8TH ANNUAL

Resident Research Fair

2023

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

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Research-at-a-Glance

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

Available research projects can be divided into 5 overall catergories:

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

Message from the Program Director

Dr. Stephen Gauthier
Program Director, Core Internal Medicine Program

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

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

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

On behalf of the QIM program, I would like to thank the Department of Medicine faculty 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

- *Anxiety in allergic rhinitis patients during the COVID-19 pandemic*
- *Comparison of commercially available SARS-CoV-2 tests to clinically validated assays*
- *Serum biomarkers and bacterial carriage in allergen-induced allergic rhinitis models*

Allergy & Immunology

Peer Reviewed Publications:

1. Linton S, Xu K, Hossenbaccus L, BottingH, Garvey S, Sunavsky A, Steacy LM, Tripp DA, Ellis AK. Anxiety in adult swith asthma during the coronavirus disease 2019 pandemic: a Canadian perspective. Allergy Asthma Clin Immunol. 2023 Aug 23;19(1):73. doi: 10.1186/s13223-023-00833-z.
2. Casale TB, Ellis AK, Nowak-Wegrzyn A, Kaliner M, Lowenthal R, Tanimoto S. Pharmacokinetics/Pharmacodynamics of Epinephrine After Single and Repeat Administration of neffy, EpiPen, and Manual Intramuscular Injection. J Allergy Clin Immunol. 2023 Aug 19:S0091-6749(23)01059-X. doi: 10.1016/j.jaci.2023.08.007. Epub ahead of print.
3. Lorenzo A, Kthupi A, Liu W, Hamza C, Todorova AA, Kuburi S, Ellis AK, Keown-Stoneman C, Fadel SA, Gagnon F. The mental health impact of the COVID-19 pandemic on post-secondary students: A longitudinal study. Psychiatry Res. 2023 Sep;327:115401. doi: 10.1016/j.psychres.2023.115401. Epub 2023 Jul 30.
4. Linton S, Hossenbaccus L, Ellis AK. Evidence-based use of antihistamines for treatment of allergic conditions. Ann Allergy Asthma Immunol. 2023 Jul 28:S1081-1206(23)00524-0. doi: 10.1016/j.anai.2023.07.019. Epub ahead of print.
5. Greenhawt M, Dribin TE, Abrams EM, Shaker M, Chu DK, Golden DBK, Akin C, Anagnostou A, ALMuhizi F, Alqurashi W, Arkwright P, Baldwin JL, Banerji A, Bégin P, Ben-Shoshan M, Bernstein J, Bingemann TA, Bindslev-Jensen C, Blumenthal K, Byrne A, Cahill J, Cameron S, Campbell D, Campbell R, Cavender M, Chan ES, Chinthrajah S, Comberiati P, Eastman JJ, Ellis AK, Fleischer DM, Fox A, Frischmeyer-Guerrerio PA, Gagnon R, Garvey LH, Grayson MH, Isabwe GAC, Hartog N, Hendron D, Horner CC, Hourihane JO, Iglesia E, Kan M, Kaplan B, Katelaris CH, Kim H, Kelso JM, Khan DA, Lang D, Ledford D, Levin M, Lieberman JA, Loh R, Mack DP, Mazer B, Mody K, Mosnaim G, Munblit D, Mustafa SS, Nanda A, Nathan R, Oppenheimer J, Otani IM, Park M, Pawankar R, Perrett KP, Peter J, Phillips EJ, Picard M, Pitlick M, Ramsey A, Rasmussen TH, Rathkopf MM, Reddy H, Robertson K, Rodriguez Del Rio P, Sample S, Sheshadri A, Sheik J, Sindher SB, Spergel JM, Stone CA, Stukus D, Tang MLK, Tracy JM, Turner PJ, Vander Leek TK, Wallace DV, Wang J, Wasserman S, Weldon D, Wolfson AR, Worm M, Yacoub MR. Updated guidance regarding the risk of allergic reactions to COVID-19 vaccines and recommended evaluation and management: A GRADE assessment and international consensus approach. J Allergy Clin Immunol. 2023 Aug;152(2):309-325. doi: 10.1016/j.jaci.2023.05.019. Epub 2023 Jun 7.
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Conference Presentations:

1. 2023 – COVID-19 Immunity Task force Scientific Meeting

Burrows AG, Linton SL, Thiele J, Sheth PM, Vanner S, Ellis AK. Characterizing SARS-CoV-2 vaccine and post-infection humoral an soluble immune responses

