascites, and therefore likely prevented a complication such as a perforation or failed procedure
- POCUS tends to deflect the needle insertion site superiolaterally, which is further away from vital structures such as the inferior epigastric artery and the bladder
- Shortcomings of this study include the relatively small sample size, the lack of a randomized-clinical trial, the preponderance of junior residents, as well as the homogenous ascites population that consisted primarily of patients with cirrhosis
- Nonetheless, this study demonstrates the utility of POCUS in bedside paracentesis and supports its continued use in clinical care and incorporation into medical education

Affiliations

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Queen's University | School of Medicine

Pleural Fluid Echogenicity – POCUS Characteristics to Differentiate Transudative and Exudative Pleural Effusions

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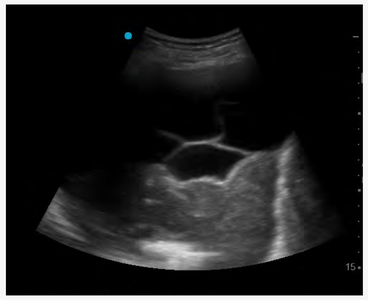
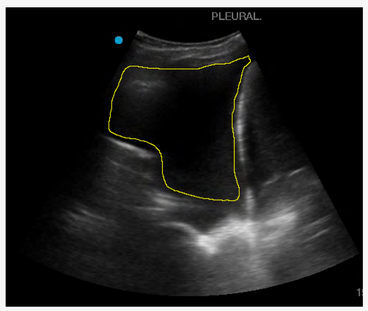
Introduction

Pleural effusions are a common complication, and management can vary based on the type of pleural effusion. Ultrasound can be used to characterize pleural effusions as simple, complex septated, complex nonseptated, and homogeneously echogenic, with the use of Lights Criteria to differentiate between transudative and exudative effusions.

Since ultrasound has become standard of care for thoracentesis, there has been increased efforts to compare ultrasound characteristics to Lights Criteria, with mixed results. Evan et al. (2021) was unable to demonstrate predictive value of anechoic ultrasound images but did demonstrate high predictive value of septations for exudative effusions. Soni et al (2022) utilized pixel density analysis in addition to subjective ultrasound findings in an exploratory retrospective study and found that pixel density in addition to subjective criteria (loculations, fibrin stranding, and floating debris) may provide the ability to create a scoring system to better characterize pleural effusions prior to thoracentesis.

The ability to better predict pleural effusion type prior to pleural effusion fluid sampling may lead to earlier development of management plans and determining the appropriateness of procedures (i.e. thoracentesis vs chest tube).





Purpose

1°- To determine if ultrasound characteristics can be utilized to differentiate transudative & exudative pleural effusions to guide care prior to thoracentesis.
2° - To determine reliability of pleural fluid ultrasound image analysis between assessors.

Pixel Intensity & Standardization
ImageJ v1.54i was used to analyze pixel Intensity/density, with images being standardized from 0-255 to give a full 8-bit integer range

Methods

Participants were recruited through inpatient medicine units and the outpatient pleural space clinic. We were notified of 71 diagnostic thoracenteses. Of these, 38 individuals were invited to participate in the study. Exclusion criteria included inability to provide informed consent, insufficient data for Lights Criteria, use of lung view on POCUS, and current admission for end-of-life care.

Table 1 – Demographic Data

	Sex	Age (years)	Transudative	Exudative	Inpatient	Outpatient
Male	29	73 ± 12	12	17	9	20
Female	9	59 ± 16	1	8	2	7
Total	38	70 ± 15	13	25	11	27

Images were reviewed by 2 residents & 1 staff physician familiar with POCUS and assessed for floating debris, fibrin stranding, & loculations. The subjective characteristics were considered present if ≧ 2/3 assessors agreed it was present. Images were then analyzed using ImageJ software to assess pixel intensity. Each image was assessed twice, first with absolute pixel intensity, then standardized where the most anechoic area was assigned a value of 0 and the most hyperechoic a value of 255. Images were then re-analyzed to attempt to minimize variation operator ultrasound gain preference.

Analysis

The Intraclass correlation coefficient (ICC) (continuous data) and Cohen's weighted Kappa (binary data) were used to measure agreement between assessors. Pixel intensity measurements were not normally distributed and therefore analyzed with the Mann-Whitney U test. Categorical data were compared with the Fisher's Exact test.

Results

- There was a high level of absolute agreement in subjective characteristics between assessors but low weighted Kappas (Range of 0.14 to 0.78) due to results being heavily loaded towards one group.
- Interclass correlation coefficients demonstrated very good correlation between assessors for mean pixel intensity (ICC 0.861) and minimum pixel intensity (ICC 0.953), with moderate reliability for maximum pixel intensity (ICC 0.534).
- There were no statistically significant results, but the following trends were identified:
  - Outpatients were more likely to have exudative effusions (74.1%; p=0.092)
  - Individuals with transudative effusions were on average older than those with exudative effusions (81yrs vs 71yrs; p=0.06)
  - Females were more likely to have exudative effusions (88.9%; p=0.126)
  - Maximum pixel intensity was higher in transudative effusions than exudative effusions (97.1 vs 78.9; p=0.079)

Figure 1– Pixel Intensity

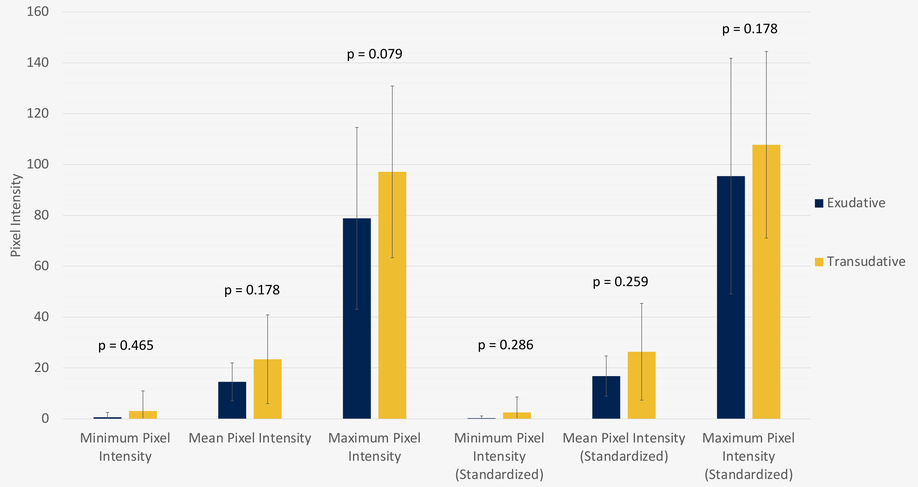


Table 2 – Results by effusion classification

	Transudative (n= 13)	Exudative (n=25)	Significance
Min Pixel Intensity	3.2 ± 7.9	0.7 ± 1.9	p = 0.465
Mean Pixel Intensity	23.5 ± 17.5	14.6 ± 7.5	p = 0.178
Max Pixel Intensity	97.1 ± 33.6	78.9 ± 35.8	p = 0.079
Min Pixel Intensity (Standardized)	2.6 ± 6.1	0.3 ± 0.9	p = 0.286
Mean Pixel Intensity (Standardized)	26.4 ± 19	16.9 ± 7.9	p = 0.259
Max Pixel Intensity (Standardized)	107.8 ± 36.7	95.4 ± 46.4	p = 0.178
Floating Debris	2	4	p = 1.0
Fibrin Stranding	1	0	p = 0.342
Loculations	0	2	p = 0.538

Discussion, Conclusions, & Next Steps

- Point of Care Ultrasound has become standard of care for thoracentesis, but more research is required to determine its utility in characterizing pleural effusions.
- Pleural effusion image analysis can be reliable between multiple assessors, facilitating ongoing research in this field.
- Pixel intensity analysis and qualitative characteristics are not sufficient to differentiate transudative and exudative effusions in our sample. Next steps will include using our data with a novel pleural fluid ultrasound score[1] to assess our results with previously tested systems.
- Pixel intensity standardization does not appear to provide benefit in improving ultrasound image quality, and other methods of reducing variation of user preference in ultrasound gain should be considered moving forward.
- Additional data, including a better representative demographics as well as variety of inpatient and outpatient thoracentesis will be beneficial to support more in-depth analysis moving forward and provide more generalizability of findings.

A special thank you to the following members of the Kingston Health Sciences Centre (KHSC) Pleural Space Clinic for their part in data collection:
Dr. Susan Moffatt, Dr. Christina Liak, Dr. Sebastian Rodriguez, Dr. Christopher Parker, Dr. Christopher Davis, Amy Mussell, Kim Spearing, & Delanya Podgers

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Cancer and cardiovascular disease: can understanding the mechanisms of cardiovascular injury guide us to optimise care in cancer survivors?

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Abstract

Cancer and cardiovascular disease (CVD) are the leading causes of morbidity and mortality. Therefore, CVD deaths in cancer survivors remain a major challenge in improving cancer outcomes, especially in low and middle income countries (LMICs). Cancer and CVD share many common risk factors, both modifiable risk factors (obesity, diabetes and smoking) and non-modifiable factors such as inflammation. Additionally, some cancer therapies are associated with cardiac toxicity. These mechanisms drive increased CVD outcomes in cancer survivors, and understanding this relationship allows us to target therapies to combat such risks. Several commonly used pharmacotherapies for CVD demonstrate promise in cancer survivors for both primary and secondary prevention. Beta blockers and Angiotensin converting enzyme (ACE)-inhibitors have been shown in several studies to improve left ventricular ejection fraction (LVEF) in patients with already established LVEF decline following cancer therapy. Statin use during chemotherapy was associated with lower risk of heart failure and smaller declines in LVEF. Recent studies into the effects of anti-inflammatory medications on cardiovascular events in the non-cancer population have demonstrated promising results and may prove to be an area of further investigation and possible benefit in the cancer population [Canakinumab Anti-Inflammatory Thrombosis Outcomes Study (CANTOS) and Colchicine Cardiovascu-lar Outcomes Trial (COLCOT)]. Additionally, several other medications including PCSK9 inhibitors, sodium-glucose cotransporter-2 inhibitors (SGLT2i) and glucagon-like peptide 1 (GLP-1) agonists have been shown to modify inflammation, and therefore may provide cardiovascular benefits. While common pharmacotherapies used in CVD show promise in cancer survivors, their exact mechanisms remain poorly understood. Few studies evalu-ate their clinical effectiveness specifically in cancer survivors, as this patient population is excluded from most studies. Further investigation is warranted with more representation of cancer survivors before cost-effective recommendations are made. This is especially true in LMICs where resources are sparse for primary and secondary prevention in order to optimise care in this unique, high-risk population for CVD.

Keywords: *chemotherapy-induced cardiotoxicity, cardiovascular disease, cancer survivors, cancer survivorship, chemotherapy-related cardiac dysfunction, heart failure, coronary artery disease, primary prevention, secondary prevention, cardio-oncology*

Review

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ecancer 2022, **16**:1430
https://doi.org/10.3332/ecancer.2022.1430

Published: 14/07/2022
Received: 03/03/2022

Publication costs for this article were supported by *ecancer* (UK Charity number 1176307).

Effect of Monetary Incentives on Peer Review Acceptance and Completion: A Quasi-Randomized Interventional Trial

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Abid Alam, MA[1]
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OBJECTIVES: Peer review typically relies on experts volunteering their time to review research. This process presents challenges for journals that may face a shortage of qualified referees, resulting in either delay in handling papers or less thorough review than is optimal. We experimentally tested the impact of providing cash incentives to complete peer review assignments at *Critical Care Medicine*.

DESIGN: Quasi-randomized, blinded, interventional study with an alternating treatment design.

SETTING: *Critical Care Medicine (CCM)*, a peer-reviewed specialty journal.

SUBJECTS: All reviewers receiving requests from *CCM* to review research articles during a 6-month period from September 2023 to March 2024 (excluding a 2-wk holiday window).

INTERVENTIONS: In alternating 2-week blocks, reviewer invitation letters were sent out, including either an offer of $250 for accepting the peer review request (treatment) or the standard letter with no cash offer (control). Reviewers who fulfilled incentivized invitations received a $250 check from the journal.

MEASUREMENTS AND MAIN RESULTS: Our primary outcome was the rate of invitation-to-completed-review conversion, defined as the number of reviews submitted divided by the number of reviewer invitations sent out. Secondary outcomes included the "on-time" conversion rate, invitation acceptance rate, time to invitation acceptance, time to review submission, and review quality. Seven hundred fifteen reviewer invitations were sent out, 414 of which (57.9%) included an incentive offer. Two hundred eighteen (52.7%) of the incentivized invitations were accepted, compared with 144 (47.8%) in the control group. A greater proportion of reviewer invitations led to submitted peer review reports in the incentive group than in the control group (49.8% [206/414] vs. 42.2% [127/301]; $p = 0.04$). In a "survival analysis," invitations sent with an incentive offer were fulfilled faster on average (Cox proportional hazard ratio, 1.30 [1.04–1.62]; $p = 0.02$), corresponding to quicker review times of approximately 1 day (11 vs. 12 d). Of the 333 reviewer reports submitted, 205 (61.6%) were assessed by editors, with no difference in review quality noted between study arms.

CONCLUSIONS: Providing cash incentive for completing peer review reports resulted in a modest increase in the share of invited reviewers who complete reviews for a specialty medical journal.

KEYWORDS: behavioral economics; health policy; peer review; publishing; scholarly communication

Peer review is often regarded as a cornerstone of scholarly publishing, its roots extending back centuries as a critical means of ensuring the credibility and quality of scientific communications (1). Historically, it has relied on the volunteer labor of experts who, without monetary compensation, assess articles submitted to journals and provide recommendations for their

DOI: 10.1097/CCM.0000000000006637

Received: 19 February 2025 | Accepted: 28 May 2025

DOI: 10.1111/hiv.70058

REVIEW ARTICLE

Patient-reported outcomes in clinical trials assessing the effectiveness of cabotegravir + rilpivirine long-acting injections as antiretroviral therapy: A systematic review

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Abstract

Introduction: Human immunodeficiency virus-1 (HIV-1) continues to have a high global burden, with approximately 39.9 million people currently living with the virus. Despite the clinical success of antiretroviral therapy (ART), adherence remains a significant challenge, often due to emotional distress and HIV-related stigma. Long-acting injectables (LAIs) such as the combination of cabotegravir (CAB) and rilpivirine (RPV) have emerged as promising alternatives, reducing the burden of daily pill regimens.

Methods: This systematic review explores the role of CAB + RPV-LA injectables in antiretroviral therapy (ART), with a focus on patient-reported outcomes from five key clinical trials.

Results: Findings reveal that CAB + RPV-LA maintains high levels of viral suppression comparable to daily ART while improving patient satisfaction and quality of life. Meta-analysis of HIV Treatment Satisfaction Questionnaire (HIVTSQc) scores across multiple trials demonstrated consistent positive outcomes, with a mean score of 28.83 out of a possible range from −33 to +33, indicating a substantial improvement in patient satisfaction compared to baseline. Qualitative data highlight the psychological and logistical benefits of LAIs, including reduced stigma and enhanced treatment convenience.

Conclusions: This review underscores the potential of CAB + RPV-LA in improving patient adherence and satisfaction while offering insights for future studies on longer-term outcomes of LAI use.

KEYWORDS

cabotegravir and rilpivirine, HIV therapy, long acting injectable, patient perspective, patient-reported outcomes

Chen *et al.*
Intensive Care Medicine Experimental (2023) 11:2
https://doi.org/10.1186/s40635-022-00490-3

Intensive Care Medicine Experimental

METHODOLOGIES Open Access

A deep learning model for the classification of atrial fib illation in critically ill patients

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Abstract

Background: Atrial fibrillation (AF) is the most common cardiac arrhythmia in the intensive care unit and is associated with increased morbidity and mortality. New-onset atrial fibrillation (NOAF) is often initially paroxysmal and fleeting, making it difficult to diagnose, and therefore difficult to understand the true burden of disease. Automated algorithms to detect AF in the ICU have been advocated as a means to better quantify its true burden.

Results: We used a publicly available 12-lead ECG dataset to train a deep learning model for the classification of AF. We then conducted an external independent validation of the model using continuous telemetry data from 984 critically ill patients collected in our institutional database. Performance metrics were stratified by signal quality, classified as either clean or noisy. The deep learning model was able to classify AF with an overall sensitivity of 84%, specificity of 89%, positive predictive value (PPV) of 55%, and negative predictive value of 97%. Performance was improved in clean data as compared to noisy data, most notably with respect to PPV and specificity.

Conclusions: This model demonstrates that computational detection of AF is currently feasible and effective. This approach stands to improve the efficiency of retrospective and prospective research into AF in the ICU by automating AF detection, and enabling precise quantification of overall AF burden.

Keywords: Atrial fibrillation, Deep learning, Critical care

Background

New-onset atrial fibrillation (NOAF) is the most common cardiac dysrhythmia in critically ill patients with a reported incidence as high as 46% [1]. It is most often described in patients with sepsis with an incidence of 10–40% [2], but is seen in a variety of illnesses such as acute respiratory distress syndrome [3], non-cardiac thoracic surgery [4, 5], and trauma [6]. Critical illness is an independent driver of NOAF due to arrhythmogenic triggers such as electrolyte disorders, vasoactive medications, fluid overload and hypoxia [7]. Acute events during critical illness (e.g., infection, ischemia) accelerate cardiac remodeling and fibrosis, begetting further arrhythmias [8]. NOAF is independently associated with prolonged duration of hospital stay [2, 9] and significant morbidity and mortality [10]. Patients with NOAF are at an increased risk for in-hospital ischemic

nature medicine

PERSPECTIVE

https://doi.org/10.1038/s41591-022-01843-x

Redefining critical illness

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Research and practice in critical care medicine have long been defined by syndromes, which, despite being clinically recognizable entities, are, in fact, loose amalgams of heterogeneous states that may respond differently to therapy. Mounting translational evidence—supported by research on respiratory failure due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection—suggests that the current syndrome-based framework of critical illness should be reconsidered. Here we discuss recent findings from basic science and clinical research in critical care and explore how these might inform a new conceptual model of critical illness. De-emphasizing syndromes, we focus on the underlying biological changes that underpin critical illness states and that may be amenable to treatment. We hypothesize that such an approach will accelerate critical care research, leading to a richer understanding of the pathobiology of critical illness and of the key determinants of patient outcomes. This, in turn, will support the design of more effective clinical trials and inform a more precise and more effective practice at the bedside.

A 66-year-old woman is admitted to the intensive care unit (ICU) with fever, cough and difficulty breathing. She is diagnosed with pneumonia, intubated and placed on mechanical ventilation. The following day, her chest X-ray reveals bilateral infiltrates, and arterial blood gas analysis shows severe hypoxemia. Her treating clinicians consider what to do next.

Were this patient admitted in 2019, her management might have been beset by more questions than answers. She has both sepsis, a syndrome of life-threatening organ dysfunction in the face of infection, and acute respiratory distress syndrome (ARDS), a syndrome of respiratory failure associated with lung injury and impaired gas exchange. Both of these syndromes have been the subject of many epidemiological and interventional studies, yet little of the resulting evidence is clinically actionable. There are no specific treatments for her sepsis beyond antmicrobials[1], and the ventilation strategies used to treat ARDS might reasonably be applied to any patient in the ICU[2].