2. 2023 – American Academy of Allergy, Asthma, and Immunology
   Linton SL, Davis A, Thiele J, Steacy L, Ellis AK. Reporting on the Levels of Ragweed Specific and Total Immunoglobulin-E Following a Nasal Allergen Challenge Developed by the Allergic Rhinitis Clinical Investigator Collaborative (AR-CIC)
3. 2023 – American Academy of Allergy, Asthma, and Immunology
   Hossenbaccus L, Walker T, Linton SM, Ellis AK. Reproducibility of the Specialized PArticulate Control Environmental Exposure Unit (SPAC-EEU) as a Novel Controlled Cat Dander Exposure Room
4. 2022 – Canadian Society of Allergy and Clinical Immunology
   Davis A, Linton SM, Thiele J, Hossenbaccus L, Botting H, Walker T, Steacy L, Ellis AK. Analyzing phenotypes post-exposure in allergic rhinitis (APPEAR): comparing phenotype distribution in the Environmental Exposure Unit and nasal allergen challenge.
5. 2022 – American Academy of Allergy, Asthma, and Immunology
   Hunt K, Foley M, **Ellis AK**, Connors L, Hildebrand K. Trends in the proportion of women speakers at North American allergy and immunology conferences over a 12-year period. J Allergy Clin Immunol 01 Feb 2022. 149(2):AB119.
6. 2022 – American Academy of Allergy, Asthma, and Immunology
   Linton S, Thiele J, Steacy LM, **Ellis AK**. Cytokine analysis of serum before and after nasal allergen challenge with ragweed extract. J Allergy Clin Immunol 149(2):AB218 Feb 01 2022. (accepted for virtual poster presentation)
7. 2022 – American Academy of Allergy, Asthma, and Immunology
   Hossenbaccus L, Linton S, Thiele J, Steacy L, Walker T, Malone C, **Ellis AK**. Biological Responses to House Dust Mite Exposure in the Environmental Exposure Unit.
   J Allergy Clin Immunol. 149(2):AB228. Feb 01 2022.
8. 2022 – Canadian Respiratory Conference
   Xu K, Linton S, Sunavsky A, Garvey S, Steacy LM, Hopman WM, Tripp DA, **Ellis AK**. Anxiety in allergic rhinitis (AR) patients during the Coronavirus disease 2019 (COVID-19) pandemic. (accepted as a moderated poster)

Anxiety in Allergic Rhinitis (AR) Patients During the Coronavirus Disease 2019 (COVID-19) Pandemic

Kayley Xu[1], Sophia Linton[1,2,3], Adam Sunavsky[4], Sarah Garvey[2,3], Lisa M Steacy[2,3], Wilma M Hopman[5], Dean A Tripp[1,6], Anne K Ellis[1,2,3,7]

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INTRODUCTION

Allergic Rhinitis (AR) and Anxiety

- AR is an inflammatory disease of the nasal mucosa resulting from an IgE-mediated response to allergen exposure
- AR is a historically trivialized condition of high prevalence and poor symptom control, estimated to affect **nearly one in every four Canadians**[1]
- There is evidence of a positive relationship between AR and anxiety syndromes and symptoms, but the body of literature on these topics remains somewhat conflicted[2]

Context of Coronavirus Disease 2019 (COVID-19) Pandemic

- **Symptom overlap** between AR and the initial presentation of COVID-19 (cough, rhinorrhea, nasal congestion, conjunctivitis) makes AR patients a population of interest[3]
- Increased pandemic-time anxiety has been reported with allergic conditions, including AR, though study is limited[4,5]
- **No literature currently exists exploring the AR-anxiety relationship during the COVID-19 pandemic in a North American context**

OBJECTIVES

A. Compare anxiety in a group of survey respondents with AR against a control group

B. Explore factors associated with anxiety within the AR subgroup

METHODS

Survey Design

- COVID-19 Associated Anxiety in Allergic Rhinitis and asthma patients Experiencing Symptoms (CAAARES) Survey
- Data collection period
  - April-August 2020
  - Spring allergy season (grass, tree, mold)
- Population: adults (18+) residing in Ontario
- Distributed virtually on the "Qualtrics XM" platform
- **Response: 835 participants**

Measures

- Generalized Anxiety Disorder Assessment-7 (GAD-7)[6]
  - Score: 0-21
  - 0-4: minimal anxiety
  - 5-9: mild
  - 10-14: moderate
  - 15-21: severe
- Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ)[7]
  - Score: 0-6, greater AR burden of disease with higher score
  - 7 domains

RESULTS

AR Group vs. Control Group Analysis

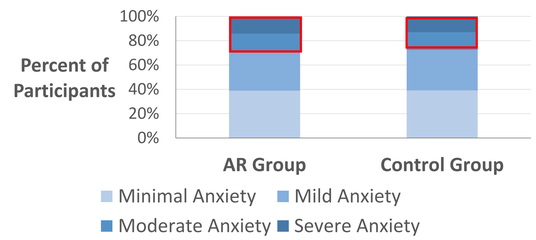

Figure 1. High levels of anxiety were found in both the AR group (n=143) and the control group (n=608). 28.0% of participants in both groups (indicated by red boxes) reported GAD-7 scores ≥10, which is the threshold for diagnosis of Generalized Anxiety Disorder (GAD).[6]

Predictor Variables	Regression 1				Regression 2			
	B	95% CI Lower	95% CI Upper	*p* Value	B	95% CI Lower	95% CI Upper	*p* Value
Gender (0=Man, 1=Woman)	0.243	-0.610	1.095	0.577	0.242	-0.611	1.095	0.577
Age	-0.731	-0.971	-0.490	0.000	-0.739	-0.983	-0.494	0.000
Asthma status (0=N, 1=Y)	0.192	-0.506	0.890	0.590	0.171	-0.536	0.878	0.635
Previous anxiety diagnosis (0=N, 1=Y)	4.004	3.270	4.738	0.000	4.001	3.266	4.736	0.000
Past access of Mental Health Services (MHS) (0=N, 1=Y)	0.662	-0.084	1.407	0.082	0.662	-0.084	1.408	0.082
Current access of MHS (0=N, 1=Y)	1.002	-0.045	2.049	0.061	1.000	-0.047	2.048	0.061
General COVID-19-related worry	0.924	0.552	1.296	0.000	0.925	0.553	1.297	0.000
Perceived COVID-19 stress of others	0.686	0.511	0.861	0.000	0.685	0.510	0.860	0.000
AR status (0=N, 1=Y)	--	--	--	--	0.161	-0.692	1.013	0.711

Dependent variable: GAD-7 Score

Table 1. After controlling for other predictor variables in a Hierarchal Multiple Regression (HMR) model, AR status had no significant predictive effect on GAD-7 score (B=0.161, *p*=0.711). In Regression 1, the overall regression was statistically significant (R^2=0.397, F(8,703)=57.822, p<.001). After adding AR status in Model 2, ΔR^2=.000, F(1,702)=0.137, p=0.711. Predictor variables significant at the p<0.05 level are indicated in red.