Were she admitted today—and depending on geography and time of year—her condition might well be the result of critical Coronavirus Disease 2019 (COVID-19). She would still meet diagnostic criteria for both sepsis and ARDS and would ostensibly face a similar degree of therapeutic uncertainty. However, in the last few years, many large randomized trials have provided a wellspring of evidence suggesting that a patient in her condition is likely to benefit from corticosteroids[3] and interleukin-6 receptor antagonists[4,5] but that treatments for milder disease, including remdesivir[6] and systemic anticoagulation[7], are unlikely to provide substantial benefit. To the great relief of many, the once arid landscape of clinical evidence in critical care has begun to germinate.

In what follows, we examine how advances in translational critical care brought us to this inflection point in our field and how these advances stand to fundamentally alter the way that we conceptualize and classify critical illness.

A new era in translational critical care research

The field of critical care medicine can be described by three stages of development (Fig. 1). In the first stage ('Foundations', c. 1955–1980s), mechanical ventilation and continuous monitoring of physiologic parameters were introduced to the care of the critically ill, along with higher nurse-to-patient ratios, standardized practices and an emerging recognition of critical care as a standalone medical specialty. These technological advances provided the basis for a physiology-based understanding of the host response to injury and saved the lives of patients who might otherwise have died. Critical illness was defined as organ-level pathophysiology (for example, shock and respiratory failure), and the delivery of intensive care services was centered on maintaining organ-level homeostasis (for example, assisted breathing and circulatory support).

A second stage of development in the critical care field ('Acceleration', c. 1980s–2020) arose alongside advances in translational research that proffered an improved understanding of the pathophysiology of the host response. In this era, the field acquired

A full list of affiliations appears at the end of the paper.

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.*
- *Investigating appropriate prescribing for medically complex older adults*
- *Pharmacoepidemiology including dementia treatment*
- *Improving health care access with age friendly options in healthcare settings*
- *Improving the management of cognitive impairment and technology*

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. Leah Nemiroff (Division Chair):
Dr. Nemiroff can offer medical education opportunities, with ideas that could be launched with an interested resident. Dr. Nemiroff is involved in funded research focused on the following topics:
- A multicentre implementation study of generative AI to reduce EHR-related documentation burden
- Using simulation to increase competence in assessment of capacity in Geriatric Psychiatry trainees
- Developing a novel local Geriatric Medicine and Geriatric Psychiatry collaborative triage model

Dr. John Puxty:
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.

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.

However, I've attached some relevant documents that might be worth including in the research catalogue, including:

1. An overview page with the names of division members, possible project areas of focus, and contact information

2. Some recent publications by various division members (some of which include recent trainees) - of note, Dr. Chris Frank has a series of articles in the journal Canadian Family Physician with some of them co-authored by Queen's Care of the Elderly trainees. Here's a link to Chris' author page at Canadian Family Physician:https://www.cfp.ca/search/author1%3Afrank%252C%2Bchris%20numresults%3A10%20sort%3Arelevance-rank%20format_result%3Astandard

3. And here is the link to another publication authored by two division members that might also be a useful addition to the research catalogue: https://pubmed.ncbi.nlm.nih.gov/36515053/

Approach to inappropriate sexual behaviour in people with dementia

Petra Joller MD CCFP **Neeraj Gupta** MSc **Dallas P. Seitz** MD FRCPC **Christopher Frank** MD FCFP
Michelle Gibson MD CCFP **Sudeep S. Gill** MD MSc FRCPC

Abstract

Objective To provide family physicians with an update on the approach to diagnosis and management of inappropriate sexual behaviour (ISB) in persons with dementia.

Sources of information MEDLINE and EMBASE were searched for relevant articles published before June 2012. No level I studies were identified; most articles provided level III evidence.

Main message Inappropriate sexual behaviour is common in people with dementia. A variety of factors (eg, cultural, religious, societal views of geriatric sexuality, medicolegal issues) might complicate evaluation of this behaviour, and must be considered to allow suitable management of individual patients. Tools to assist in documenting ISB are available. Creative nonpharmacologic interventions for ISB might be effective when tailored to individual patients. A number of drug treatments (eg, antidepressant, antiandrogen, antipsychotic, and anticonvulsant medications) have been proposed for symptoms that do not adequately respond to nonpharmacologic interventions. However, evidence to support drug treatments is limited, adverse effects remain an important consideration, and it is unclear which should be used as first-line versus second-line treatments.

Conclusion Although there is no empirically established treatment algorithm for dementia-related ISB, existing literature provides some evidence for various nonpharmacologic and pharmacologic treatments. Further high-quality research is urgently needed to guide family physicians who manage patients with dementia-related ISB.

A broad spectrum of behavioural and psychological symptoms can develop in Alzheimer disease and related dementias, and increase the risk of poor outcomes for both patients and their caregivers.[1,2] While dementia is usually accompanied by apathy and decreased sexual interest,[3,4] disinhibition and inappropriate expressions of sexuality can also emerge.[4,5] Inappropriate sexual behaviour (ISB) can be very troubling for family members and other caregivers and can present substantial challenges for the treating clinician.

All individuals—regardless of their age or medical condition—need love, touch, companionship, and intimacy.[6] Clinicians should look past societal stereotypes of elderly people as asexual beings, as these stereotypes can cause negative attitudes toward healthy expressions of sexuality. Care must be taken not to pathologize appropriate sexual behaviour.

Perceptions of what constitutes appropriate behaviour vary between individuals, and might be influenced by a host of factors, such as religious beliefs or prevailing societal views of elderly persons.[6-8] The effect of sexual behaviour on others is especially relevant in the nursing home setting, where there is relatively little privacy and many different attitudes toward sexuality. Examples of ISB include lewd or suggestive language, implied sexual acts (eg, requesting unnecessary genital care, viewing pornography in public), and overt sexual acts (eg, touching, grabbing, or disrobing of self or others, public masturbation).

In this article, we provide an update on the evaluation and management of dementia-related ISB. Details regarding

KEY POINTS Caution is needed when evaluating inappropriate sexual behaviour to ensure that events have not been perceived incorrectly, and that treatment is in fact warranted. An initial careful evaluation and nonpharmacologic treatments should precede attempts to treat behaviour with medications. No randomized controlled trials of treatments of dementia-related inappropriate sexual behaviour have been reported. We must instead rely on evidence from case reports and a few small studies (ie, level II or III evidence). When using a pharmacologic treatment, keep in mind the drug's toxicity profile, communicate the potential for benefits and harms to patients and caregivers, and carefully document these discussions.

This article has been peer reviewed.
Can Fam Physician 2013;59:255-60

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La traduction en français de cet article se trouve à **www.cfp.ca** dans la table des matières du numéro de **mars 2013** à la **page e135.**

ORIGINAL RESEARCH

Pre-Clerkship Observerships to Increase Early Exposure to Geriatric Medicine

Peng You, BHSc[1], Marie Leung, BSc[1], Victoria Y. Y. Xu, BHSc[1], Alexander Astell, BSc[1], Sudeep S. Gill, MD, MSc, FRCPC[2], Michelle Gibson, MD, MEd, CCFP[2], Christopher Frank, MD, FCFP[2]

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DOI:http://dx.doi.org/10.5770/cgj.18.184

ABSTRACT

Background and Purpose

To foster interest in geriatric care, the Queen's Geriatrics Interest Group (QGIG) collaborated with the Division of Geriatric Medicine to arrange a Geriatrics Pre-Clerkship Observership Program.

Methods

Forty-two pre-clerkship medical students participated in the program between October 2013 and May 2014. Participants were paired with a resident and/or attending physician for a four-hour weekend observership on an inpatient geriatric rehabilitation unit. The program was assessed using: (1) internally developed Likert scales assessing student's experiences and interest in geriatric medicine before and after the observership; (2) University of California Los Angeles–Geriatric Attitudes Scale (UCLA-GAS); and (3) narrative feedback.

Results

All participants found the process of setting up the observership easy. Some 72.7% described the observership experience as leading to positive changes in their attitude toward geriatric medicine and 54.5% felt that it stimulated their interest in the specialty. No statistically significant change in UCLA–GAS scores was detected (mean score pre- versus post-observership: 3.5 ± 0.5 versus 3.7 ± 0.4; p=.35). All participants agreed that the program should continue, and 90% stated that they would participate again.

Conclusions

The observership program was positively received by students. Structured pre-clerkship observerships may be a feasible method for increasing exposure to geriatric medicine.

Key words: geriatrics, undergraduate medical education, attitude, intervention

INTRODUCTION

Currently, those aged 65 years and older constitute the fastest growing segment of the Canadian population.(1) In 2012, there were only 230–242 specialists in geriatric medicine in Canada; to meet the health-care needs of the elderly population, an increase in the number of physicians specialized in geriatric care is needed.(1,2)

Career intentions are strongly influenced by exposure to role models in a particular clinical field and early patient contact.(3) However, many Canadian medical students make career choices early, often without much exposure to the field of geriatric medicine.(4) In addition, clerkship rotations in geriatric medicine are only mandated in seven Canadian undergraduate medical programs. Thus, many students do not have any exposure to geriatric medicine throughout their entire undergraduate medical career.(5)

Pre-clerkship medical students have noted that a lack of clinical exposure to certain specialties precluded them from making informed career decisions.(6) Previous interventions involving early clinical exposure to Emergency Medicine and Infectious Diseases have been shown to increase interest in those specialties.(6,7) Furthermore, interventions involving clinical contact with the elderly have also demonstrated an increase in positive attitudes towards caring for geriatric patients.(3,8)

The Queen's Geriatrics Interest Group (QGIG) is a student-run initiative at the Queen's University School of Medicine and was developed to foster interest in the field of geriatric medicine. A new QGIG initiative, the Geriatrics Pre-Clerkship Observership Program, was developed in collaboration with the Division of Geriatric Medicine at Providence Care–St. Mary's of the Lake Hospital in Kingston, Ontario.

The purpose of this study was to evaluate the impact of pre-clerkship observerships on student experiences and attitudes towards geriatric medicine.

Canadian Medical Education Journal

Brief Reports

Prescribing competency assessment for Canadian medical students: a pilot evaluation

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Published: March 13, 2019

CMEJ 2019, 10(1):e103-e110 Available at http://www.cmej.ca

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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CANADIAN COLLEGE OF HEALTH LEADERS
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We can do better: Addressing ageism against older adults in healthcare

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Healthcare Management Forum
2022, Vol. 35(2) 118–122

DOI: 10.1177/08404704221080882
journals.sagepub.com/home/hmf
SAGE

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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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*
- *Clinical trials on improving transfusion practice for patients undergoing chemotherapy and stem cell transplants*
- *Modern Scurvy and Hematology: A Retrospective Chart Review in Kingston, ON*

Resident Research Projects –
Hematology Current/Past Projects 2025

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. Inherited Bleeding Disorders

Dr. Paula James and Dr. Jennifer Leung lead the Inherited Bleeding Disorders Program of Southeastern Ontario. Their research program spans laboratory and clinical research focused on patients with inherited bleeding disorders, including bleeding assessment tools. Interested residents can reach out to Dr. James or Dr. Leung for further discussion.
Supervisor: Dr. Paula James (jamesp@queensu.ca) or Dr. Jennifer Leung (Jennifer.Leung@kingstonhsc.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 focused 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 focused 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
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
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

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

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□ 70 g/L) vs. liberal (2 units for Hgb □ 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

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

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

MODERN SCURVY AND HEMATOLOGY: A RETROSPECTIVE CHART REVIEW IN KINGSTON, ONTARIO

R. Mainland[1], P. Ganguli[2], P. James[2], J. Lui[2], N. Satkunam[2], J. Leung[2]

1. Division of General Internal Medicine, Department of Medicine, Queen's University, Kingston, ON, Canada
2. Division of Hematology, Department of Medicine, Queen's University, Kingston, ON, Canada

INTRODUCTION

- Humans have lost the ability to synthesize Vitamin C, unlike most mammals, and must consume it in diet.
- Vitamin C is a co-factor in collagen biosynthesis and contributes to the integrity of blood vessels and other tissues.
- Vitamin C deficiency can lead to bleeding (i.e., peri-follicular hemorrhage), bruising, dermatologic and hair changes (i.e., corkscrew hairs).
- There are no randomized controlled trials on Vitamin C replacement in patients who are deficient and no evidence-based or society-supported guidelines on the work up and management of Vitamin C deficiency.
- A recognized increase in the number of patients diagnosed with Vitamin C deficiency at Kingston Health Sciences Centre (KHSC) prompted a need to re-evaluate the prevalence, predisposing factors, and management of this nutritional deficiency.

AIM

This study evaluated the prevalence, predisposing factors, and management of Vitamin C deficiency among patients in Kingston, Ontario.

METHODS

- We conducted a retrospective chart review of patients evaluated by the Hematology service at KHSC between March 2017 and June 2023 who were found to be Vitamin C deficient (defined as a Vitamin C level <25 µmol/L).
- From each patient chart, data pertaining to the following was extracted: patient demographics, socioeconomic status, diet, comorbidities, clinical presentation, concurrent hematologic abnormalities, and treatment strategies.
- This study was approved by the Queen's University Health Sciences & Affiliated Teaching Hospitals Research Ethic Board.

RESULTS

- **Twenty-three patients with Vitamin C deficiency were evaluated by Hematology at KHSC between March 2017 and June 2023.**

DEMOGRAPHICS

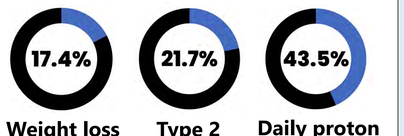
AGE (YEARS)	<40	40 – 60	>60
	30.4% (n=7)	56.5% (n=13)	13.0% (n=3)

SEX AT BIRTH	Male	Female
	65.2% (n=15)	34.8% (n=8)

SOURCE OF INCOME	Actively Employed	Government Funded	Retired
	30.4% (n=7)	34.8% (n=8)	34.8% (n=8)

RECREATIONAL DRUGS / ALCOHOL	Daily Use	>10 Standard Drinks/Week
	69.6% (n=16)	26.1% (n=6)

COMORBIDITIES



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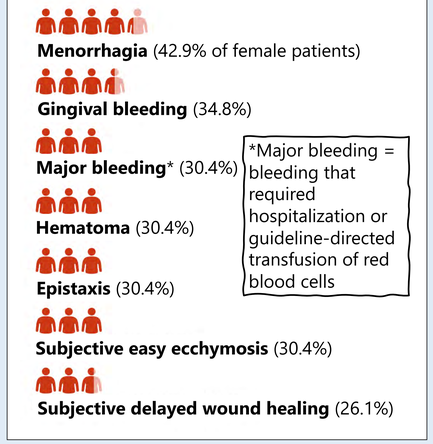
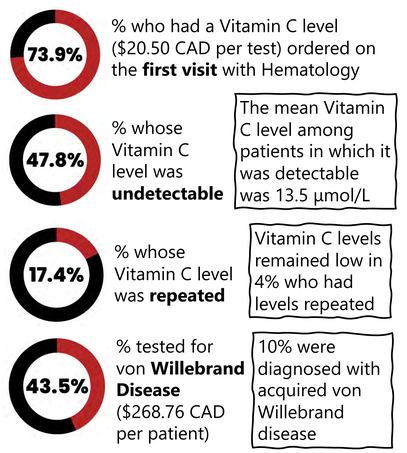


WORK UP



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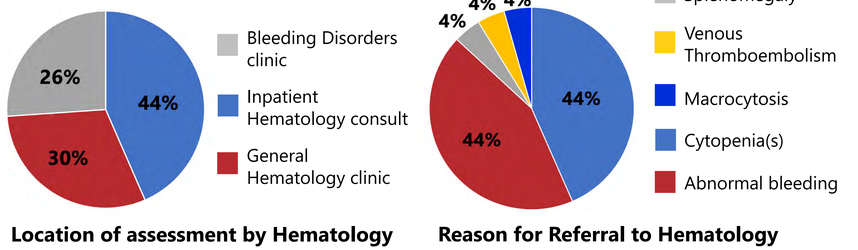
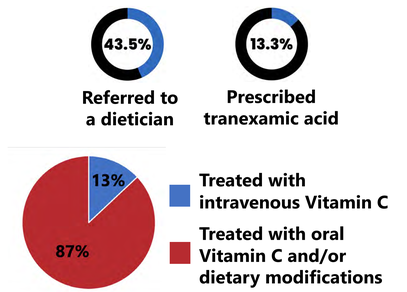


MANAGEMENT



CONCLUSIONS

- Despite its perceived rarity in modern times, Vitamin C deficiency has contributed to a variety of presentations of bleeding diathesis encountered by Hematologists in Kingston, Ontario.
- Detailed dietary and social histories, with consequent consideration of Vitamin C status, should be undertaken in the assessment of undifferentiated bleeding disorders.
- Increased awareness of the prevalence and presentation of Vitamin C deficiency could facilitate earlier diagnosis and appropriate management, including a decrease in costly testing for other bleeding disorders.

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A 22-Hospital Audit of Platelet Transfusions Demonstrates Substantial Practice Variability

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Introduction

- Audits of platelet transfusion have found varying rates of inappropriate use, ranging from 6.4[1] to 41.5%[2]
- Harms of platelet transfusion have been seen in randomized trials:
  - In 660 pre-term infants a prophylactic threshold of 50,000/mcL (vs. 25,000/mcL) was associated with new major bleeding or death[3]
  - In 190 adults with intracranial hemorrhage on an antiplatelet drug there was higher death or disability in the platelet transfused arm[4]
  - In 372 patients with dengue-induced thrombocytopenia, prophylactic transfusion at <20,000/mcL (vs. supportive care) increased transfusion-related adverse events without decreasing bleeding[5]
- This underscores the importance of judicious platelet transfusion use

Project Aim

- **Characterize platelet transfusions** across a large, hospital data sharing platform to understand the **patients being transfused**, platelet transfusion **thresholds**, and **practice variability** across prescribers and hospitals.

Methods

- **Design**: retrospective, multicenter, observational
- **Data source**: hospitals participating in the GEMINI data sharing network, with linked patient-level administrative and clinical data from any patient admitted to a medicine ward or intensive care unit (ICU)[6]
- **Inclusion**: adults admitted to a GEMINI site Jan 1, 2017 to June 30, 2022
- **Exclusions**: incomplete transfusion data, low-volume platelet use, incomplete ICU admission data, transfusions occurring before admission or after discharge, transfusion events with 5+ units
- **Primary outcome**: platelet transfusion guideline compliance ***(Table 1)*** across hospital sites, prescriber characteristics and patient groups
- **Secondary outcomes**: patient demographics of those transfused vs not, median pre-transfusion platelet count
- **Statistical analysis**: regression analysis of guideline compliance with random effect of most responsible physician (MRP), controlled by hospital type, MRP gender, MRP years out of practice and MRP specialty

Table 1 Recommended platelet transfusion thresholds and how we defined guideline compliance across various clinical criteria.

Clinical Criteria	Recommended Threshold (/mcL)	Defined as "Guideline Compliant" (/mcL)
Prophylaxis		
Immune-mediated thrombocytopenia (HIT, TTP, ITP)	No transfusion[7]	No transfusion unless other clinical criteria met
On ECMO	<50,000[8], <80,000[9]	<100,000
Therapeutic anticoagulation	<50,000[10]	<50,000
All others	<10,000[7,11,12]	<10,000
Pre-Procedure		
Neurosurgery or high-risk ophthalmic procedure	<100,000[7]	<100,000
Major non-neuraxial surgery	<40,000[11], <50,000[7, 11,12]	<50,000
Other invasive procedure	Central line: <20,000[7,12,13] Bone marrow: <20,000[11, 13], none[7] LP: <20,000[13], <40,000[7,11], <50,000[11,12]	<50,000
Bleeding		
Intracranial, polytrauma, brain injury, eye injury	<100,000[7]	<100,000
During bypass surgery	<50,000 or if on antiplatelet drug[14]	<100,000
On ECMO	<100,000[9]	<100,000
All others	WHO Grade 3-4: <50,000[7] WHO Grade 2: <30,000[7]	<50,000 if ≥ 1u RBC or 2g/dL Hgb drop in 24hr

Results

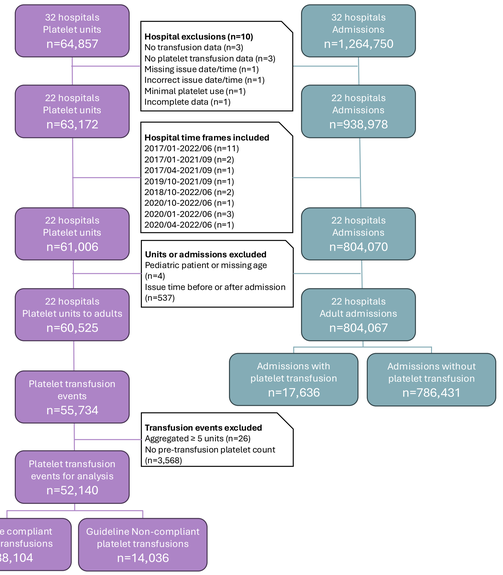

Figure 1 Inclusions and exclusions for platelet transfusion events (purple) and admissions (green).

- Most guideline non-compliant transfusion events occurred at platelet counts > 50,000/mcL (n=6,517, 46.4% of all guideline non-compliant)
- We observed higher rates of guideline compliant transfusion later during hospitalization by both the transfusion index and day of admission
- Guideline compliant platelet transfusion and median pre-transfusion platelet count varied widely by MRP specialty and hospital ***(Figure 2)***
- There was a significant impact of hospital type and MRP specialty on guideline compliance, but not MRP gender or MRP years out of practice ***(Figure 3)***

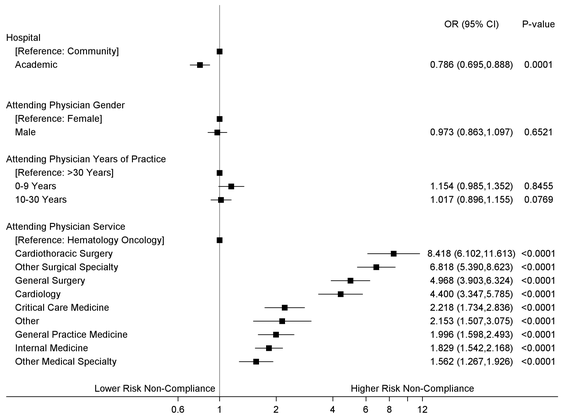

Figure 3 Generalized linear regression model, with random effect of MRP, across hospital type, MRP gender, MRP years out of practice and MRP specialty.

Table 2 Patient demographics stratified by receipt of platelet transfusion during admission.

	Platelet Transfusion (n=17,636)	No Transfusion (n=786,431)	Overall (n=804,067)
Sex			
Female	6954 (39.4%)	370547 (47.1%)	377501 (46.9%)
Age at Admission			
Mean (SD)	61.9 (15.7)	66.9 (18.4)	66.8 (18.3)
Charlson Comorbidity Index			
Median [Q1, Q3]	2 [0-2]	1 [0-2]	1 [0-2]
In-Hospital Mortality			
Yes	4247 (24.1%)	54269 (6.9%)	58516 (7.3%)
Inpatient Length of Stay (days)			
Median [Q1, Q3]	13 [7-26]	5 [3-10]	5 [3-10]
ICU Stay			
Yes	9362 (53.1%)	179628 (22.8%)	188990 (23.5%)
ICU Length of Stay (days)			
Median [Q1, Q3]	6 [3-13]	4 [2-6]	4 [2-7]
Most Responsible Diagnosis			
Malignant diseases	4406 (25%)	49569 (6.3%)	53975 (6.7%)
Circulatory diseases	3366 (19.1%)	190771 (24.3%)	194137 (24.1%)
Classical hematologic diseases	1843 (10.5%)	12927 (1.6%)	14770 (1.8%)
Digestive diseases	1816 (10.3%)	73442 (9.3%)	75258 (9.4%)
Trauma	1569 (8.9%)	55714 (7.1%)	57283 (7.1%)
Infectious diseases	1565 (8.9%)	42624 (5.4%)	44189 (5.5%)
Respiratory diseases	846 (4.8%)	84394 (10.7%)	85240 (10.6%)
Genitourinary disorders	283 (1.6%)	38667 (4.9%)	38950 (4.8%)
Endocrine disorders	146 (0.8%)	34953 (4.4%)	35099 (4.4%)
Discharging Physician Specialty			
Hematology & Oncology	5244 (29.7%)	31242 (4.0%)	36486 (4.5%)
Internal Medicine	4414 (25%)	392396 (49.9%)	396810 (49.4%)
Cardiothoracic Surgery	2263 (12.8%)	13068 (1.7%)	15331 (1.9%)
General Practice Medicine	1334 (7.6%)	124221 (15.8%)	125555 (15.6%)
Critical Care Medicine	838 (4.8%)	13254 (1.7%)	14092 (1.8%)
General Surgery	803 (4.6%)	17139 (2.2%)	17942 (2.2%)
Cardiology	433 (2.5%)	81789 (10.4%)	82222 (10.2%)
Neurosurgery	185 (1%)	5796 (0.7%)	5981 (0.7%)

Table 3 Platelet transfusion guideline compliance by clinical context.

	Guideline Non-Compliant Platelet Transfusions	Guideline Compliant Platelet Transfusions
Overall	**14036 (26.9%)**	**38104 (73.1%)**
Neurologic, ophthalmic, ICH	197 (11%)	1587 (89%)
On ECMO	59 (10.1%)	528 (89.9%)
Cardiopulmonary bypass surgery	1885 (62.4%)	1134 (37.6%)
Invasive procedure	4714 (32.8%)	9652 (67.2%)
Bleeding	5668 (17.3%)	27040 (82.7%)
Anticoagulated	309 (11.4%)	2392 (88.6%)
Antiplatelet drug	1480 (57.8%)	1079 (42.2%)
HIT, TTP or ITP	676 (42.4%)	920 (57.6%)
Primary prophylaxis	8040 (51.2%)	7655 (48.8%)

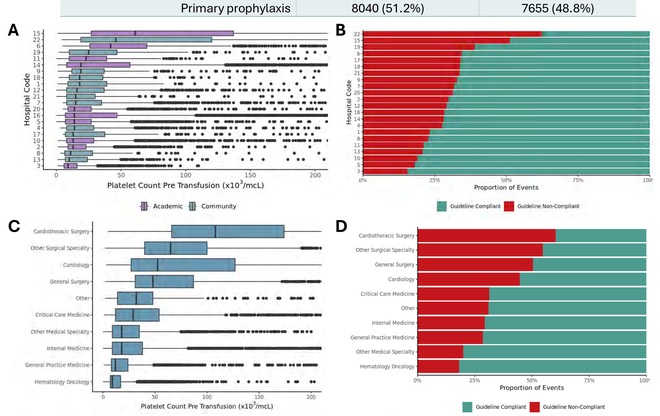

Figure 2 Median pre-transfusion threshold by (A) hospital site and (C) prescriber specialty. Platelet transfusion guideline compliance by (B) hospital site and (D) prescriber specialty.

Discussion

- The highest rates of non-compliant transfusions were observed in clinical contexts involving antiplatelet therapy, cardiopulmonary bypass surgery, invasive procedures, and immune-mediated thrombocytopenia.
- Hematology & Oncology prescribers had the lowest rates of guideline non-compliant transfusions of any specialty, but as heavy platelet users, this contributed over 25% of guideline non-compliant transfusions
- We observed high platelet transfusion thresholds being used in bypass surgery, with over 60% of transfusions occurring over 100,000/mcL
- Prophylactic platelet transfusion in patients with HIT and TTP occurred in about 40% of cases, which is potentially dangerous due to the increased thrombotic risk observed with platelet transfusion in this population[15]
- Limitations: retrospective design, unavailable data, assumed more liberal thresholds, no point-of-care tests captured, surgical admissions only included if they had an ICU stay, transfusions tied to MRP (ignoring consulting service or medical learners)
- This study represents a substantial effort to characterize platelet transfusion practice across academic and community hospitals through a comprehensive, multicenter database
- We observed variability in platelet transfusion practice and suggest key areas where targeted interventions may improve judicious platelet use
- Our simple, automated guideline compliance criteria could inform local quality improvement projects and standardize benchmarking
- In the future we aim to create a transfusion dashboard for physicians at GEMINI sites to see how their practice compares to peers

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Acknowledgements

This research is funded The Kenneth Fyke Award from Canadian Blood Services

GEMINI https://geminimedicine.ca/

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Evaluating the Efficacy and Tolerability of PJP prophylaxis with TMP-SMX in Autologous Stem Cell Transplants for Lymphoma or Myeloma: A Retrospective Cohort Study

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Introduction

- Patients undergoing allogeneic (HSCT) and autologous stem cell transplantation (ASCT) are at risk of opportunistic infections, including *Pneumocystis jirovecii* pneumonia (PJP).[1, 2, 5, 6]
- PJP is associated with high morbidity and mortality rates.[2, 3, 6]
- Trimethoprim-sulfamethoxazole (TMP-SMX or Septra) is recommended as routine PJP prophylaxis for patients undergoing HSCT.[1]
  - Prior to routine PJP prophylaxis, the incidence of PJP post-HSCT was estimated to be 9-16%.[3, 6]
  - Now reduced to <1% after the institution of routine PJP prophylaxis.[3, 4, 5, 6]
- However, its routine use in ASCT is debated.
  - Relatively lower incidence of PJP in post-ASCT.[1]
  - Adverse effects associated with TMP-SMX include hypersensitivity, renal impairment, myelosuppression and gastrointestinal disturbance.[1]
- Kingston Health Sciences Centre (KHSC) implemented routine PJP prophylaxis in ASCT patients in October 2020 in align with regional practice patterns.

Objective

To evaluate the adverse effects, tolerability, rate of adherence, and efficacy of TMP-SMX prophylaxis post-ASCT.

Methods and Cohort

2018 - 2022

Retrospective chart review of adults undergoing ASCT at **Kingston Health Sciences Centre (KHSC)**

No PJP Prophylaxis = 113

PJP Prophylaxis x 3 months = 86

	No PJP Prophylaxis	PJP Prophylaxis x 3 months
Age (Mean ± SD):	61.5 years ± 8.3	62.2 years ± 8.6
	34.5% ♀ 65.5% ♂	45.3% ♀ 54.7% ♂
Multiple Myeloma:	72.6%	65.1%
Lymphoma:	27.4%	34.9%

Data & Lab values collected:
- Pre-prophylaxis
- At 1-month post ASCT
- At 3-months post ASCT
- All Cause Mortality – March 2024 Data Cut-off

RStudio (v1.4.1717)

Results

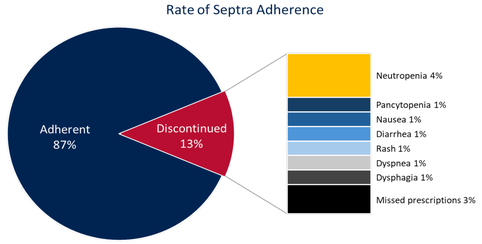

Figure 1. Rate of PJP prophylaxis adherence with TMP-SMX (Septra) and reasons for discontinuation. Reasons for discontinuation include cytopenia (n = 4), gastrointestinal symptoms (n = 3), skin rash (n = 1) , dyspnea (n = 1), and missed prescriptions (n = 2).

Cases of acute kidney injury:
No Septra = Vs. Septra =

No cases of hepatotoxicity in both cohorts

No cases of engraftment delay in both cohorts

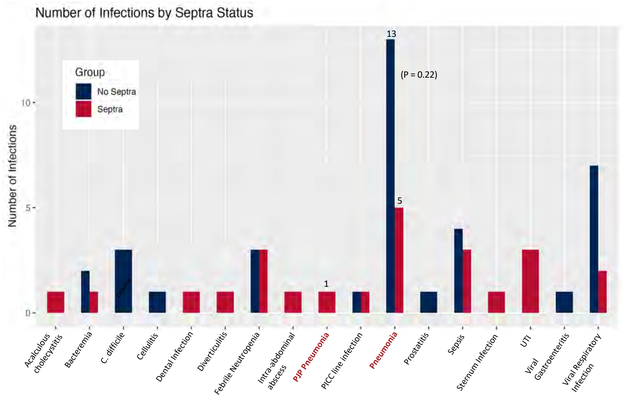

Figure 2. Incidence of infections between no PJP prophylaxis and PJP prophylaxis cohorts. Total of 36 infections in no prophylaxis cohort and 24 infections in prophylaxis cohort (P = 0.88). There were no significant differences between the proportion of specific type of infections between the two cohorts. 1 case of PJP pneumonia was captured in PJP prophylaxis cohort in setting of non-adherence.

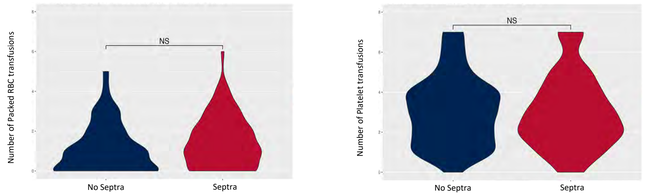

Figure 3 & 4. Violin Plot of RBC and platelet transfusions between no PJP prophylaxis and PJP prophylaxis cohorts. No significant differences were observed in RBC and platelet transfusions during the first month between the cohorts (P=0.055 and 0.74, respectively).

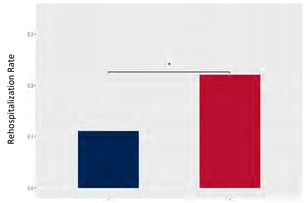

Figure 5. Rate of rehospitalization was 2.3 times higher in the prophylaxis cohort (P=0.048). No significant difference in rate of ICU admissions between the no prophylaxis cohort (n = 2) and prophylaxis cohort (n = 3) (P =0.66).

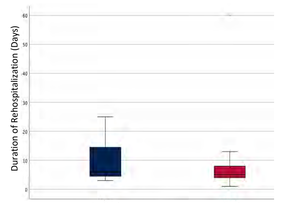

Figure 6. No significant difference in length of rehospitalization between two cohorts (P = 0.28).

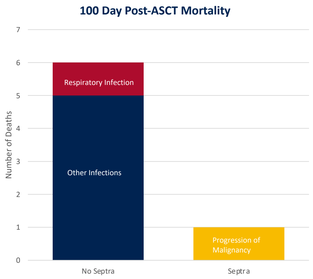

Figure 7. 100-day Post-ASCT Mortality Rate and Cause between no PJP prophylaxis versus PJP prophylaxis cohorts. No PJP-related deaths.

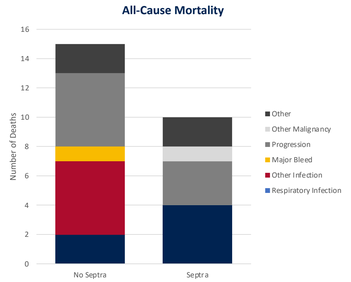

Figure 8. Post-ASCT All-Cause Mortality and Cause between no PJP prophylaxis versus PJP prophylaxis cohorts. No PJP-related deaths. No significant difference in mortality rate between two cohorts (P = 0.83).

Conclusion & Future Directions

- TMP-SMX (Septra) can be considered in post-ASCT for PJP prophylaxis.
  - Safe & well-tolerated with minimal adverse events.
  - High rates of adherence seen.
- This study captured 1 case of PJP pneumonia related to non-adherence to prophylaxis.
  - Suggests some protection against PJP infection post-ASCT.
  - However, this study was not able to evaluate the efficacy against PJP infection and mortality.
    - Insufficient cases captured and small population size of study.
    - Low incidence of PJP infections in the ASCT population.
- Future Directions:
  - Increased rehospitalization in prophylaxis cohort warrants further investigations into contributing factors.
  - Larger prospective or retrospective population studies are needed:
    - To capture sufficient cases of PJP pneumonia.
    - To determine the impact of TMP-SMX prophylaxis on reducing PJP-related morbidity and mortality in ASCT.

Acknowledgements

The authors gratefully acknowledge the partnership with Myeloma Canada and the local Kingston chapter who were instrumental in raising funds through local initiatives, resulting in a fund-sharing grant to support this project. We also extend our appreciation to the Quality Assurance Team in the Stem Cell Transplant and Cellular Therapy Program at the Cancer Centre of Southeastern Ontario (Kingston Health Sciences Center) for their invaluable support.

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Infectious Disease

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Summary

- *Effectiveness of chronic suppressive therapy for patients with prosthetic joint infection undergoing DAIR.*
- *Building the HIV database for the IIC clinic*
- *Hospital onset bacteremia as a quality metric for hospitals: A scoping review*
- *Risk of severe influenza in people who inject drugs: A population-based study*
- *Hospital-onset bacteremia as a quality metric for Ontario hospitals: A population-based study*
- *Description of recurrent Staphylococcus aureus infection*

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. Hospital onset bacteremia as a quality metric for hospitals: A scoping review

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

Methods: Scoping review

Summary: This is a scoping review to describe and summarize the current literature landscape on hospital onset bacteremia as a quality metric for infection control purposes in hospitals.

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 4. Risk of severe influenza in people who inject drugs: 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 determine if people who inject drugs are at an increased risk of severe influenza requiring hospitalization in Ontario.

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

Project 5. Hospital-onset bacteremia as a quality metric for Ontario hospitals: 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 rates of hospital-onset bacteremia cross Ontario hospitals and determine the association between hospital-onset bacteremia with mortality, length-of-stay in hospital and hospital cost.

Resident role: Resident will participate in data analysis meetings, perform a background literature search and help write-up of the manuscript as a co-author.

Time frame: 1 year

Project 6. Description of recurrent *Staphylococcus aureus* infection

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

Methods: Retrospective chart review study

Summary: This is a retrospective chart review study of patients who had recurrent serious *Staphylococcus aureus* infections at KHSC. The bacterial isolates will be tested to determine if the recurrent infections are due to the same or different *S. aureus* strains.

Resident role: Resident will assist with chart review / data collection and help write-up of the manuscript as a first author.

Time frame: 2 years

BMJ Open Quality

Increasing evidence-based care practices for patients with *Staphylococcus aureus* bacteraemia through required infectious diseases consultation in a tertiary care hospital: a quality improvement initiative

Arunima Soma Dalai,[1] Emma B Monti,[2] Raghad Mallesho,[3] Michael Obeda,[3] Gerald A Evans,[1] Santiago Perez-Patrigeon,[1] Evan Wilson,[1] Jorge L Martinez-Cajas,[1] Prameet M Sheth,[4] Lewis Tomalty,[4] Heather Wise,[5] Kiarah Shchepanik,[5] Amelia Wilkinson,[1] Geneviève C Digby,[1] Anthony D Bai [1]

To cite: Dalai AS, Monti EB, Mallesho R, *et al*. Increasing evidence-based care practices for patients with *Staphylococcus aureus* bacteraemia through required infectious diseases consultation in a tertiary care hospital: a quality improvement initiative. *BMJ Open Quality* 2025;**14**:e003243. doi:10.1136/bmjoq-2024-003243

Received 28 November 2024
Accepted 22 March 2025

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ABSTRACT

Background *Staphylococcus aureus* bacteraemia had a higher mortality rate than average at Kingston Health Sciences Centre (KHSC). Infectious diseases specialist consultation has been shown to improve outcomes for *S. aureus* bacteraemia by increasing adherence to evidence-based care practices. Yet, infectious disease specialists were not involved in many cases at KHSC.