AR Subgroup Analysis

	1	2	3	4	5	6	7	8	9
1. GAD-7	--								
2. Total RQLQ	.470	--							
3. RQLQ (Activity limitations)	.283	.807	--						
4. RQLQ (Sleep problems)	.257	.779	.655	--					
5. RQLQ (Non-nose/eye symptoms)	.629	.719	.451	.448	--				
6. RQLQ (Practical problems)	.301	.847	.707	.615	.416	--			
7. RQLQ (Nose symptoms)	.299	.847	.683	.632	.420	.841	--		
8. RQLQ (Eye symptoms)	.244	.792	.587	.592	.435	.629	.610	--	
9. RQLQ (Emotional function)	.385	.884	.710	.657	.486	.787	.768	.693	--

All correlations significant at the 0.01 level (2-tailed).

Table 2. Significant positive correlations were found between GAD-7 and burden of disease for the total RQLQ score and all 7 domain scores (*p*<.001 for all), **with the non-nose/eye symptom domain having the strongest correlation** (*r*=0.629). Correlations with GAD-7 indicated in red.

Predictor Variables	Regression 1				Regression 2			
	B	95% CI Lower	95% CI Upper	*p* Value	B	95% CI Lower	95% CI Upper	*p* Value
Gender (0=Man, 1=Woman)	-0.129	-1.060	0.802	0.785	-0.352	-1.243	0.538	0.437
Age	-0.774	-1.049	-0.499	0.000	-0.786	-1.049	-0.523	0.000
Previous anxiety diagnosis (0=N, 1=Y)	3.648	2.837	4.460	0.000	3.285	2.505	4.065	0.000
Past access of Mental Health Services (MHS) (0=N, 1=Y)	0.794	-0.019	1.607	0.056	0.815	0.039	1.591	0.040
Current access of MHS (0=N, 1=Y)	1.084	-0.067	2.235	0.065	0.797	-0.304	1.898	0.156
Perennial AR (0=N, 1=Y)	0.486	-0.255	1.227	0.198	-0.109	-0.833	0.616	0.768
General COVID-19-related worry	0.529	0.114	0.944	0.013	0.581	0.184	0.978	0.004
Perceived COVID-19 stress of others	0.647	0.454	0.840	0.000	0.549	0.363	0.736	0.000
Being treated differently when showing AR symptoms (0=N, 1=Y)	0.254	-0.732	1.240	0.613	-0.225	-1.174	0.724	0.642
Worry about mistaking AR symptoms for COVID-19 (0=N, 1=Y)	0.400	-0.022	0.821	0.063	0.064	-0.348	0.476	0.761
Worry about increased COVID-19 risk (0=N, 1=Y)	0.655	0.225	1.085	0.003	0.417	0.002	0.832	0.049
RQLQ	--	--	--	--	1.519	1.121	1.916	0.000

Dependent variable: GAD-7 Score

Table 3. After controlling for other predictor variables in an HMR model, RQLQ score had a significant predictive effect on GAD-7 score (B=1.519, *p*<.001). In Regression 1, the overall regression was statistically significant (R^2=0.431, F(11,565)=38.878, p<.001). After adding RQLQ in Model 2, ΔR^2=0.052, F(1,564)=56.211, p<.001. Predictor variables significant at the p < 0.05 level are indicated in red.

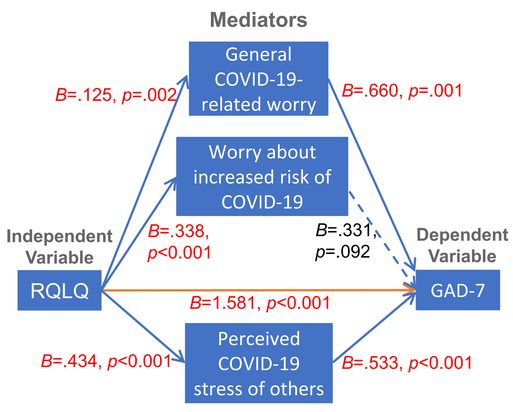

Figure 2. General COVID-19-related worry and perceived COVID-19 stress of others mediated the relationship between RQLQ and GAD-7 score in a parallel mediation model (IE=.083, 95% CI=[.016,.167] and IE=.231, 95% CI=[.120,.367], respectively). Worry about increased risk of COVID-19 did not have a significant mediation effect (IE=.112, 95% CI=[-.031,.254]).