Aim To improve adherence to evidence-based care practices by increasing the proportion of patients with *S. aureus* bacteraemia who receive a formal infectious diseases consultation.

Interventions A multimodal intervention consisting of (1) daily automated email of positive blood culture results to the infectious diseases team; (2) standardisation of prompts attached to positive blood culture results on the electronic medical record; (3) policy of mandatory infectious diseases consultation and (4) education of resident physicians.

Implementation and evaluation The outcome measure was adherence to evidence-based care practices, defined as echocardiography, repeating blood cultures and treatment with a first-line antibiotic. A secondary outcome measure was 90-day mortality. The process measure was the proportion of patients receiving formal infectious diseases consultation. A balancing measure was hospital length of stay. All measures were monitored semimonthly using statistical process control charts for time periods before and after intervention.

Results There were 171 and 186 patients with *S. aureus* bacteraemia in the preintervention and postintervention period, respectively. Between these two periods, the proportion of those who received evidence-based care practices increased from 73% to 82% (p=0.031) and demonstrated special cause variation. Mortality changed from 29% to 24% (p=0.400). The proportion of patients receiving an infectious diseases consultation increased from 47% to 90% (p<0.001) and demonstrated special cause variation. The median (IQR) length of stay was 18 (11–30) days and 17 (11–42) days in the preintervention and postintervention period, respectively (p=0.442).

Conclusions A multimodal intervention that implemented mandatory infectious diseases consultation significantly improved evidence-based care practices for *S. aureus* bacteraemia.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ *Staphylococcus aureus* bacteraemia is a common infection with a high mortality rate. Infectious diseases consultation is shown to improve adherence to evidence-based practices and outcomes.

WHAT THIS STUDY ADDS

⇒ This quality improvement initiative study demonstrated that a multimodal intervention that implemented mandatory infectious diseases consultation for *S. aureus* bacteraemia significantly improved evidence-based care practices.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ In other hospitals, similar quality improvement initiatives can be effective in improving the quality of care for *S. aureus* bacteraemia.

INTRODUCTION

Staphylococcus aureus bacteraemia is a common infection with an estimated annual incidence of 22 episodes per 100 000[1] and 90-day all-cause mortality of 27%.[2]

There are established quality-of-care indicators for *S. aureus* bacteraemia including thorough examination for metastatic foci, echocardiography to assess for endocarditis and repeat blood cultures to document clearance of bacteraemia.[3–5] Recommended

Aspiration pneumonia

Vincent Girard MD, Anthony D. Bai MD MSc

■ Cite as: *CMAJ* 2023 October 23;195:E1417. doi: 10.1503/cmaj.230628

1 Aspiration pneumonia causes 5%–15% of community-acquired pneumonias and an unknown proportion of hospital-acquired pneumonias[1]

Microaspiration is normal in healthy people and contributes to most causes of pneumonia. In contrast, aspiration pneumonia arises after a macroaspiration event. The mortality rate for aspiration pneumonia is more than twice that of other pneumonias.[1]

2 Aspiration pneumonia is a clinical diagnosis and is differentiated from other pneumonias based on clinical history and radiographic features

Risk factors include dysphagia and altered level of consciousness.[1] Macroaspiration events are usually unwitnessed but may be elicited on history.[1] Suggestive radiographic features include a right lower lobe infiltrate on chest radiography. Computed tomography may show bronchopneumonia or bronchiolitis in a gravity-dependent distribution.[2]

3 Routine anaerobic coverage is not indicated

Anaerobic bacteria are not major pathogens in aspiration pneumonia.[3] A current guideline recommends that aspiration pneumonia be treated with the same antibiotic regimen as community- or hospital-acquired pneumonia,[3] and that additional anaerobic-specific coverage (e.g., clindamycin, metronidazole) should be given only to patients with empyema, abscess or necrosis.[3]

4 Aspiration pneumonitis is clinically distinct from aspiration pneumonia, and management differs accordingly

Aspiration pneumonitis is an acute chemical lung injury from inhaled gastric contents immediately following an aspiration event.[4] It is distinct from pneumonia because symptom onset is rapid (minutes to hours) and resolution occurs after 24–48 hours. It is managed with supportive care that maintains airway and oxygenation, such as oropharyngeal suctioning and supplemental oxygen.[4] Aspiration pneumonitis is not a consequence of infection and does not benefit from antibiotic therapy.[4]

5 Macroaspiration is not an indication for gastric tube feeding

Compared with oral feeding, feeding by nasogastric or percutaneous gastrostomy tube does not decrease the risk of aspiration or pneumonia.[5] Routine measures to prevent aspiration pneumonia include swallowing assessments, positioning during feeding, texture modification of diet and mouth care.[1]

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Competing interests: None declared.

This article has been peer reviewed.

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CHEST

Anaerobic Antibiotic Coverage in Aspiration Pneumonia and the Associated Benefits and Harms

A Retrospective Cohort Study

Anthony D. Bai, MD; Siddhartha Srivastava, MD; Geneviève C. Digby, MD; Vincent Girard, MD; Fahad Razak, MD; and Amol A. Verma, MD

BACKGROUND: Antibiotics with extended anaerobic coverage are used commonly to treat aspiration pneumonia, which is not recommended by current guidelines.

RESEARCH QUESTION: In patients admitted to hospital for community-acquired aspiration pneumonia, does a difference exist between antibiotic therapy with limited anaerobic coverage (LAC) vs antibiotic therapy with extended anaerobic coverage (EAC) in terms of in-hospital mortality and risk of *Clostridioides difficile* colitis?

STUDY DESIGN AND METHODS: We conducted a multicenter retrospective cohort study across 18 hospitals in Ontario, Canada, from January 1, 2015, to January 1, 2022. Patients were included if the physician diagnosed aspiration pneumonia and prescribed guideline-concordant first-line community-acquired pneumonia parenteral antibiotic therapy to the patient within 48 h of admission. Patients then were categorized into the LAC group if they received ceftriaxone, cefotaxime, or levofloxacin. Patients were categorized into the EAC group if they received amoxicillin-clavulanate, moxifloxacin, or any of ceftriaxone, cefotaxime, or levofloxacin in combination with clindamycin or metronidazole. The primary outcome was all-cause in-hospital mortality. Secondary outcomes included incident *C difficile* colitis occurring after admission. Overlap weighting of propensity scores was used to balance baseline prognostic factors.

RESULTS: The LAC and EAC groups included 2,683 and 1,316 patients, respectively. In hospital, 814 patients (30.3%) and 422 patients (32.1%) in the LAC and EAC groups died, respectively. *C difficile* colitis occurred in five or fewer patients (≤ 0.2%) and 11 to 15 patients (0.8%-1.1%) in the LAC and EAC groups, respectively. After overlap weighting of propensity scores, the adjusted risk difference of EAC minus LAC was 1.6% (95% CI, –1.7% to 4.9%) for in-hospital mortality and 1.0% (95% CI, 0.3%-1.7%) for *C difficile* colitis.

INTERPRETATION: We found that extended anaerobic coverage likely is unnecessary in aspiration pneumonia because it was associated with no additional mortality benefit, only an increased risk of *C difficile* colitis.

CHEST 2024; 166(1):39-48

KEY WORDS: antibiotic treatment; aspiration pneumonia; mortality

ABBREVIATIONS: ATS = American Thoracic Society; CAP = community-acquired pneumonia; CIF = cumulative incidence function; EAC = extended anaerobic coverage; ICD-10-CA = International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Canada; IDSA = Infectious Diseases Society of America; IQR = interquartile range; LAC = limited anaerobic coverage; mLAPS = modified Laboratory-Based Acute Physiology Score; sHR = subdistribution hazard ratio

AFFILIATIONS: From the Division of Infectious Diseases (A. D. B.), the Division of General Internal Medicine (S. S.), the Division of Respirology (G. C. D.), the Internal Medicine Residency Program (V. G.), Department of Medicine, Queen's University, Kingston, the

JAMA Network Open

Original Investigation | Medical Journals and Publishing

Comparison of Preprint Postings of Randomized Clinical Trials on COVID-19 and Corresponding Published Journal Articles

A Systematic Review

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Abstract

IMPORTANCE Randomized clinical trials (RCTs) on COVID-19 are increasingly being posted as preprints before publication in a scientific, peer-reviewed journal.

OBJECTIVE To assess time to journal publication for COVID-19 RCT preprints and to compare differences between pairs of preprints and corresponding journal articles.

EVIDENCE REVIEW This systematic review used a meta-epidemiologic approach to conduct a literature search using the World Health Organization COVID-19 database and Embase to identify preprints published between January 1 and December 31, 2021. This review included RCTs with human participants and research questions regarding the treatment or prevention of COVID-19. For each preprint, a literature search was done to locate the corresponding journal article. Two independent reviewers read the full text, extracted data, and assessed risk of bias using the Cochrane Risk of Bias 2 tool. Time to publication was analyzed using a Cox proportional hazards regression model. Differences between preprint and journal article pairs in terms of outcomes, analyses, results, or conclusions were described. Statistical analysis was performed on October 17, 2022.

FINDINGS This study included 152 preprints. As of October 1, 2022, 119 of 152 preprints (78.3%) had been published in journals. The median time to publication was 186 days (range, 17-407 days). In a multivariable model, larger sample size and low risk of bias were associated with journal publication. With a sample size of less than 200 as the reference, sample sizes of 201 to 1000 and greater than 1000 had hazard ratios (HRs) of 1.23 (95% CI, 0.80-1.91) and 2.19 (95% CI, 1.36-3.53) for publication, respectively. With high risk of bias as the reference, medium-risk articles with some concerns for bias had an HR of 1.77 (95% CI, 1.02-3.09); those with a low risk of bias had an HR of 3.01 (95% CI, 1.71-5.30). Of the 119 published preprints, there were differences in terms of outcomes, analyses, results, or conclusions in 65 studies (54.6%). The main conclusion in the preprint contradicted the conclusion in the journal article for 2 studies (1.7%).

CONCLUSIONS AND RELEVANCE These findings suggest that there is a substantial time lag from preprint posting to journal publication. Preprints with smaller sample sizes and high risk of bias were less likely to be published. Finally, although differences in terms of outcomes, analyses, results, or conclusions were observed for preprint and journal article pairs in most studies, the main conclusion remained consistent for the majority of studies.

JAMA Network Open. 2023;6(1):e2253301. doi:10.1001/jamanetworkopen.2022.53301

Key Points

Question How do preprints of randomized clinical trials (RCTs) on COVID-19 differ from their corresponding published journal articles?

Findings In this systematic review of 152 COVID-19 RCT preprints posted in 2021, 119 (78%) were subsequently published in a scientific, peer-reviewed journal. When preprint and journal article pairs were compared, there were differences in terms of outcomes, analyses, results, or conclusions in 65 of 119 studies (55%); however, the main conclusion remained consistent for all but 2 studies (2%).

Meaning These findings suggest that although there were differences in the outcomes, analyses, results, or conclusions between RCT preprint and journal article pairs in most cases, the main conclusion remained consistent for the majority of studies.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

Clinical Microbiology and Infection 28 (2022) 1076–1084

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Systematic review

Staphylococcus aureus bacteraemia mortality: a systematic review and meta-analysis

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ARTICLE INFO

Article history:
Received 11 January 2022
Received in revised form
9 March 2022
Accepted 12 March 2022
Available online 23 March 2022

Editor: M. Paul

Keywords:
Staphylococcus aureus
Bacteraemia
Mortality
Meta-analysis

ABSTRACT

Background: Precise estimates of mortality in *Staphylococcus aureus* bacteraemia (SAB) are important to convey prognosis and guide the design of interventional studies.
Objectives: We performed a systematic review and meta-analysis to estimate all-cause mortality in SAB and explore mortality change over time.
Data sources: The MEDLINE and Embase databases, as well as the Cochrane Database of Systematic Reviews, were searched from January 1, 1991 to May 7, 2021.
Study eligibility criteria: Human observational studies on patients with *S. aureus* bloodstream infection were included.
Participants: The study analyzed data of patients with a positive blood culture for *S. aureus*.
Methods: Two independent reviewers extracted study data and assessed risk of bias using the Newcastle–Ottawa Scale. A generalized, linear, mixed random effects model was used to pool estimates.
Results: A total of 341 studies were included, describing a total of 536,791 patients. From 2011 onward, the estimated mortality was 10.4% (95% CI, 9.0%–12.1%) at 7 days, 13.3% (95% CI, 11.1%–15.8%) at 2 weeks, 18.1% (95% CI, 16.3%–20.0%) at 1 month, 27.0% (95% CI, 21.5%–33.3%) at 3 months, and 30.2% (95% CI, 22.4%–39.3%) at 1 year. In a meta-regression model of 1-month mortality, methicillin-resistant *S. aureus* had a higher mortality rate (adjusted OR (aOR): 1.04; 95% CI, 1.02–1.06 per 10% increase in methicillin-resistant *S. aureus* proportion). Compared with prior to 2001, more recent time periods had a lower mortality rate (aOR: 0.88; 95% CI, 0.75–1.03 for 2001–2010; aOR: 0.82; 95% CI, 0.69–0.97 for 2011 onward).
Conclusions: SAB mortality has decreased over the last 3 decades. However, more than one in four patients will die within 3 months, and continuous improvement in care remains necessary. **Anthony D. Bai, Clin Microbiol Infect 2022;28:1076**

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https://doi.org/10.1016/j.cmi.2022.03.015
1198-743X/

Clinical Infectious Diseases

BRIEF REPORT

How Generalizable Are Randomized Controlled Trials (RCTs) in *Staphylococcus aureus* Bacteremia? A Description of the Mortality Gap Between RCTs and Observational Studies

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In *Staphylococcus aureus* bacteremia, mortality rates in randomized controlled trials (RCTs) are consistently lower than observational studies. Stringent eligibility criteria and omission of early deaths in RCTs contribute to this mortality gap. Clinicians should acknowledge the possibility of a lower treatment e! ect when applying RCT results to bedside care.

Keywords. *Staphylococcus aureus*; bacteremia; mortality; trials.

To evaluate the e! ect of interventions on mortality in *Staphylococcus aureus* bacteremia (SAB), there have been increasing e! orts to conduct pragmatic randomized controlled trials (RCTs). " e results from these RCTs are intended to inform SAB management at the bedside. Yet to be generalizable to clinical practice, patients in pragmatic RCTs should be similar to patients who are going to be treated outside of trials in terms of baseline characteristics and prognosis. Unfortunately, this may not be the case in RCTs for several reasons. For example, external validity is reduced when eligibility criteria are stringent or if a delay due to consent and enrollment processes omits the sickest patients who died early. " is will be ampli#ed in trials where enrollment occurs later into the treatment course, such as trials evaluating stepdown to oral antibiotics or antibiotic duration.

By contrast, observational studies on SAB are more likely to represent the general SAB patient population with respect to mortality, because most observational studies recruit consecutive patients with minimal exclusion criteria and typically capture all patients from the time of blood culture collection—including those who die early.

We recently conducted a systematic review and meta-analysis on mortality in SAB [1]. In this secondary analysis, we compared the all-cause mortality rates observed in RCTs versus observational studies. We hypothesized that there is a substantial gap in the observed mortality between observational studies and RCTs. " is would be important when translating trial results to patient care at the bedside and when designing future RCTs.

METHODS

The systematic review protocol was registered (PROSPERO CRD42021253891) and described elsewhere [1]. To summarize, a literature search was performed using MEDLINE, Embase, and the Cochrane Database of Systematic Reviews for dates between 1 January 1991 and 7 May 2021 using MeSH terms to capture *S. aureus*, bacteremia, and mortality. Studies (RCTs and observational studies) that included patients with SAB based on positive blood culture(s) and reported numbers for all-cause mortality were included. Studies that included bacteremia due to bacteria other than *S. aureus* were excluded. Two independent reviewers extracted the data in duplicate.

In this secondary analysis, RCTs were compared to observational studies in 2 ways. First, RCTs were compared to all observational studies. In our original systematic review [1], a meta-regression model showed that the decade and geographic continent that the study was conducted in as well as methicillin resistance were important predictors of mortality. " erefore, for the second comparison, we matched each RCT to 4 observational studies involving patients from the same decade, describing the same population in detail (all SAB including methicillin-resistant *S. aureus* [MRSA] and methicillin-susceptible *S. aureus* [MSSA], only MRSA, or only MSSA), and reporting mortality at the same timepoint(s) as the RCT. For

Received 31 December 2021; editorial decision 25 February 2022; published online 4 March 2022.

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Clinical Infectious Diseases® 2022;XX(XX):1–4

https://doi.org/10.1093/cid/ciac177

Open Forum Infectious Diseases

MAJOR ARTICLE

What Is the Optimal Follow-up Length for Mortality in *Staphylococcus aureus* Bacteremia? Observations From a Systematic Review of Attributable Mortality

Anthony D. Bai,[1,2] Carson K. L. Lo,[3] Adam S. Komorowski,[2,4] Mallika Suresh,[5] Kevin Guo,[6] Akhil Garg,[7] Pranav Tandon,[8] Julien Senecal,[9] Olivier Del Corpo,[10] Isabella Stefanova,[5] Clare Fogarty,[11] Guillaume Butler-Laporte,[12] Emily G. McDonald,[13] Matthew P. Cheng,[14] Andrew M. Morris,[15] Mark Loeb,[3] and Todd C. Lee[13]

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Background. Deaths following *Staphylococcus aureus* bacteremia (SAB) may be related or unrelated to the infection. In SAB therapeutics research, the length of follow-up should be optimized to capture most attributable deaths and minimize nonattributable deaths. We performed a secondary analysis of a systematic review to describe attributable mortality in SAB over time.

Methods. We systematically searched Medline, Embase, and Cochrane Database of Systematic Reviews from 1 January 1991 to 7 May 2021 for human observational studies of SAB. To be included in this secondary analysis, the study must have reported attributable mortality. Two reviewers extracted study data and assessed risk of bias independently. Pooling of study estimates was not performed due to heterogeneity in the de! nition of attributable deaths.

Results. Twenty-four observational cohort studies were included. " e median proportion of all-cause deaths that were attributable to SAB was 77% (interquartile range [IQR], 72%–89%) at 1 month and 62% (IQR, 58%–75%) at 3 months. At 1 year, this proportion was 57% in 1 study. In 2 studies that described the rate of increase in mortality over time, 2-week follow-up captured 68 of 79 (86%) and 48 of 57 (84%) attributable deaths that occurred by 3 months. By comparison, 1-month follow-up captured 54 of 57 (95%) and 56 of 60 (93%) attributable deaths that occurred by 3 months in 2 studies.

Conclusions. " e proportion of deaths that are attributable to SAB decreases as follow-up lengthens. Follow-up duration between 1 and 3 months seems optimal if evaluating processes of care that impact SAB mortality.

Clinical Trials Registration. PROSPERO CRD42021253891.

Keywords. attributable mortality; bacteremia; follow-up; mortality; *Staphylococcus aureus*; systematic review.

Staphylococcus aureus bacteremia (SAB) is a common bloodstream infection with a high mortality rate [1]. The mortality in SAB varies greatly across studies from 10% to 30% [1, 2]. One contributing factor to the wide range of mortality estimates is a lack of consensus on the optimal follow-up duration for SAB, which is reflected by varied length of follow-up across studies ranging from 2 weeks [3, 4] to 1 year [5, 6].

In principle, follow-up should be long enough to capture most deaths attributable to SAB. However, as follow-up lengthens, deaths that are not attributable to SAB will accumulate and, at a certain time point, the ability to determine the impact of processes of care on SAB becomes confounded by the competing risk of death from all other causes. For example, consider an intervention where patients received combination antibiotic therapy in the ! rst 5 days. If the patient dies within the ! rst week, that may have a strong correlation to the treatment whereas if a patient dies of lung cancer in month 11, it is extremely unlikely to be related. In fact, once the bacteremia is cured, outside of a relapse or major irreversible drug toxicity, it is unlikely that any death beyond a certain time point would be related to the initial therapy. Based on the same logic, a study that examines risk factors for mortality over a long period would converge on general predictors of life expectancy that are unrelated to the management of SAB.

Received 1 December 2021; editorial decision 16 February 2022; accepted 19 February 2022; published online 10 April 2022.

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Open Forum Infectious Diseases®2022

https://doi.org/10.1093/ofid/ofac096

International Journal of Infectious Diseases 122 (2022) 405–411

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Review

Staphylococcus aureus bacteremia mortality across country income groups: A secondary analysis of a systematic review

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ARTICLE INFO

Article history:
Received 24 March 2022
Revised 29 May 2022
Accepted 14 June 2022

Keywords:
Staphylococcus aureus
Bacteremia
Mortality
Low and middle income countries

ABSTRACT

Objectives: *Staphylococcus aureus* bacteremia (SAB) is a common infection worldwide. We compared SAB mortality in low- and middle-income countries (LMIC) versus high-income countries (HIC) in a meta-analysis.

Methods: We searched MEDLINE, Embase, and Cochrane Database of Systematic Reviews from 1991-2021 and included observational, single-country studies on patients with positive blood cultures for *S. aureus*. The main outcome was the proportion of patients with SAB who died in the hospital. A generalized linear mixed random-effects model was used to pool estimates, and a meta-regression was used to adjust for study-level characteristics.

Results: A total of 332 studies involving 517,671 patients in 39 countries were included. No study was conducted in a low-income country. Only 33 (10%) studies were performed in middle-income countries (MIC), which described 6,216 patients. The pooled in-hospital mortality was 32.4% (95% confidence interval [CI] 27.2%-38.2%, $T^2 = 0.3063$) in MIC and 22.3% (95% CI 20.1%-24.6%, $T^2 = 0.3257$) in HIC. In a meta-regression model, MIC had higher in-hospital mortality (adjusted odds ratio 1.37, 95% CI 1.11-1.71; $P = 0.0042$) than HIC.

Conclusion: In SAB studies, LMIC are poorly represented. In-hospital mortality was significantly higher in MIC than in HIC. Research should be conducted in LMIC to characterize differences in care processes driving the mortality gap.

Introduction

Staphylococcus aureus bacteremia (SAB) is a common cause of bloodstream infection and is associated with significant morbidity and mortality. In previous studies, estimates for the incidence

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https://doi.org/10.1016/j.ijid.2022.06.026

Nephrology

Dr. David Holland
Division Chair

Summary

- *Quality improvement interventions for patients with acute kidney injury*
- *Association of Primary Care Continuity with Home Dialysis, Transplantation, and Utilization of Medical Services for Patients Starting Hemodialysis*
- *Quality Improvement Pilot: The Safety and Efficacy of Weight-Based MMF Dosing in Kidney Transplant Patients*

- Samuel Silver MD, MSc
- Clinical training University of Toronto
- MSc quality improvement and patient safety
- Veteran’s Affairs Quality Scholar (UCSF)
- Fellowship in acute kidney injury (AKI) health services research Stanford University

Interests:

- Administrative data to inform the design of quality improvement interventions
- Systematic reviews and meta-analyses
- Delivery of care for patients with AKI, both during the inpatient and outpatient setting

Current Projects:

- Specialized follow-up after AKI (blood pressure trends, quality of life, perspectives of primary care providers)
- Strategies to promote kidney recovery after AKI (survey of nephrologist practice patterns)

Healthcare Provider Awareness Of AKI In Patients With Advanced CKD Undergoing Surgery: A Descriptive Study of Preoperative Notes

Jonah Buckstein[1], Sarah Hammond[1], Tyrone Harrison[2] Samuel Silver[1]
Division of Nephrology, Kingston Health Sciences Center[1], University of Calgary[2]

1. INTRODUCTION

- The KDIGO guidelines offer a bundle of preventative strategies to mitigate AKI risk.
- Our study examined how often the risk of post-operative AKI and elements of the KDIGO bundle were mentioned by preoperative healthcare providers in their assessments.

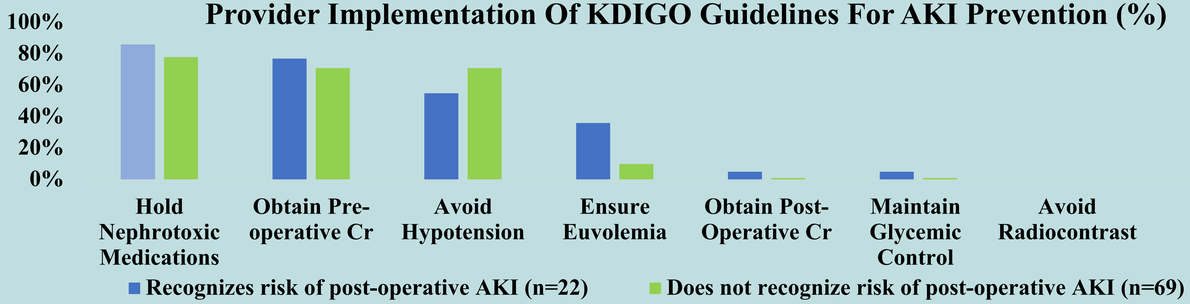
2. METHODOLOGY

- We conducted a retrospective chart review of 91 patients seen in an advanced CKD clinic who underwent an elective surgical procedure that included an anesthesia pre-operative assessment between 2017-2022.
- We extracted data on provider awareness of AKI, inclusion of KDIGO bundle elements in preoperative assessments, and qualitative comments on AKI risk assessment.
- We analyzed the quantitative data descriptively, stratifying our findings by preoperative healthcare provider awareness of AKI.

Primary Outcome: Frequency of provider awareness of post-operative AKI risk

Secondary Outcomes: Frequency of specific provider recommendations to mitigate post-operative AKI risk in keeping with the KDIGO strategies

3. RESULTS



3. RESULTS CONTINUED

Mean age: 76 (±13)
75% Male
96% category 4/5 CKD

24% **Of providers comment on postoperative AKI risk**

40% **Of providers comment on postoperative cardiac risk**

In qualitative comments, providers who recognized postoperative AKI risk frequently mentioned the potential for dialysis (n=12/22, 55%), rarely utilized risk scores (n=1/22, 5%), and did not provide any actionable postoperative orders (n=0/22, 0%)

Postoperative AKI & dialysis frequencies were 13% and 1%, respectively

"I did discuss the perioperative risk with the patient and the potential need for post-operative hemodialysis, either temporarily or permanently"

4. CONCLUSIONS

- Our study demonstrates that providers infrequently document the risk of postoperative AKI.
- However, providers recognize the potential cardiac risk at almost double the rate, highlighting the possible discrepancy in attention these complications receive pre-operatively.
- Opportunities may exist to improve the perioperative care of patients with advanced CKD by increasing awareness of AKI risk and the KDIGO bundle elements.

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Association of Primary Care Continuity with Home Dialysis, Transplantation, and Utilization of Medical Services for Patients Starting Hemodialysis

Cole Wyman[1], Maya Djerboua[2], Kristin Clemens[3, 2], Manish M. Sood[4], Samuel A. Silver[2, 5]

1. Western University, ON, Canada. 2. Institute for Clinical Evaluative Sciences, Toronto, ON, Canada. 3. Division of Endocrinology and Metabolism and Department of Epidemiology and Biostatistics, Western University, London, ON, Canada. 4. University of Ottawa Faculty of Medicine, Ottawa, ON, Canada. 5. Division of Nephrology, Kingston Health Sciences Center, Queen's University, Kingston, ON, Canada

1. Background

- Transition to maintenance hemodialysis is a challenging period for patients
- Primary care management may provide emotional support and healthcare guidance through this transition

2. Objectives

- We aimed to understand if pre-dialysis continuity with the same Primary Care Physician (PCP) can:

1. Influence uptake of home dialysis or transplantation
2. Improve access to healthcare services

3. Methods

- Using administrative databases in Ontario, Canada we conducted a retrospective population-based study, propensity matching patients initiating maintenance dialysis between 2007 to 2017
- We identified high PCP continuity using the usual provider of care (UPC) index (>75% of PCP visits over 2-years with the same PCP)

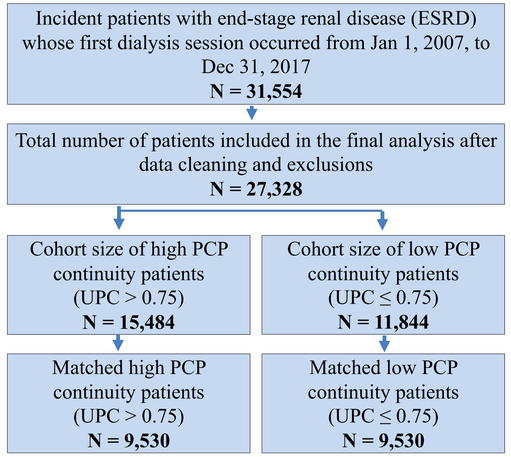

Figure 1: Cohort build for propensity score matching

Baseline Characteristics	Low Continuity (n=9530)	High Continuity (n=9530)	Standardized Difference
Age (years), median (IQR)	67 (56-77)	67 (56-77)	0.01
Female, n (%)	3666 (38.5)	3666 (38.5)	0.00
Rural residence, n (%)	1115 (11.7)	1138 (11.9)	0.01
Rostered to a primary care physician, n (%)	8009 (84.0)	8009 (84.0)	0.00
Physician's dialysis patient volume in previous year, n (%)			
0	1680 (17.6)	1682 (17.7)	0.001
1	1977 (20.8)	1965 (20.6)	0.003
2	1679 (17.6)	1689 (17.7)	0.003
3	1260 (13.2)	1296 (13.6)	0.01
4	853 (9.0)	826 (8.7)	0.01
≥5	2081 (21.8)	2072 (21.7)	0.002

Table. 1: Baseline characteristics of patients starting maintenance hemodialysis propensity matched on PCP continuity

4. Results for Main Outcomes

- High PCP continuity prior to maintenance hemodialysis initiation was only associated with a significant increase in the utilization of colon cancer screening, influenza vaccination, and comprehensive diabetes care

Outcome and Exposure	No. (%) of Events	Event per 100 Patient-Years	Hazard Ratio (95% CI)
Home dialysis			
Low continuity	2930 (30.8)	14.0	Referent
High continuity	2939 (30.8)	14.0	1.00 (0.97-1.04
Kidney transplantation			
Low continuity	1384 (14.5)	4.5	Referent
High continuity	1329 (13.9)	4.3	0.97 (0.90-1.04)

Table 2: Association of home dialysis and kidney transplantation with primary care physician continuity in 9530 propensity-matched patients

Outcome and Exposure	No. Events per Patient-Year	Hazard Ratio (95% CI)
Colon cancer screening		
Low continuity	0.10	Referent
High continuity	0.11	**1.07 (1.01-1.14)**
Influenza immunization		
Low continuity	0.22	Referent
High continuity	0.29	**1.33 (1.27-1.39)**
Diabetes assessment		
Low continuity	0.45	Referent
High continuity	0.55	**1.23 (1.14-1.33)**

Table 3: Association of colon cancer screening, influenza immunization, and diabetes assessment with primary care physician continuity in 9530 propensity-matched patients

Healthcare services outcomes with non-significant results:

- **Specialist Visits**: Cardiology, Endocrinology, Psychiatry, Palliative Care
- **Cancer Screening**: Mammography, PAP, PSA
- **Other Preventative Care**: Diabetes vision screening

5. Conclusions

- High PCP continuity before dialysis initiation was not associated with increased utilization of home dialysis or transplantation
- We observed only small effects of high PCP continuity on medical care outside of influenza vaccination and comprehensive diabetes care
- Given the competing health and time demands of patients on maintenance hemodialysis, additional work is needed to clarify how primary care may best benefit this patient population

For enquiries, please contact cwyman3@uwo.ca

Expedited Pre-kidney Transplant Workup

A Quality Improvement Study

Abdelrahman Elsebaie, BHSc[1], Natalie Witton, RN, BScN[2], Wilma Hopman , MA[1,2], David Holland, MD, MSc[1,2], and M. Khaled Shamseddin, MD, MSc[1,2]

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BACKGROUND AND RATIONALE

- Failure to complete a comprehensive pre-kidney transplant workup in a timely fashion results in:
  - Increased dialysis exposure
  - Poorer post-transplant survival
  - Higher resource demands.
- Candidates are worked-up by our transplant program post-referral rather than by their dialysis programs
- We aimed to assess quality metrics at our program, focusing on variability in the duration of pre-Tx workup after adopting a more frequent and scheduled chart review process by our newer coordinator to expedite pre-transplant workup

METHODS AND COHORT

Retrospective Single Center Study

***W/U*: Jan. 1, 2021 – Dec. 31, 2022**

***F/U*: Mar. 1, 2024**

Kingston Kidney Transplant Program (KKTP)

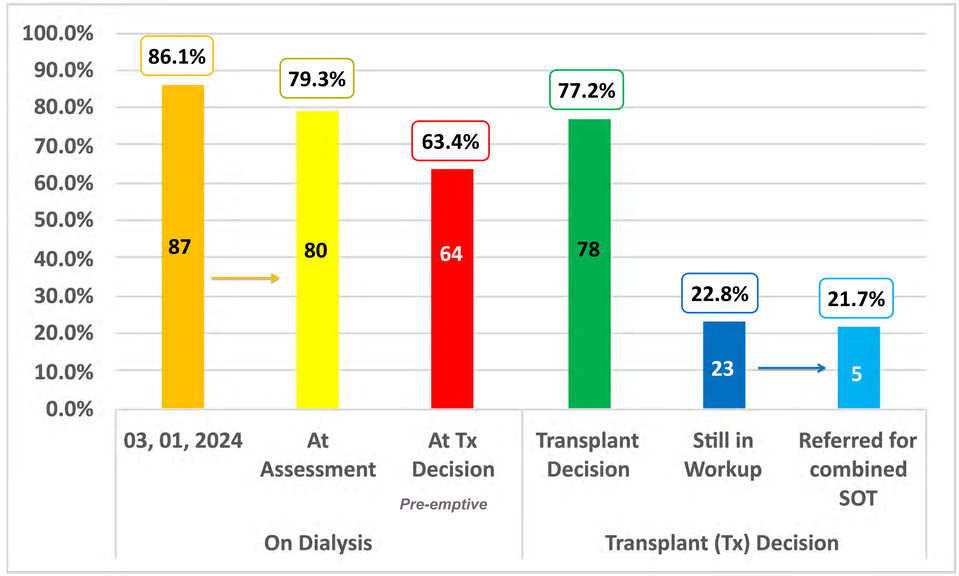
101 Kidney Transplant Candidates

42.6% ♀ 57.4% ♂

Caucasian: 76.2%

Age: 55.4 ± 13.1 years

RESULTS



Median (IQR) Time of Pre-Tx Workup: Time from Assessment-to-Transplant Decision (*months*)		
More Regular Pre-Transplant Chart Review	12.8 (7.2-20.4)	*P* <0.001
Historical Candidates Workup (Old Practice)	23.3 (14.3-37.1)	

Median (IQR) Time from Dialysis-to-Initial Assessment (*months*)		
More Regular Pre-Transplant Chart Review	7.9 (2.9-32.1)	*P* <0.12
Historical Candidates Workup (Old Practice)	5.6 (7.0-20.8)	

Median (IQR) Time from Dialysis-to-Transplant Decision (*months*)		
More Regular Pre-Transplant Chart Review	24.1 (12.3-43.2)	*P* <0.89
Historical Candidates Workup (Old Practice)	31.6 (5.9-52.4)	

CONCLUSIONS

- Frequent and scheduled chart review of pre-transplant candidates results in shorter:
  - Pre-transplant workup
  - Dialysis vintage
- Dialysis vintage can be reduced further by earlier referral for pre-transplant assessment

ABBREVIATIONS

Tx: transplant; P***re-Tx:*** pre-transplant; ***W/U:*** workup; ***IQR:*** interquartile range; ♀: female; ♂: male.

ACKNOWLEDGEMENT

We thank Ms. Wilma Hopman for her excellent statistical analysis.

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In-Limbo Pre-kidney Transplant Workup

A Quality Assessment/Process Improvement Program

Abdelrahman Elsebaie, BHSc[1], Natalie Witton, RN, BScN[2], Wilma Hopman , MA[1,2], David Holland, MD, MSc[1,2], and M. Khaled Shamseddin, MD, MSc[1,2]

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

BACKGROUND AND RATIONALE

- Failure to complete a comprehensive pre-kidney transplant workup in a timely fashion results in:
  - Increased dialysis exposure
  - Poorer post-transplant survival
  - Higher resource demands
- As referrals come to transplant centers, patients who are in 'pending activation limbo' are either neglected or detract from new patients' evaluation
- Candidates are worked-up by our transplant program post-referral rather than by the dialysis programs
- We aimed to assess metrics of quality at our program focusing on variability in the duration of pre-transplant workup among different coordinators, processes, and populations

METHODS AND COHORT

Retrospective Single Center Study

W/U Started: Prior to Jan. 01, 2021

F/U: Mar. 01, 2024

Kingston Kidney Transplant Program (KKTP)

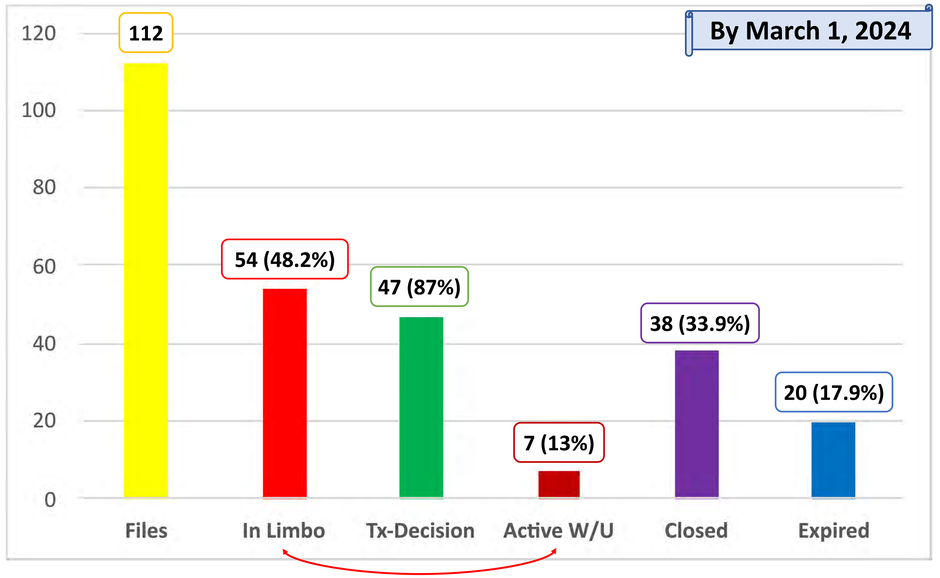
112 Kidney Transplant Candidate's Files

44.4% ♀ 55.6% ♂

Caucasian: 74.1%

Age: 54.5 ± 10.7 years

RESULTS



Median (IQR) Time of Pre-Transplant (Tx) Workup for "In Limbo" Candidates (*months*)		
Time from Assessment-to-Transplant Decision	23.3 (14.3-37.1)	
➢ *With More Frequent Pre-Transplant Assessments*	20.2 (9.7-32.1)	*P* = 0.037
➢ *With Once Pre-Transplant Assessment*	27.1 (18.6-40.1)	
Time from Chart Review-to-Transplant Decision	7.7 (3-16)	
Time from Assessment-to-Date (Active W/U)	44.6 (42.4-55.7)	

Dialysis Prevalence & Vintage of "In Limbo" Candidates at the Time of Transplant Decision		
38 (81%)	< 12 months	> 24 months
	24 (63%)	9 (24%)

CONCLUSIONS

- "In Limbo" pre-transplant assessment represents a significant challenge for transplant programs
- "In Limbo" candidates often undergo a prolonged pre-transplant workup
- Increasing the frequency of pre-transplant assessments can significantly shorten the duration of pre-transplant workup
- Expediting the pre-transplant workup helps reduce dialysis vintage

ABBREVIATIONS

Tx: transplant; ***Pre-Tx:*** pre-transplant; ***W/U:*** workup; ***IQR:*** interquartile range; ♀: female; ♂: male.