CONCLUSIONS

- High levels of anxiety exist during the COVID-19 pandemic regardless of AR status
- Within the AR subgroup, there were significant positive correlations between anxiety and burden of disease, with non-nose/eye symptoms having the strongest correlation
- General COVID-19-related worry and perceived COVID-19 stress of others were identified as mediators of the relationship between RQLQ score and GAD-7 score
- **These findings indicate the importance of early anxiety screening in all patients and highlights the importance of non-nose/eye symptoms in AR management**

FUTURE DIRECTIONS

- Longitudinal study of participants to examine time-dependent trends (e.g. different allergy seasons, COVID-19 case incidence)
- Investigate changes in anxiety levels with developments over the course of the COVID-19 pandemic (e.g. policy changes to mask mandates, vaccine rollout, etc.)
- Explore pandemic-time anxiety in groups of patients with other allergic or respiratory diseases in a North American context

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Serum biomarkers and Staphylococcus aureus carriage in ragweed-induced allergic rhinitis using the nasal allergen challenge model

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Abstract

Background: The relationship between *Staphylococcus aureus* (SA) nasal carriage and allergic rhinitis blood biomarkers is not known. The current study compares ragweed(RW) specific(s) immunoglobulin-E(IgE) levels and serum cytokine levels and in RW-allergic participants colonized with and without SA. The allergen exposure was modeled using the nasal allergen challenge model (NAC), which consists of a screening and challenge visit.

Methods: Nasal SA carriage was assessed using culture-based screening methods in 15 RW-allergic participants before their NAC with individualized RW-extract doses determined using a titration challenge. Peripheral blood samples collected at the screening visit were used to evaluate sIgE levels, while those collected at the challenge visit were used to evaluate serum cytokine (baseline, 6- and 24-hour post-NAC). The cytokines IL-1b, IL-4, IL-5, IL-6, IL-10, IL-13, TNF-a, IFN-g, MCP-1, MIP-1b, and RANTES were measured using Luminex xMAPTM technology, and sIgE concentrations were measured using an ImmunoCAP assay on the Phadia 100 machine. All statistical analyses were performed on GraphPad Prism 9.0.

Results: Four RW-allergic participants were colonized with antibiotic-sensitive SA (SA+), and 11 were not (SA-). The sIgE (p=0.3429) levels were not significantly different between the two populations. The concentration of MCP-1 at 24-hours was significantly higher in SA+ than SA- (p=0.0399). MIP1-b (p=0.0170) and IFN-g (p=0.0214) concentrations were significantly elevated in SA- at 24-hours compared to baseline. Individual cytokine levels were widely distributed, and therefore the change in cytokine levels from baseline was calculated. The change in IL-5 concentration at 6-hours compared to baseline was significantly greater in SA+ than SA- (p=0.0148).

Conclusion: There is differential cytokine expression in the blood of SA+ and SA- populations post-NAC while sIgE levels were not significantly different. These results suggest that SA carriage may impact the allergic response to RW exposure in the peripheral blood, however more investigations are needed to support these findings and identify potential mechanistic pathways.

Background

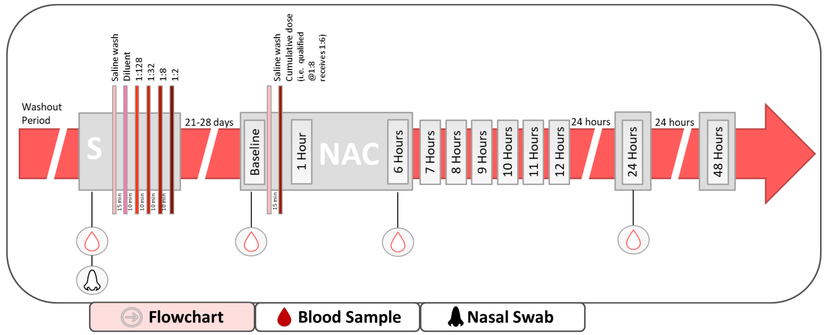
Allergic Rhinitis (AR)
- Immunoglobulin-E (IgE) mediated inflammatory disease caused by allergen exposure

Nasal Allergen Challenge (NAC)
- Optimized and validated model of AR
- Controlled and direct delivery of an individualized concentration of allergen extract into the nasal cavity

***Staphylococcus aureus* (SA)**
- Gram-positive, Firmicute
- Associated with atopic dermatitis, chronic rhinosinusitis, and food allergy (1-3)
- The relationship between SA nasal carriage and AR blood biomarkers is not known.

AIM: The current study compares ragweed (RW) specific IgE levels and serum cytokine levels and in RW-allergic participants coonized with and without SA.

Study Design & Methods



- RW sIgE measured using ImmunoCAP assay on the Phadia 100 machine
- The cytokines IL-1b, IL-4, IL-5, IL-6, IL-10, IL-13, TNF-a, IFN-g, MCP-1, MIP-1b, and RANTES were measured using Luminex xMAP™ technology on a Bioplex 200 analyzer.

Flowchart | Blood Sample | Nasal Swab

- Nasopharyngeal swabs analyzed using a culture and sensitivity test to assess SA carriage and susceptibility to antibiotics.
- Performed by Microbiology Laboratory at Kingston Health Sciences Center – KGH Site.