ACKNOWLEDGEMENT

We thank Ms. Wilma Hopman for her excellent statistical analysis.

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The Safety and Efficacy of Weight-Based MMF Dosing in Kidney Transplant Patients: A Quality Improvement Pilot

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BACKGROUND AND RATIONALE

- MMF ↓ the risk of AR in KTRs and ↑ graft survival.
- MMF is usually prescribed in fixed doses at 2 g/day.
- Due to its side effects, doses often require reduction.
- Weight-based MMF dosing (10-16 mg/kg) was correlated with therapeutic level in Asian KTRs.
- We are aiming to evaluate the safety and efficacy of weight-based MMF dosing at 15 mg/kg/day, adopted by our program at KGH in September 2021.

METHODS AND COHORT

Retrospective Single Center Study
Snapshot: 08/31/2023 (Presented)
Retrospective: 09/01/2021 – 08/31/2023

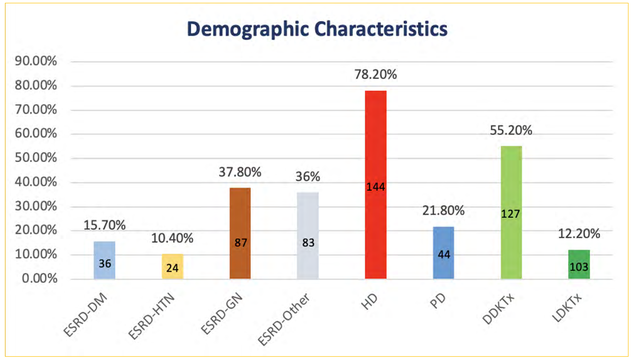
Kingston Kidney Transplant Program (KKTP)

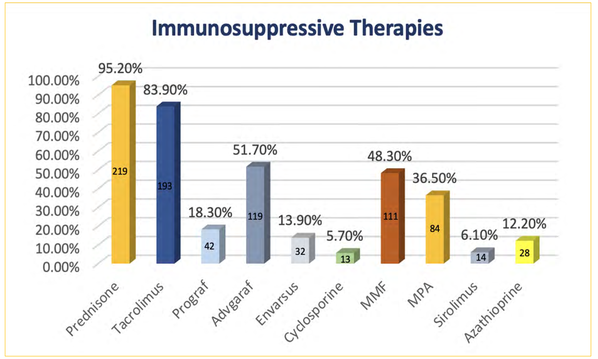
230 Kidney Transplant Patients

♀ 36.1% ♂ 63.9%

Caucasian 87.8%
Age: 56.9±14.4 years

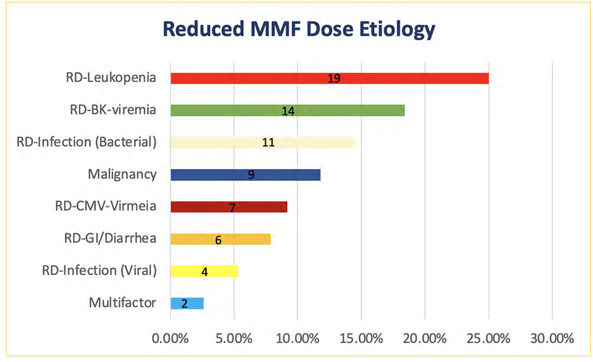
RESULTS





MMF		
Wgt-Based	Fixed Dose	Reduced Dose
18 (7.8%)	17 (7.4%)	76 (33%)
15.9 (14.9-18.1) mg/kg	20.7 (17.2-26.2) mg/gh	14.4 (10.4-16.9) mg/kg

Table 1: MMF Dosage Regimens.



Last Visit				
eGFR	ACR	Leukopenia	BK-Viremia	CMV-Viremia
56.5 (43.8-69.3)	3.6 (1.5-12.4)	4 (1.7%)	7 (3%)	1 (0.4%)

Table 2: Last Visit Outcomes.

	Tacrolimus		Sirolimus	
	On	Off	On	Off
uACR	15.8	32.9	56.1	16.1
P Value	0.032		0.007	

Table 3: Tacrolimus and Sirolimus Impact on uACR.

CONCLUSIONS

- 111 (48.3%) patients were on MMF.
- 33% of MMF patients were on reduced doses due to adverse effects, most notably leukopenia (25%).
- Only 18 patients were on weight-based MMF dosage; however, it is likely more patients were on weight-based dosage before doses were reduced further due to side effects.
- Snapshot data showed a low rate of leukopenia, BK- and CMV-viremia/infection, likely due to effective MMF dose reduction.
- Further analysis to be done through our next retrospective cohort study to evaluate outcomes.

ABBREVIATIONS

MMF: mycophenolate mofetil; ***MPA:*** mycophenolic acid; ***AR:*** acute rejection; ***KTRs:*** kidney transplant recepients; ***ESRD:*** end-stage renal disease; ***HD:*** hemodialysis; ***PD:*** peritoneal dialysis; ***DDKTx:*** deceased donor kidney transplant ***LDKTx:*** live donor kidney transplant ***RD:*** reduced dose ***eGFR:*** estimated glomerular filtration rate ***uACR/ACR:*** urine albumin-creatinine ratio

ACKNOWLEDGEMENT

We thank Ms. Wilma Hopman for her excellent statistical analysis.

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Dr. Craig Goldie
Division Co-Chair

Summary

- *A Quality Improvement Pilot: Systematic Screening for Risk of Aberrant Opioid Use Behaviour with the Opioid Risk Tool*
- *Streamlining administrative burden: Using a standardized letter to improve communication between specialist palliative care physicians and family physicians regarding new consults*
- *Educational Interventions to Improve Medical Learners' Competency in Goals Of Care Discussions*
- *Trauma Informed Care in Substance Use Disorder*

**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

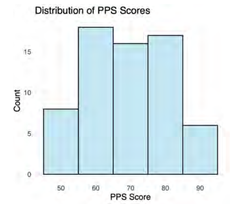
Create acceptability surveys for prospective data collection

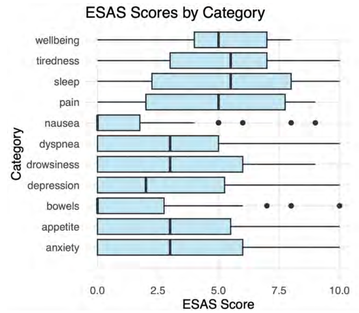
Results from Retrospective Chart Review

- $n = 68$
- 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.**

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

Queen's University

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

Queen's University

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 Goldie, MD, CCFP(PC), FRCPC
Dr. Majid Iqbal, MD, PhD, CCFP(PC)
Dr. Danielle Kain, MA, MD, CCFP(PC)
Dr. Jean Mathews, MBBS MD
Dr. Adrienne Selbie, MD, CCFP(PC)
Dr. Aynharan Sinnarajah, MD, MPH, CCFP(PC)
Dr. Anna Voeuk, MD, CCFP(PC), FCFP, MPH, DTM&H
Dr. Hasitha Welihinda, 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

Queen's University

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 G512 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 G512). 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

Queen's University

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

Queen's University

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.

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

Ana Julia Canabrava Carvalho[1] MD, David Barber[2] MD CCFP, and Jean Mathews[3] MBBS MD
Family Medicine Department[1,2] and Department of Medicine[3], Queen's University

Department of Family Medicine

Introduction

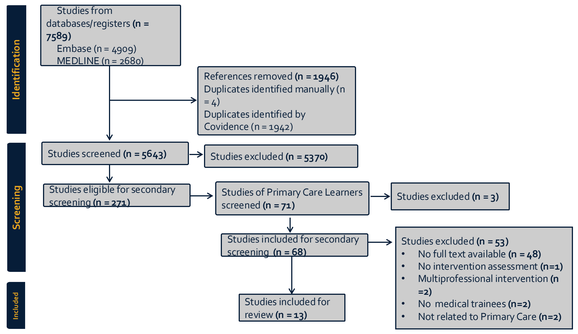
Advance care planning (ACP) is the process by which clinicians engage patients in conversations about illness understanding, elicit their wishes and values for their care, and designate a substitute decision-maker (SDM). Goals of care (GOC) discussions incorporate a patient's current wishes and values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

Trauma Informed Care in Substance Use Disorder: A Review

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Background

- Substance use disorder (SUD) is characterized by harmful patterns of substance use resulting in physical and mental health harm, as well as functional impairment (Volkow & Blanco, 2023).
- In Canada, 21% of the population, about 6 million people, meet the criteria for substance addiction at some point in their lives (CMHA, 2024).
- In 2020, 74,000 Canadians died from substance-related harm (Health Canada, 2023). The shortened lifespan in individuals with SUD is multifactorial, including challenges in engaging with traditional healthcare practices (Trimbur et al., 2024).
- Trauma-informed care (TIC) is a growing approach that takes into account a patient's trauma history when developing management plans (Dobischok, Archambault & Goyer, 2024).
- This literature review explores the research on TIC for patients with SUD, particularly in the context of serious illness.

Methods

- A narrative review was conducted by analyzing primary sources published on PubMed.
- Key findings focused on participant perceptions of TIC and its impact on substance use patterns..

- Inclusion criteria: Primary sources, people with SUD, TIC intervention, outcomes related to substance use and on Pubmed.
- Exclusion criteria: Editorials, opinion pieces, commentaries, conference abstracts, reviews and non-peer-reviewed sources

Results

- Nine primary sources were reviewed (table 1).
- Of these, 8 studies (88.9%) were conducted in high-income countries
- Two studies were qualitative method and 7 studies were quantitative method, including 1 randomized control trial (RCT).
- The total sample size in included studies was n=685.

First author/year/country	Study design	Participants (sample size, mean age, %Female, %White, Diagnosis)
Tolou-Shams, 2021, USA	RCT	n=113; 16yrs; 100%F.
Schuman-Olivier, 2022, USA	Cohort	n=18; 47.4yrs; 27.8%F; 88.9%White.
O'Malley, 2020, USA	Cohort	n=220; 100%F, 56.4%White.
Bray, 2022, USA	Cohort	n=215, 27.3yrs, 100%F, 43.7%White.
Edwards, 2023, USA	Cohort	n= 59; 41.6yrs; 100%F; 79.7%White.
Myers, 2019, South Africa	Cohort	n=60; ages 18-25yrs; 100%F.
Powel, 2012, USA	Cohort	n=152; 83.1%F; 45.1%White.
Mefodeva, 2022, Australia	Qualitative	Staff: n=20; 36yrs; 75%F. Clients: n=18; 28yrs; 44%F.
Fatkin, 2021, USA	Qualitative	n=25; 47.4yrs; 27.8%F; 94.4%White.

Table 1: Descriptions of studies included

- The 7 quantitative studies showed TIC interventions generally linked to decreased substance use among individuals with SUD (table 2, figure 1).
- Three studies (42.8%) were conducted in an outpatient setting, 2 (28.6%) were in an inpatient hospital, and 2 (28.6%) did not specify.

Results

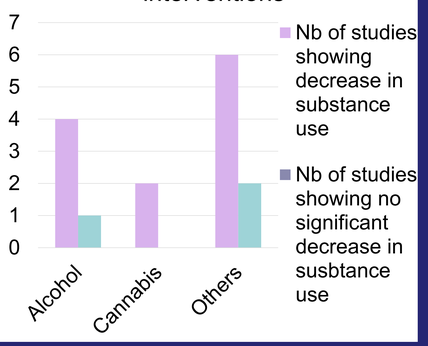
First author	Setting	Details of intervention	Findings
Tolou-Shams	Outpatient (schools and hospitals)	*VOICES,* a gender-responsive substance use intervention for girls, delivered in twelve in-person group sessions over 20 weeks. Control: Non-trauma informed intervention named GirlHealth.	Decrease in cannabis, alcohol and other substances used for up to 6 months post intervention when compared to the control.
Schuman-Olivier	Outpatient (group sessions in a clinic)	*Mindful Recovery OUD Care Continuum (M-ROCC),* a 24 week mindfulness training provided along side buprenorphine and naloxone treatment.	Decrease in cocaine and benzodiazepines post-intervention. No difference in use of illicit opioids and alcohol following the intervention.
O'Malley	Outpatient (at home)	*The Team for Infants Exposed to Substance abuse (TIES)* Program, a multi-disciplinary model for maternal SUD.	Decrease in mean maternal substance use post-intervention.
Bray	Inpatient (residential substance use treatment centre)	*MIRRORS (Maternal Initiative for Reflective Recovery-Oriented Residential Services)* program, a prevention and recovery support program for women and children.	Decrease in percentage of participants admitting to using alcohol and other drugs within 30 days.
Edwards	Inpatient (Sober living home)	*Support, Education, Empowerment, and Directions (SEEDs)* program, providing transitional housing to women with histories of domestic partner violence and SUD.	Decrease in alcohol and drug use decreased (most significant decrease in the first 6 months of starting the intervention).
Myers	Location not specified	*Trauma-informed Women's Health Coop (WHC),* a substance use and sexual risk reduction intervention for young South African women.	Decrease in frequency of heavy episodic drinking, methamphetamine use and cannabis use at 3 months post-intervention.
Powel	Location not specified	*The Pima County Family Drug Court program* where trauma-informed mental health therapy is provided alongside alcohol and other drug treatment.	Decrease in alcohol with treatment. The changes in other drug use were not statistically significant.

Table 2: TIC interventions and findings of the quantitative method studies.

In reviewing qualitative data:

- Fatkins (2021): high satisfaction and good retention of participants. All the participants stated they would refer to a friend.
- Mefodeva (2022): many clinicians are not practicing TIC due to misunderstanding and confusing TIC with PTSD treatment. Residential settings are not ideal for TIC, as clients did not always feel physically safe (an important component of TIC).

Figure 1: Patterns in substance use following TIC interventions



Defining Trauma Informed Care

Of the 9 studies, 6 provided a definition of trauma informed care (Table 3).

First author	Definition/theoretical framework of TIC	Source of definition
Tolou-Shams	"ten principles of trauma-informed care, including emphasizing strengths and resilience and recognizing the impact of victimization on development and coping strategies."	Markoff et al, 2005
Mefodeva	"understands the widespread impact of trauma and provides a recovery-oriented environment that focuses on trauma-specific recovery."	Elliott et al, 2005
Schuman-Olivier	consists of 6 principles, "safety, trust/transparency, peer support, collaboration/mutuality, empowerment/voice/choice, cultural/historical/gender issues"	SAMHSA, 2014
Edwards	"consider the role of trauma in etiology, onset, and recovery; avoid triggering reactions or retraumatization; support women's coping capacities; and promote empowerment so that survivors can manage their trauma symptoms successfully."	Covington, 2008 / Fallot & Harris, 2002 / Purtle, 2020
Powel	"Developing a strong therapeutic relationship, education about normal responses to trauma, anger and anxiety management, parent training, constructing a coherent trauma narrative, employing strategies that allow exposure to traumatic memories in tolerable doses, empowerment activities, and closure."	No source given
Fatkin	"adhere to six principles of care, including creating safety, maintaining transparency, cultivating peer support, bringing a stance of collaboration and mutuality, empowering patients by providing choice, and paying attention to cultural, historical, and gender issues"	SAMHSA, 2014

Table 3: Trauma informed care definitions from reviewed articles

Discussion

- TIC supports recovery by addressing trauma as a driver of substance use and fostering a sense of safety and empowerment.
- Gender-responsive, community-based, and holistic approaches may enhance effectiveness.
- Quantitative studies generally showed decrease in substance use following TIC interventions.
- Qualitative studies emphasized the benefits of TIC, as well as high satisfaction suggesting strong acceptability.
- Inpatient setting were described as less ideal for TIC due to less sense of safety, although quantitative studies showed good SUD recovery.
- Challenges in TIC implementation include misunderstanding TIC. Definitions above for TIC were different and came from diverse sources (other than 2). Many articles did not even provide a definition.
- Limitations of current literature include that studies take place mainly in the United-States and only 1 RCT.
- A limitation of this review is that it was not systematic.

Conclusion

- While the findings are promising, further research is required to assess long-term outcomes and effectiveness in diverse populations and treatment settings.
- Although TIC is often talked about as important h in the care of patients with SUD and serious illness, there is a gap in the evidence.
- Future research needs to study TIC interventions for SUD specifically in patients with serious illness.

References

Respirology & Sleep Medicine

Dr. Genevieve Digby
Division Co-Chair

Dr. Christopher Parker
Division Co-Chair

Summary

- *Redesign clinical pathways and processes to provide multiple interventions in patients with MPE within a single timeframe.*
- *Use pleural physiology measures (i.e. pleural manometry, ultrasound guided atelectasis displacement measurements) to improve clinical outcomes during pleural procedures.*
- *Design and implementation of an augmented large language model as a conversational resource for providing support to patients newly diagnosed with obstructive sleep apnea.*
- *Characterizing motivations for/against oral nicotine product consumption*
- *Combining pulmonary function imaging and clinical respiratory physiology to uncover the structural determinants of wasted ventilation in dyspneic patients at the initial stages of COPD*
- *Improving timeliness of care for patients undergoing evaluation for suspected lung cancer in Southeastern Ontario*

Division of Respirology and Sleep Medicine – Resident Research Fair Submission

Active Projects

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

PLEURAL SPACE RESEARCH

The pleural space clinic manages over 30 patients with pleural effusion 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. Amirali Mahpour
Email: amirali.mahpour@kingstonhsc.ca

Research Opportunities: The Intersection of Medicine and Artificial Intelligence

Areas of investigations:

1. Design and implementation of an augmented large language model as a conversational resource for providing support to patients newly diagnosed with obstructive sleep apnea.
2. Assessment of clinical bias in large language models.
3. Investigating the strengths and weaknesses of artificial intelligence tools for electronic medical records data curation and data quality assessment.

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

Research projects/opportunities - Interstitial Lung Diseases

- Comparison of different diagnostic criteria of Progressive Pulmonary Fibrosis.
- 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 and prognosis of CT patterns on presentation in patients with CTD related ILD.
- Prognosis of different clinical, radiological and serologic domains in IPAF.
- Validation of CTD questionnaire used in ILD clinic.
- Prognosis of patients with chronic HP after antigen identification and avoidance achieved using a comprehensive exposure investigation approach.