Flowchart | Blood Sample | Nasal Swab

Results

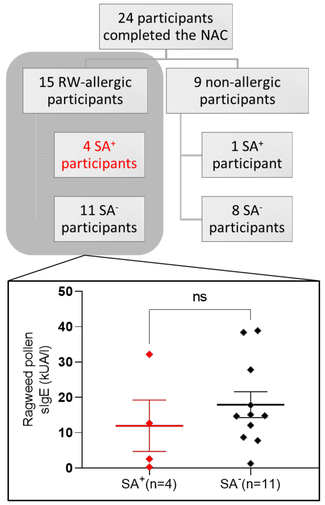


Figure 1. SA nasal carriage distribution and sIgE concentrations. Four RW-allergic participants were colonized with antibiotic-sensitive SA (SA+), and 11 were not (SA-). Of the allergics, the sIgE (p=0.3429) levels were not significantly different between SA+ and SA- populations.

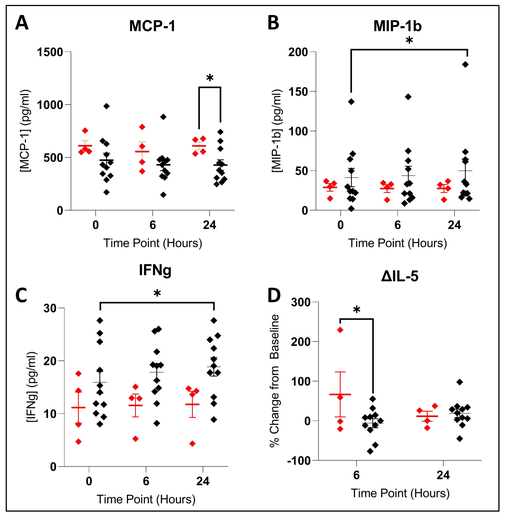


Figure 2. Serum cytokine concentrations. (A) The concentration of MCP-1 at 24-hours was significantly higher in SA+ than SA- (p=0.0399). MIP1-b (B; p=0.0170) and IFN-g (C; p=0.0214) concentrations were significantly elevated in SA- at 24-hours compared to baseline. (D) The change in IL-5 concentration at 6-hours compared to baseline was significantly greater in SA+ than SA- (p=0.0148)

Summary & Discussion

- Allergic participants had a higher carriage rate of antibiotic-sensitive SA.
- There is differential cytokine expression in the blood of SA+ and SA- populations post-NAC while sIgE levels were not significantly different.
- These results suggest that SA carriage may impact the allergic response to RW exposure in the peripheral blood.
  - We have previously shown there is no association between SA carriage and peripheral blood cell counts except SA+ participants had significantly higher levels of lymphocytes in the blood at 6 hours (4).
  - More investigations are needed to support these findings and identify potential mechanistic pathways.
- This study is limited by small sample sizes (n=24 participants).

Acknowledgements

This study was supported by the Division of Allergy & Immunology at Kingston General Hospital, the Spear Endowment Funds and the Department of Medicine at Queen's University.

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Poster #1

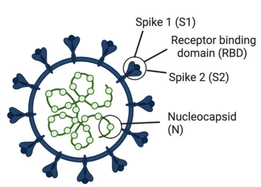
Comparing Commercially Available SARS-CoV-2 Immunoglobulin-G Immunoassays to a Clinically Validated Assay to Determine Seroprevalence.

Alyssa G. Burrows BHSc[1,2], Jenny Thiele MSc[1,2], Sophia Linton BSc[1,2], Prameet M. Sheth PhD[3,4,5], Stephen Vanner MD, MSc[1,4], Anne K. Ellis MD, MSc[1,2,3]

Abstract

Background: Globally, severe-acute-coronavirus disease-2 (SARS-CoV-2) has caused over 500 million infections and over 6 million deaths, respectively (1). Monitoring SARS-CoV-2 seroprevalence is crucial to determining population immunity.
Methods: Serum samples were collected prospectively from Queen's University Faculty of Health Sciences (FHS) students and recovered community members to determine asymptomatic carriage and seroprevalence to SARS-CoV-2. A clinically validated SARS-CoV-2 Immunoglobulin (Ig)-G assay (Abbott) was used to detect Ig-G for SARS-CoV-2 nucleocapsid in all serum samples. Subsequently, samples were selected and compared to two commercially available immunoassays (Bio-Plex(Bio-Rad) & MILLIPLEX® (MilliporeSigma)) for IgG antibodies to four SARS-CoV-2 proteins (spike-1, spike-2, nucleocapsid, receptor-binding-domain). GraphPad 9.2 was used for statistical analysis.
Purpose: Determine the reliability and variability of the Bio-Plex and MILLIPLEX® compared to the Abbott immunoassay.
Results: From May 2020-June 2021, 1,229 and 16 serum samples were collected from 457 FHS participants and 11 recovered community participants, respectively. Nine samples were selected for further assay-validation purposes. Using a two-tailed Spearman correlation to compare the R^2-values for the Bio-Plex vs. Abbott assay were: 0.53 (p=0.1492), 0.37 (p=0.3268), 0.795 (p<0.0143), and 0.444 (p=0.2333) MILLIPLEX® vs. Abbott assay, the R^2-values were: 0.99 (p<0.0001), 0.9743 (p<0.0001), 0.95 (p<0.0004) and 0.89 (p<0.0022) for 1:100, 1:250, 1:500, and 1:1000 dilutions, respectively. The inter-assay CV% for the 1:100 and 1:500 dilutions ranged from 0.75-19.66 and 4.49-18.88 (MILLIPLEX®), and 17.26-91.55 and 16.79-91.65 (Bio-Plex).
Conclusion: The reliability and variability of the MILLIPLEX® immunoassay was superior and will be used to determine the seroprevalence of IgG to all four SARS-CoV-2 proteins in all serum samples.
References: (1) COVID-19 Map [Internet]. Johns Hopkins Coronavirus Resource Center. [cited 2022 May 5]. Available from: https://coronavirus.jhu.edu/map.html

Background



- SARS-CoV-2 has 29 proteins
- Recovered= antibodies to all SARS-CoV-2 proteins
- Vaccinated= antibodies to S1, S2, RBD

Abbott ARCHITECTi1000SR

- Clinically validated
- Detects IgG antibodies to N protein indicating prior infection
- Expensive/ less accessible

Bio-Plex 200

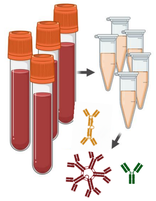
- Commercially available assays
- Bio-Plex and Millipore SARS-CoV-2 detects IgA, IgM, IgG antibodies to N, S1, S2, RBD
- Can differentiate between infection and vaccinated individuals
- Less expensive/ more accessible

Monitoring SARS-CoV-2 seroprevalence is crucial to understanding a susceptible population and guiding appropriate public health response.

Affiliations

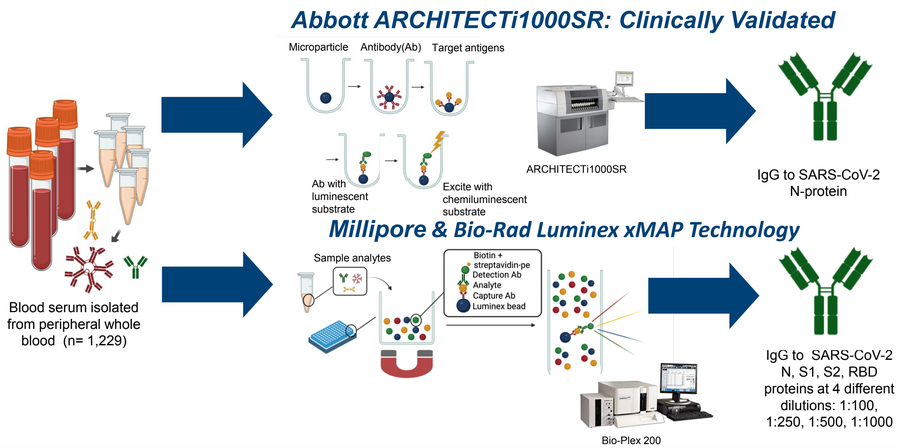
1. Department of Medicine, Queen's University, Kingston, ON, Canada,
2. Allergy Research Unit, Kingston, ON, Canada,
3. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada,
4. Gastrointestinal Disease Research Unit (GIDRU), Faculty of Health Science, Queen's University, Kingston, ON, Canada,
5. Pathology & Molecular Medicine, Queen's University, Kingston, ON, Canada

Study Design



Serum samples collected from peripheral whole blood May 27, 2020 – June 23 2021 over 1 to 5 visits.

Methods



Results

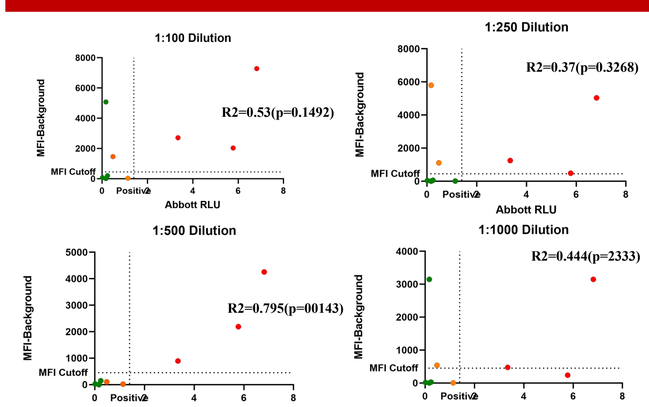


Figure 1. No significant correlations were observed between the Bio-Plex and Abbott Immunoassays. Legend: Red= positive(>1.40RLU), Orange= medium (0.48-1.14RLU) , Green= negative (<0.02-0.24RLU).

Abbreviations: MFI= Mean Fluorescent Index, RLU= Relative Light Unit.

Results

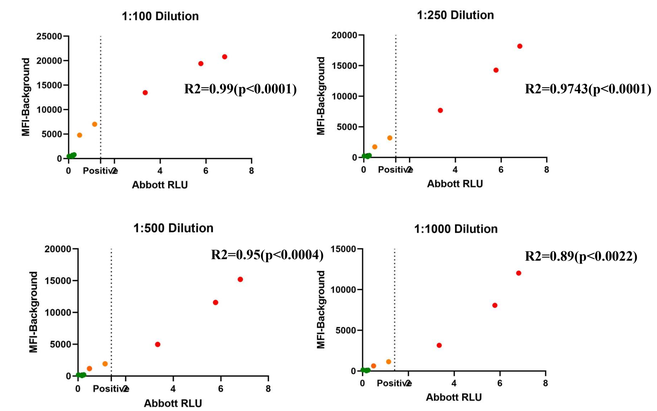


Figure 2. Positive and significant correlations were observed between MILLIPLEX® and Abbott Immunoassays at all dilutions.
Legend: Red= positive(>1.40RLU), Orange= medium (0.48-1.14RLU), Green= negative (<0.02-0.24RLU) Abbreviations: MFI= Mean Fluorescent Index, RLU= Relative Light Unit.