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

Resident Research Opportunities:

General Areas of Inquiry:

- Clinical physiology (focus on sleep and exercise in health and respiratory disease) - prospective studies
- Retrospective (cohort / chart) analyses
- Medical / Science Education

Potential Projects:

1. Characterizing motivations for/against oral nicotine product consumption (qualitative / quantitative analysis of a completed survey of post-secondary students)
2. Does sleep quality at baseline impact on the longitudinal trajectory of physical fitness and exertional breathlessness in health and COPD (CanCOLD cohort database)
3. Let's talk! Many of the best projects are co-created. Please reach out if you have ideas for retrospective (e.g., chart review, sleep lab database, our research team's database, available cohorts) or prospective projects you are interested in pursuing; I'd be happy to discuss how we might make this happen.

Principal Investigator: Dr. M Diane Lougheed
Email: 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. J Alberto Neder
Email: alberto.neder@queensu.ca

Active Areas of Research:

- Combining pulmonary function imaging and clinical respiratory physiology to uncover the structural determinants of wasted ventilation in dyspneic patients at the initial stages of COPD
- 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)

Principal Investigator: Dr. Vanessa Martelli
Email: vanessa.martelli@kingstonhsc.ca

Research interests are real world-evidence and health economic evaluation, pertaining to sleep disorders and circadian science. She has experience conducting population-based research using health administrative datasets. Her current project is funded by an American Academy of Sleep Medicine Focused Projects Grant for Junior Investigators, and seeks to evaluate preference-based health utility instruments in patients with obstructive sleep apnea.

Principal Investigator: Dr. Geneviève Digby
Email: genevieve.digby@kingstonhsc.ca
Active Areas of Research:

- Improving timeliness of care for patients undergoing evaluation for suspected lung cancer in Southeastern Ontario
- Exploring factors within models of care that influence physician burnout and engagement
- Choosing Wisely Canada – Optimizing Utilization and Improving Climate Sustainability
- GoZero Inhaler Recycling Project – feasibility and Quality Improvement study evaluating the impact of an inhaler recycling project across a tertiary care, academic hospital

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

Allarakhia S[1], Morra A[2,3], Theal R[4], Moloney M[2], Gupta S[5,6], To T[7,8], Digby G[3], Barber D[4,9], Queenan J[4], Lougheed MD [1,2,3,10]

[1] Kingston Health Sciences Centre, Kingston ON, [2] Asthma Research Unit, Kingston General Hospital, 72 Stuart Street, Kingston, Ontario, Canada, [3] Division of Respirology, Department of Medicine, Queen's University, Kingston, Ontario, Canada, [4] Canadian Primary Care Sentinel Surveillance Network (Eastern Ontario Network), Kingston, Ontario Canada, [5] Division of Respirology, Department of Medicine, St. Michael's Hospital, Toronto, Ontario, Canada, [6] Li Ka Shing Knowledge Institute, University of Toronto, Toronto, Ontario, Canada. [7] Child Health Evaluative Science, The Hospital for Sick Children, Toronto, ON, Canada, [8] Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada, [9] Department of Family Medicine, Queen's University, Kingston, Ontario, Canada, [10] Department of Public Health Sciences, Queen's University, Kingston, Ontario, Canada

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

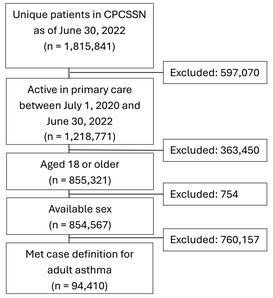
- For all unique patients with an active visit at a participating CPCSSN clinic in the 2-year period from July 1, 2020 to June 30, 2022, charts were screened to include patients who were aged 18 years or older with available sex recorded.
- The CPCSSN adult asthma case definition was applied to identify 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

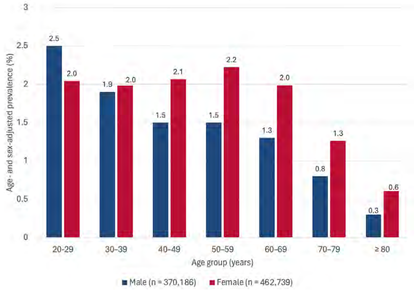


- 854,567 charts with available demographic information were identified as active adult patients in the 2-year study period.
  - 94,410 charts met criteria for suspected or confirmed asthma.

Prevalence

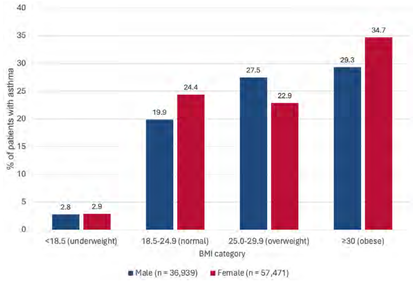
- The overall prevalence of adult asthma is 11%.
- Asthma prevalence decreases with increasing age (14% in adults aged 18-29 years compared to 8% in adults aged ≥ 80 years).
- Asthma is more common in females (12%) vs. males (10%).

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.

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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.

Acquisition of endobronchial ultrasound bronchoscopy proficiency at a Canadian academic center

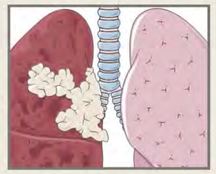
AUTHORS

Anna Tyker[1], Jennifer D'Cruz[2], Marita Stuanton[1], Yining Chen[4], Kerry Lake[5], Christopher M. Parker[1,2,3], Paul Heffernan[3], Geneviève C. Digby[1,2]

AFFILIATIONS

Department of Medicine[1], Division of Respirology[2], Department of Critical Care, Queen's University[3]; Department of Medicine, University of British Columbia[4]; Department of Medicine, Division of Respirology, McMaster University[5]

01. Introduction



- Endobronchial ultrasound (EBUS) bronchoscopy is used to assess intrathoracic lymph nodes and masses.
- EBUS skill is commonly acquired by interventional or thoracic surgery training, but there is no consensus on what constitutes appropriate training for EBUS
- EBUS at Kingston Health Sciences Center (KHSC) was instroduced in 2014, performed by Respirologists with expertise in bronchoscopy using conscious sedation
- The literature suggests the diagnostic yield of EBUS ranges from 83-96%

02. Objective

To understand and describe the attainment of EBUS skill at Kingston Health Sciences Center.

03. Methodology

- Retrospective chart review of EBUS procedures at KHSC
- Data include first 70 procedures performed by 4 respirologists between 2014 and 2019 (n=280).

All respirologists had experience with flexible bronchoscopy and had attended an accredited EBUS course.

Table 1. Patient, procedure and lymph node characteristics (n=280).

	n	%
Patient Characteristics		
Age	65	
Male	139	49.64
Female	141	50.36
Diagnosis Obtained	**241**	**86.07**
→Sufficient for Biomarkers	107	78.10
Diagnosis Not Obtained	**39**	**13.93**
Procedure Characteristics		
Indication:		
→Diagnosis	56	20.00
→Staging	43	15.36
→Both	181	64.64
Number of Days to Procedure	13	
Duration (min)	51	
Lymph Node Characteristics		
Average Number of Lymph Nodes Sampled per Procedure	1	
Total Number of Lymph Nodes Sampled	415	
Average Number of Passes (mode)	5	
Pathology		
Lung Cancer	137	48.93
Granuloma	25	8.93
Other Cancer	17	6.07
Benign Lymph Node	62	22.14
Non-diagnostic	39	13.93

04. Results

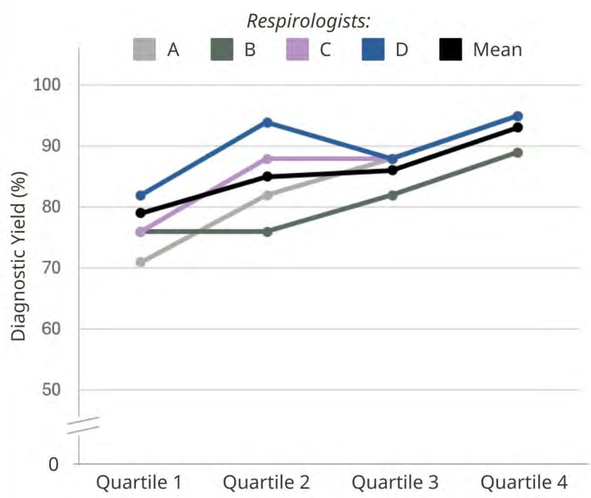


Figure 1. Diagnostic yield (%) per quartile for respirologists A to D. Quartile 1,2, and 3, n=17 procedures per respirologist per quartile, and quartile 4, n = 19 procedures per respirologist.

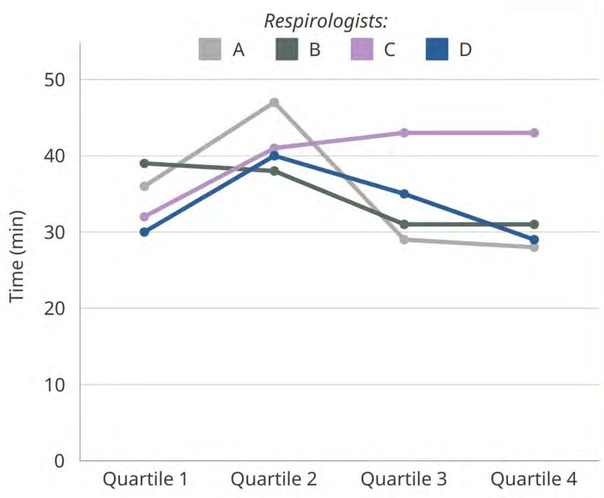


Figure 2. Time (min) per lymph node sampled per quartile for respirologists A to D. Quartile 1,2, and 3, n=17 procedures per respirologist per quartile and quartile 4, n = 18 -19 procedures per respirologist.

- Number of EBUS procedures increased from 5.3/month in 2014 to 18.3/month in 2019 and 25.5/month in 2023
- In the 1st quartile of skill acquisition, mean diagnostic yield was 76.5% (range 70.6-82.4%) compared with 93.4% in the 4th quartile (range 89.5-94.7%)
- Most common complication was coughing (8.6% of cases); serious complications such as hypoxia and bleeding were rare (2.5% and 1% of procedures, respectively)

05. Conclusion

EBUS skill acquisition and proficiency is attainable safely by non-interventional trained respirologists with experience in flexible bronchoscopy.

Funding: University Hospitals Kingston Foundation Grant

Evaluating the Impact of Interstitial Lung Diseases Nursing Support on Antifibrotic Treatment Adherence in Patients with Idiopathic Pulmonary Fibrosis

Hend Alsaleh[1],Onofre Moran-Mendoza[1], Carla Paredes[2], Lynda McCarthy[2].
[1]Queen's University - Kingston (Canada), [2]Hotel Dieu Hospital - Kingston (Canada)

Background

Idiopathic pulmonary fibrosis (IPF) has a median survival of 3-5 years without treatment.
Antifibrotic drugs slow down the progression of the disease and decrease mortality.
However, adherence to antifibrotics is a challenge, with abandonment rates of 20% over 1-year in randomized controlled trials (RCT).
We report the impact of ILD nursing support on adherence to antifibrotic treatment in IPF patients.

Objective

To evaluate the impact of an ILD nurse on the adherence to antifibrotic medications in patients with IPF in the modern era, when ancillary resources now available can help patients stay on treatment.

Methods

We evaluated adherence rates of patients with IPF started on Pirfenidone or Nintedanib at our ILD center between January 2020 and December 2023, with the support of an ILD Nurse.
We assessed the proportion of patients who required switching antifibrotics, those on full dose or reduced dose, and the adherence rates achieved with our ILD nurse to that reported by other studies.

Statistics

We calculated the percentage of patients who started anti-fibrotics, of those who switched antifibrotics, and of those who remained on antifibrotics at the end of the study period.

Results

Subjects characteristics
N= 118

Mean Age (Min-Max)	**76** (46 - 92)
Gender	M **91** F **27**
Mean Treatment Duration (min - max)	**15.5 months** (0 months – 3.75 years)
Overall compliance	**109/118** (92%)
Started on Pirfenidone	**87**
Switched to Nintedanib*	**10** (11%)
Started on Nintedanib	**50**
Switched to Pirfenidone*	**9** (18%)

*Switched due to adverse events.

Compliance to anti-fibrotics

	Current study	Real-world and RCT studies combined	
		Nintedanib[1-3]	Pirfenidone[1,4,5]
Compliance	**92%** Full Dose 90 (83%) Reduced Dose 19 (17%) **Last year of study** **N = 32** Pirfenidone 24 / 24 (100%) Nintedanib 8 / 8 (100%)	**79%-81%**	**80%-82%**

1. Hughes G. et al. J Clin Med. 2016; 5: 78-89.
2. Richeldi L. et al. Respir Med. 2016; 113: 74-9.
3. Corte et al. Respiratory Research 2015; 16:116
4. Costabel U. et al. Respiration 2017;94:408–415
5. Noble P. et al. Eur Respir J 2016; 47: 243–253

Conclusion

Support from an ILD nurse greatly enhances patient adherence to antifibrotic treatment in patients with IPF.

Disclosures: None to declare.

Hypersensitivity Pneumonitis Due To Domestic Exposure to Foam And Bamboo In Bedding And Other Sources – Microbiologic Analyses

Maria A. Coppola-Lamas[1,2], *Onofre Moran-Mendoza*[1,2]

[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

Male 43%, Female 57%
Mean age 72 years (min 50 – max 88)

Diagnosis of HP (N=14)

	Frequency	(%)
BAL Lymphocytosis (> 20%)	5	37
TBLC	3	21
VATS biopsy	3	21
3-density pattern on HRCT	3	21

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.

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.

Evaluating the Impact of Interstitial Lung Diseases Nursing Support on Antifibrotic Treatment Adherence in Patients with Idiopathic Pulmonary Fibrosis

Hend Alsaleh[1],Onofre Moran-Mendoza[1], Carla Paredes[2], Lynda McCarthy[2].
[1]Queen's University - Kingston (Canada), [2]Hotel Dieu Hospital - Kingston (Canada)

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We assessed the proportion of patients who required switching antifibrotics, those on full dose or reduced dose, and the adherence rates achieved with our ILD nurse to that reported by other studies.

Statistics

We calculated the percentage of patients who started anti-fibrotics, of those who switched antifibrotics, and of those who remained on antifibrotics at the end of the study period.

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Compliance to anti-fibrotics

	Current study	Real-world and RCT studies combined	
		Nintedanib[1-3]	Pirfenidone[1,4,5]
Compliance	**92%** Full Dose 90 (83%) Reduced Dose 19 (17%) **Last year of study** **N = 32** Pirfenidone 24 / 24 (100%) Nintedanib 8 / 8 (100%)	**79%-81%**	**80%-82%**

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Conclusion

Support from an ILD nurse greatly enhances patient adherence to antifibrotic treatment in patients with IPF.

Disclosures: None to declare.

Duloxetine Induced Interstitial Lung Disease - A Novel Case Report

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INTRODUCTION

Duloxetine is a commonly prescribed antidepressant and has been associated with eosinophilic pneumonia (EP) in one case report*.
We report here the first case of duloxetine-induced Interstitial lung disease (ILD) other than EP.

CASE REPORT

A 71-year-old female presented with a 1-month history of cough, yellow sputum, fever, vomiting, hyporexia, and 15-pound weight loss. A computed tomography pulmonary angiogram ruled out pulmonary embolism but revealed right upper lobe (RUL) consolidation and patchy consolidations/nodules in the right middle (RML) and lower lobes (RLL) (Figure 1-A). The respiratory virus panel, sputum and blood cultures, and legionella urinary antigen were negative. She was hospitalized, treated with antibiotics, and referred to Respirology.

At her clinic visit, she had dyspnea (Medical Research Council grade 2/5) and dry cough, with resolution of other symptoms.
She reported exposure to foam and bamboo in her pillow and mattress, but no exposure to chemicals, fumes, molds, or dusts.
Her medications included duloxetine (started one-year prior), simvastatin, omeprazole, levothyroxine, and bisoprolol. She had no clinical or serologic evidence of connective tissue diseases. On exam had 97% SpO_2 on room air and bibasilar fine/coarse inspiratory crackles.

INVESTIGATIONS

Laboratory tests revealed leukocytosis (12.3 x10^9/L), elevated CRP (114 mg/L), and ESR (73 mm/hr).
Pulmonary function tests showed restriction (FVC 72%, TLC 56%) and reduced diffusing capacity (DLCO 48%).

Follow-up chest CT showed resolution of RUL and RML consolidations and new consolidations in both lower lobes (Figure 1-B).
Migratory consolidations suggested organizing pneumonia (OP), from hypersensitivity pneumonitis (foam exposure), or drug-induced EP.

Bronchoalveolar lavage (BAL) from the LLL was negative for infections but showed neutrophilia (53%), eosinophilia (23%), and lymphocytosis (20%), suggesting EP or OP related to drug-induced ILD (DI-ILD).

A second BAL showed mild neutrophilia (7%) and eosinophilia (4%); transbronchial lung biopsies showed intra-alveolar foamy macrophages and mild interstitial inflammation including lymphocytes and few eosinophils. Findings were not supportive of EP.

MANAGEMENT & OUTCOME

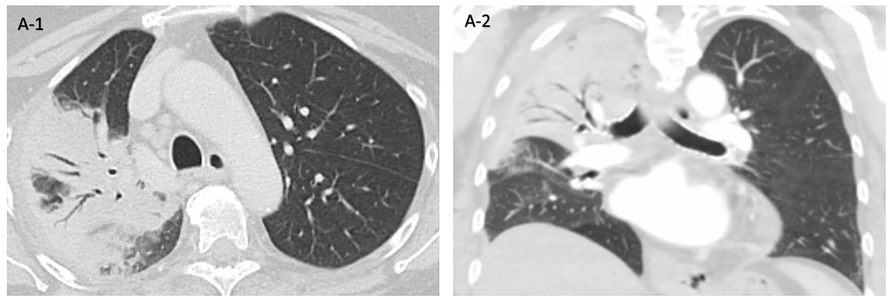
She was diagnosed with possible DI-ILD due to duloxetine that had been started a year prior.

Duloxetine was discontinued based. No immunosuppressive treatment was initiated.

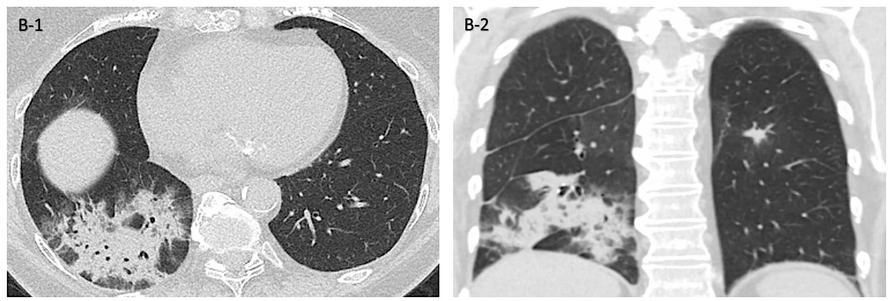
Following duloxetine discontinuation, she had complete resolution of symptoms and of the chest CT abnormalities (Figure 1-C).