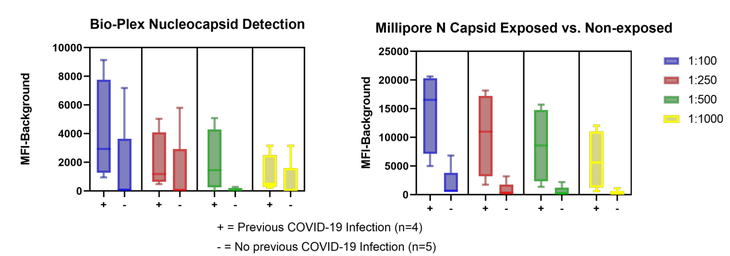


Figure 3. MILLIPLEX reliably detects IgG antibodies at different dilutions to SARS-CoV-2 Nucleocapsid while Bio-Plex does not.
Abbreviations: MFI= Mean Fluorescent Index.

Summary & Discussion

The reliability and variability of the MILLIPLEX® immunoassay was superior and will be used to determine the seroprevalence of IgG, IgA, and IgM antibodies to four SARS-CoV-2 proteins in all serum samples.

Cardiology

Dr. Damien Redfearn
Division Chair

Dr. Wael Abuzeid
Research Lead

Summary

- *Combining intraplaque neovascularization with risk stratification by carotid stress ECHO*
- *Improving management and outcomes for patients requiring admission for heart failure*
- *Expanding point-of-care ultrasound training to remote health care providers*
- *Developing tools and screening athletes for sudden cardiac death*
- *Psychology of athletic cardiovascular evaluations*
- *Female risk factors for post-infarction depression and anxiety*
- *Assess successful transcatheter mitral valve repair*
- *Creation of a structural heart disease database by examine the effects of intertribal block as predictive for atrial fibrillation patients*
- *Improving understanding of Lyme carditis*
- *Research involving pacemakers and cybersecurity*

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

CINQ

- Director: Dr Amer Johri

1. CIRCE Study: Combining Intraplaque Neovascularization with Risk Stratification by Carotid Stress echo. This is a prospective parallel 6 centre study assessing intraplaque neovascularization in stress echo patients.

   Project opportunity: Involvement in patient recruitment in echo lab and U/S image analysis

2. ARCTICA study: Point of care U/S training and expertise are unavailable to all practitioners. This study aims to implement a tele-POCUS training and consultation program for non expert users at geographically remote facilities **Project opportunity:** Participate with team to train remote health care workers to set up workshops and determine average change in pre and post training test scores

Interventional Cardiology

- Research lead: Wael Abuzeid

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

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

2. Structural heart disease database: This will involve setting up a database of all patients undergoing structural interventions and allowing us to study outcomes and factors affecting success locally. Project opportunity: examining the effect of interatrial block (ECG finding) as predictive for Atrial fibrillation patients

Interventional EP

- Research contacts Dr Baranchuk, Dr Neira

- Opportunities to be involved in Research on topics including Lyme carditis. One of the current residents was an author on a textbook covering this topic
- Opportunities to be involved in Research involving pacemakers and ICD cybersecurity
- Opportunities to be involved in Research on the effect of interatrial block as a predictor of atrial fibrillation in patients undergoing transcatheter valvular interventions

Heart Failure

- Research lead: Aws Almufleh

1. ACCELERATE-HF: Prospective clinical study examining the effectiveness HF decision aids and POCUS in reducing readmission rates for HF patients
2. Systematic review on “The utility of point of care ultrasound in identifying patients with heart failure who are at risk of hospital readmission”.

Projects opportunity: Patient recruitment, physical exams and POCUS, writing reviews and editorials

Heart Failure II

- Research lead: Aws Almufleh

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

Projects opportunity:

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

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

Cardiovascular Imaging Network Queen's

Accelerated Remote Consultation by Tele-POCUS in Cardiopulmonary Assessment (ARCTICA): A Proof-of-Concept Study

Queen's University

Nicholas Grubic[1], Salwa Nihal[1], Julia Herr[1], Jeffrey Lam[1], Sheung Wing Sherwin Wong[1], Daniel J. Belliveau[1], Stephen Gauthier[1], Steven J. Montague[1], Amer M. Johri[1]

[1]Queen's University, Kingston, Ontario, Canada

BACKGROUND

- Point-of-care ultrasound (POCUS) is recommended as a first-line imaging tool for patients with COVID-19 and cardiopulmonary symptoms.[1]
- Currently, there is no standardized teaching approach and few training opportunities for non-specialists to obtain POCUS skills.[2,3]
- The use of real-time, remotely supervised ultrasound (Tele-POCUS) can be used to provide feedback during clinical practice, which is particularly useful in settings where on-site supervision is unavailable.[4,5]

AIM & OBJECTIVE

- **Aim:** Integrate both asynchronous and synchronous teaching components into a fully virtual, live-streamed ultrasound teaching program for novice learners.
- **Objective:** Investigate the feasibility of the program at a single academic center with 6 non-expert physician learners.