IMAGES

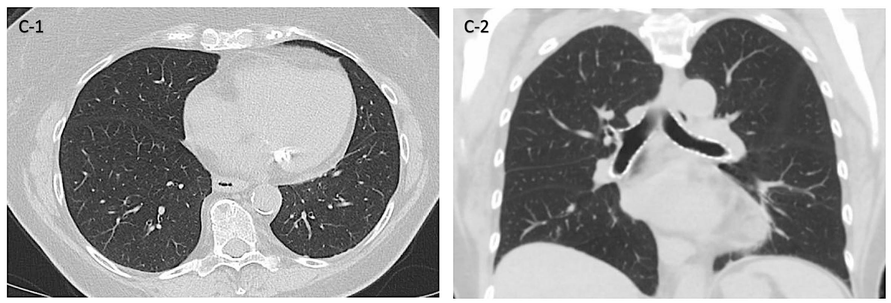
Figure 1



A (1-2): Axial and coronal images of CTPA demonstrate right upper lobe consolidation.



B (1-2): Axial and coronal images of follow up Chest CT scan demonstrate resolution of right upper lobe consolidation and new consolidations in right and left lower lobes.



C (1-2): Axial and coronal images of Chest CT scan demonstrate complete resolution of previously seen abnormalities after discontinuation of duloxetine.

DISCUSSION

We report here the first case of non-eosinophilic DI-ILD due to duloxetine, which fully resolved after drug discontinuation.

*Espeleta VJ, Moore WH, Kane PB, Baram D. Eosinophilic pneumonia due to duloxetine. Chest. 2007;131(3):901–903. doi:10.1378/chest.06-1659

Disclosures: None to declare.

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*
- *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*
- *Identification of clinical and immunological factors predicting the response to hydroxychloroquine in patients with osteoarthritis:*
- *Risk assessment of fractures in rheumatoid arthritis patients*

Rheumatology Research Projects 2025

1) Prospective cohort study of the effects of bariatric surgery on bone density, markers of bone metabolism, and health-related quality of life (HRQOL). Study would involve a pre and post design, with baseline measurements of bone density and markers of bone metabolism and HRQOL with follow up extending to 1 year from surgery-need to involve bariatric surgeons/staff. *(PI: Dr. Towheed)*

2) Risk of fragility fractures with diabetic medications (gliptins and SGL2T inhibitors): Systematic review and meta-analysis. *(PI: Dr. Towheed)*

3) Fibromyalgia Attitudes in 2023 amongst Ontario Rheumatologists: An on-line survey. *(PI: Dr. Towheed)*

4) Osteoporosis Care Gap: Causes and Solutions. Systematic review with Canadian recommendations. *(PI: Dr. Towheed)*

5) Case report and narrative review of the literature on any clinical topic in Rheumatology. *(PI: Dr. Towheed)*

6) Systematic review and meta-analysis of any other topic of interest in Rheumatology/Osteoporosis (eg Ozempic for knee osteoarthritis). *(PI: Dr. Towheed)*

7) Determine the role of the terminal complement complex in autoimmune diseases: laboratory-based experiments (ELISA, qPCR, and immunoblotting) and patient chart review for clinical and demographic data. *(PI: Dr. Nakamura)*

8) Identification of clinical and immunological factors predicting the response to hydroxychloroquine in patients with osteoarthritis: laboratory-based experiments (FACS, ELISA, and qPCR) and patient chart review for clinical and demographic data. *(PI: Dr. Nakamura)*

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Dr. Aki Nakamura (Akihiro.nakamura@queensu.ca)

Clinical Validation of Neutrophil DTL Expression in Spondyloarthritis

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Background

- Macrophage migration inhibitory factor (MIF) drives the pathology of spondyloarthritis (SpA) in curdlan-injected SKG mouse models[1]
- Neutrophils are the primary cells that produce MIF in these SKG mice, however, their mechanisms in driving the pathology of SpA remains unknown[1]
- Total RNA sequencing has identified **Denticleless E3 Ubiquitin Protein Ligase Homolog (DTL)**[2]
- *Mif* +/+ neutrophils show decreased *Dtl* expression and increased IL-23 expression compared to *Mif* -/- neutrophils in SKG mice[1]
- *DTL* negatively regulates IL-23 expression in psoriasis[2]
- *DTL* has reduced expression in human immune cells and inflammatory gut tissues[3]
- SpA spectrum diseases appear to have decreased levels of DTL in human immune cells and target tissues[3]

Hypothesis

In this pilot study, we hypothesize that neutrophil DTL expression is suppressed in patients with axial SpA (axSpA), which negatively correlates with IL-23A levels and/or disease activity.

Methods

Participant recruitment & mRNA expression

1. Blood samples were collected from 11 healthy donors and 26 patients with axSpA on NSAIDs or TNF inhibitors
2. AxSpA patients reported BASDAI scores
3. From the blood samples, neutrophils were isolated and mRNA was extracted
4. Quantitative PCR was used to measure *DTL* and *IL23A* expression

Assessing IL-23 secretion

1. Human neutrophil cell line HL-60 and peripheral blood neutrophils were stimulated using control conditions, lipopolysaccharide (100 ng/mL), and curdlan (10 µg/mL) for 20 hours
2. IL-23 secretion was assessed using ELISA

Assessing DTL expression

1. HL-60 treated under control conditions, lipopolysaccharide (100 ng/mL), curdlan (10 µg/mL), and MN-4924 (NEDD8-activating enzyme inhibitor) for 4 hours
2. Cells were collected, centrifuged, lysed, and lysates were cleared
3. DTL expression was assessed using Western blot analysis

Results

- **No significant differences** in peripheral neutrophil expression of *DTL* and *IL23A* between healthy controls and axSpA patients

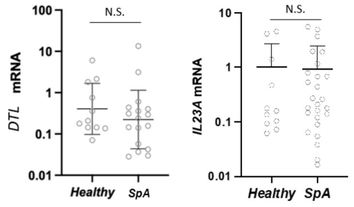


Figure 1. qPCR analysis of *DTL* and *IL23A* expression in peripheral neutrophils from healthy donors and axSpA patients

- **Strong positive correlation** between peripheral neutrophil *DTL* and *IL23A* expression (r = 0.95, p < 0.0001)

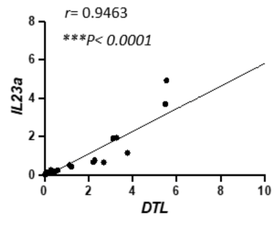


Figure 3. Correlation analysis between peripheral neutrophil *DTL* and *IL23A* expression

- **No significant correlations** in peripheral neutrophil expression of *DTL* with BASDAI scores (r = -0.10, p = 0.78) and *IL23A* with BASDAI scores (r = -0.20, p = 0.55)

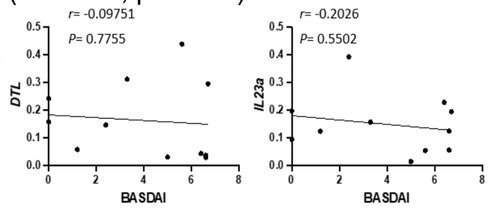


Figure 2. Correlation analysis between peripheral neutrophil *DTL* and *IL23A* expression and BASDAI scores

- **HL-60** cells showed increased IL-23 secretion and decreased DTL expression in response to curdlan, but not **human peripheral neutrophils**

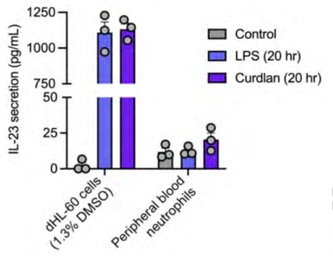
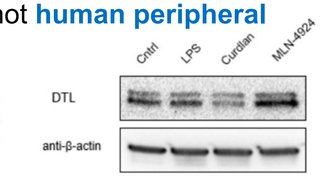


Figure 4. ELISA results showing greater IL-23 secretion by HL-60 cells under 20-hour curdlan and lipopolysaccharide stimulation compared to peripheral blood neutrophils under the same stimuli.



Legend. HL-60 cells (day 5, 1.3% DMSO) treated for 4 hours with LPS (100 ng/mL), Curdlan (10 ug/mL), or MLN-4924.

Figure 5. Western blot analysis showing decreased DTL expression in HL-60 cells under 4-hour curdlan stimulation.

Discussion

- The discrepancy between human and mouse neutrophils may be attributed to the source from which these cells were isolated
  - **Peripheral neutrophils** are known to minimally express IL-23, which may limit their ability to replicate the behaviors of their **tissue-resident or infiltrated counterparts**
- AxSpA patients do not reflect an active disease state - they have received NSAIDs and/or bDMARDs, resulting in variable BASDAI scores

Future Directions

Further testing with a larger sample size will be beneficial to validate these preliminary results.

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There is no conflict of interest related to this data.

Survey Study of Canadian Screening Practices in Rheumatoid Arthritis Related Interstitial Lung Disease

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1. McMaster University, 2. Queen's University, 3. Kingston Health Sciences Centre

Background

- Interstitial lung disease (ILD) is an extra-articular manifestation of rheumatoid arthritis (RA) with significant morbidity and mortality.[1]
- There is growing evidence that therapeutic agents for RA-ILD can slow down lung function decline.
- Some risk factors for development of RA-ILD have been identified, including male sex, older age, smoking, higher disease activity, and positive Anti-Citrullinated Peptide Antibody (ACPA)/Rheumatoid Factor (RF). [2, 3]
- There are no specific recommendations in Canadian guidelines for the screening, diagnosis, or management of RA-ILD.

Objective

- This study aimed to understand the current patterns of rheumatologist in Canada to screen for ILD in patients with RA.

Methods

- We invited all adult rheumatologist who were members of the Canadian Rheumatology Association to complete an anonymous online survey.
- The survey was developed by our authors, consisting of a Rheumatologist (MCB) and Respirologist (OM) with experience in managing RA-ILD. It is based on current typical clinical practices and informed by the results of a literature review
- Data included both quantitative metrics and qualitative free text.
- Responses were analyzed using descriptive statistics.

Results

- Forty-seven Canadian adult rheumatologists completed the survey. 56% self-identified as community physicians, 29% as academic and 15% as both community and academic.
- The results of the survey are displayed below.

Figure 1: Do you routinely screen patients with Rheumatoid Arthritis (RA) for shortness of breath (SOB)?

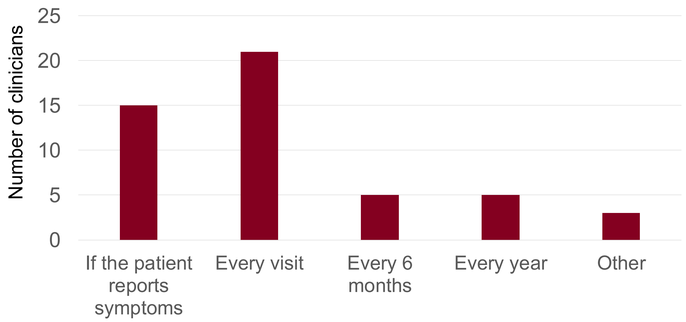


Figure 2: How often do you auscultate your RA patient's lungs for crackles?

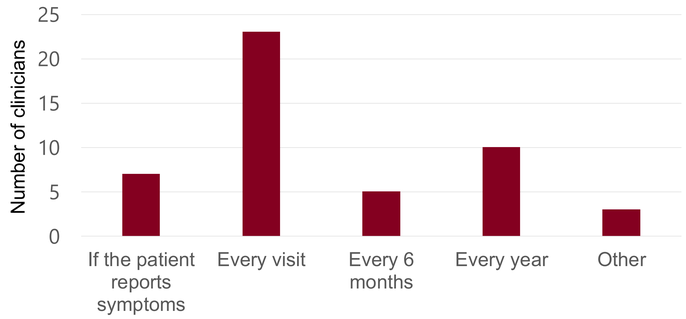


Figure 3: Do you order pulmonary function tests (PFT) for your RA patients?

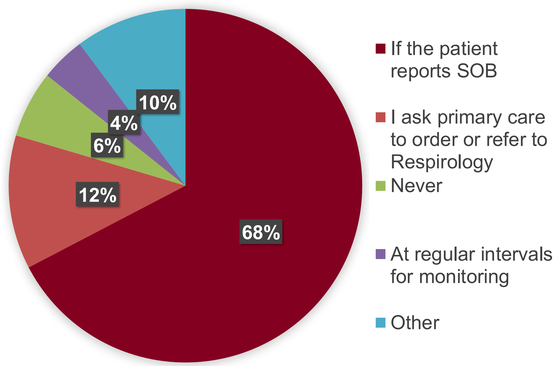


Figure 4: Are you familiar with the patient characteristics/disease features that are associated with an increased risk of RA associated ILD?

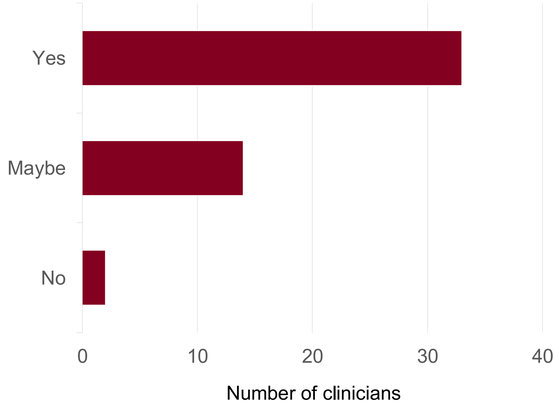
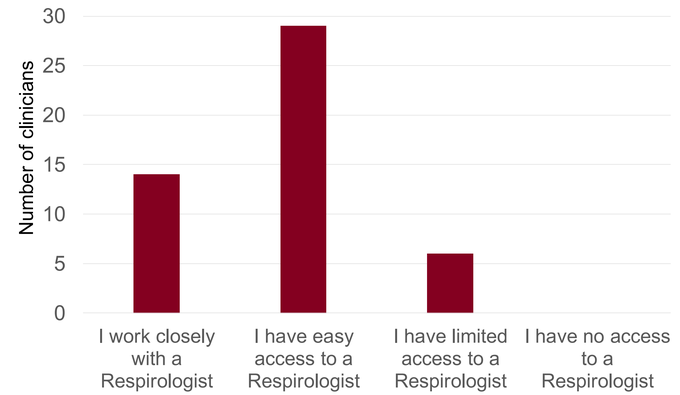


Figure 5: Do you have a Respirology colleague that you share care with for RA-ILD patients?



Conclusion

- There are inconsistent practices by Canadian Rheumatologist in the screening of RA patients for ILD.
- Many Rheumatologists may not be familiar with the risk factors for developing RA-ILD.
- Our findings emphasize the need for guidelines to address this gap and to provide evidence-based recommendations to screen RA patients for ILD.

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Clinical Features of Patients with Interstitial Lung Disease and Anti-Ro52 Antibody

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Department of Medicine, Queen's University, Kingston ON Canada

Background

- Interstitial lung disease (ILD) encompasses a heterogenous group of diseases characterized by inflammation and fibrosis of the lung parenchyma, and are associated with significant morbidity and mortality [1]
- ILD can be either primary, as in the case of idiopathic pulmonary fibrosis (IPF) or secondary to another process, such as connective tissue disease (CTD)
- In addition to careful histories and clinical exams, autoantibody panels are typically sent to exclude underlying CTD [2]
- There is growing evidence that anti-Ro52 antibodies are associated with worse outcomes in patients with ILD [3, 4, 5]

Methods

- We performed a retrospective chart review of all patients seen at the ILD clinic of a tertiary care centre since its inception until September 2020.
- All adult patients who were anti-Ro52 positive with a diagnosis of ILD by American Thoracic Society criteria were included.
- Signs and symptoms associated with CTD, serologic markers, high resolution CT (HRCT) findings and pulmonary function test (PFT) results were recorded using a standardized data extraction form.
- Proportion of patients with progression of ILD at 1-year follow-up was also recorded. This was defined as a decrease in forced vital capacity (FVC) greater than 10% of predicted or a decrease in diffusing capacity of carbon monoxide (DLCO) of greater than 15% predicted.

Results

Variables	Overall, n = 22
Mean age of onset (yrs)	70.3 ± 11.7
Female	13 (59%)
Mean symptom duration (yrs)	2.19 ± 2.11
Prior diagnosis of CTD	3 (13.7%)
Auto-antibody positivity:	
ANA > 1:40	16 (72.7%)
Anti-Ro52	22 (100%)
Anti-Ro60	8 (36.4%)
Imaging characteristics:	
NSIP	6 (27.2%)
UIP	10 (45.5%)
Other	3 (13.6%)

Table 1: Features of patients with ILD and anti-Ro52 antibody positivity. Data are presented as n (%) or mean ± std.

Variables	Initial	At 1 year follow-up
Measures of Lung Function		
Mean MRC class	2.45 ± 1.11	2.04 ± 1.25
Mean FVC	78.7% ± 23.1	77.6% ± 24.0
Mean DLCO	56.7% ± 15.8	52.9% ± 16.4
Mean 6MWT distance (meters)	423.1 ± 96.0	404.6 ± 95.0
Diagnosis of CTD		
Rheumatoid arthritis	1 (4.5%)	1 (4.5%)
SLE	2 (9.1%)	2 (9.1%)
Sjogren's syndrome	1 (4.5%)	3 (13.6%)
Anti-synthetase syndrome	0	2 (9.1%)
Mixed CTD	0	1 (4.5%)
Undifferentiated CTD	0	3 (13.6%)

Table 2: Changes in lung function and new diagnosis of CTD over 1 year follow-up.

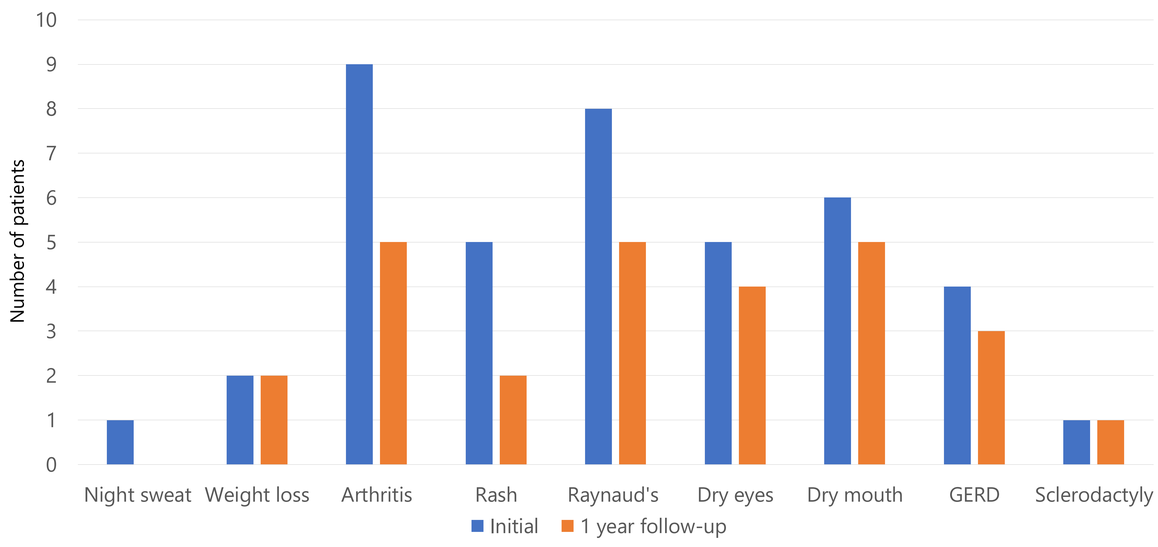

Figure 1: Changes in clinical symptoms over 1 year follow-up.

Conclusion

- ILD is often associated with CTD and auto-antibody testing may hold important prognostic value during patient assessment.
- Interdisciplinary collaboration between respirology, rheumatology and other specialty services is essential for management of these patients
- Next steps include comparing this cohort against ILD patients who are anti-Ro52 negative, or patients who are positive for other ENA auto-antibodies.

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