METHODS

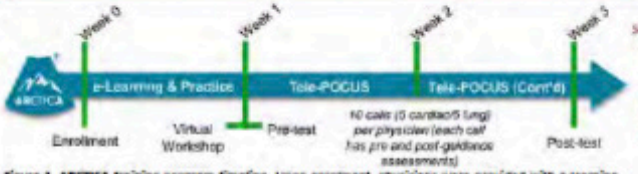
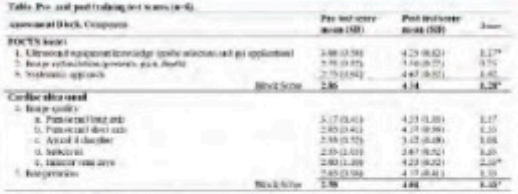


Figure 1. ARCTICA training program timeline. Upon enrolment, physicians were provided with e-learning modules and instructed to practice independently (Week 0). After one week of self-directed learning, physicians participated a live workshop led by expert imagers (Week 1). Following training, physicians were assessed through a POCUS pre-test (Week 1), prior to participating in a two-week tele-POCUS training block (Weeks 1-2). At the end of the study, physicians were assessed through a POCUS post-test (Week 3).

- To assess knowledge and skill development, the change in pre- and post-training scores (Δ_{score}) across 3 testing blocks (POCUS basics, cardiac ultrasound, and pleura/lung ultrasound) was calculated.
- Wilcoxon's signed-rank test was used to compare scores.

Figure 2. Sample tele-POCUS consultation between expert trainer and learner. Learners called expert trainers through commercially available Reacts telehealth software. All tele-POCUS scans were conducted using a Samsung Galaxy tablet equipped with a Lumify phased-array probe. Expert trainers were able to view the physical probe orientation and POCUS scans performed by learners, allowing for remotely delivered guidance and mentorship.

RESULTS



- **POCUS basics Δ_{score}=1.38 ($p<0.05$)**
- **Cardiac ultrasound Δ_{score}=1.43 ($p<0.05$)**
- **Pleura/lung ultrasound Δ_{score}=1.04 ($p<0.05$)**

- All learners improved skills in device operation, image optimization, and image acquisition following our training program, without the need for any face-to-face contact with expert teachers.

CONCLUSIONS & NEXT STEPS

- Introductory POCUS skills can be taught to remote users using an entirely virtual live-streamed format, demonstrating significant enhancement in scanning skills.
- Our program has expanded across Canada to 6 academic sites, which will provide Tele-POCUS training to 9 satellite care centers in remote, Northern, and Indigenous communities.

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FUNDING/DISCLOSURES

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CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

Canadian Cardiovascular Society

Heart&Stroke

Cardiovascular Imaging Network

PHGY115

Detection of Vulnerable Plaque to Enhance Stress Echocardiography

Michaela Spence, Shagun Jain, Julia Herr, MSc, Nabil Hawwa, MSc, Robyn Jackson, MD, Marie-France Hetu, PhD, Dathan Liblik, Samir Hazra, BSc, MD, Anthony Sanfilipo, MD, Amer M. Johri, MD, MSc, FRCPC, FASE

CINQ Lab, Queen's University, Kingston, ON.

Queen's University

INTRODUCTION

- Screening of low-intermediate risk patients for coronary artery disease is performed using a stress echocardiogram (SE) with moderate sensitivity and specificity, leading to false positives and missed diagnoses.
- Adding carotid artery ultrasound to identify plaque burden in SE enhanced the predictive value of SE for identifying patients with coronary artery disease[1].
- The European Guidelines on Cardiovascular Disease Prevention now include carotid ultrasound as class IIb recommendation.[2]
- Plaque height (thickness) of ≥ 1.5mm is associated with increased stress test sensitivity: 59% to 100%.[1]
- Pixel distribution analysis (PDA) shows that high percentages of fat or calcium tissue plaques are associated with an increased risk for cardiovascular events within 5 years.[3]
- By combining the use of PDA with the standard SE techniques, we could potentially fulfill the need for a way to rapidly and accurately identify undiagnosed patients who need treatment for CAD

HYPOTHESIS & OBJECTIVES

Combining standard SE with vulnerable carotid plaque assessment through PDA techniques would enhance the prognostic performance of the SE over standard SE alone

Objective: To identify components of plaque composition assessed by Intelliplaque, a novel PDA software, that added discriminatory and reclassification benefit to the SE.

STUDY DESIGN

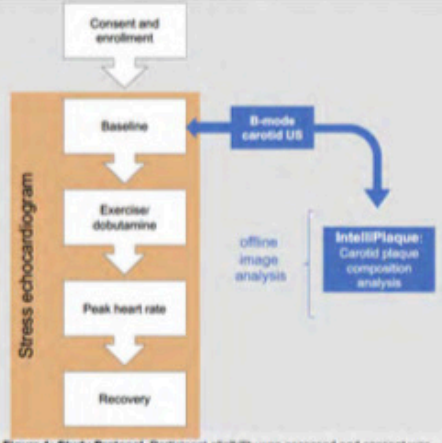

Figure 1: Study Protocol. Participant eligibility was assessed and consent was obtained before stress echocardiograms (SE) commenced. B-mode carotid ultrasound images were taken before baseline SE images. Images were analyzed offline using Intelliplaque.

METHODS

Patient Population

- Participants: 84 outpatients referred for SE at Kingston Health Sciences Centre Echo Lab → low to intermediate risk group for CAD.

Carotid Ultrasound/Stress Echocardiogram (CSE) Protocol and Data Collection (Figure 1)

- B mode CSE images taken using FOVUS protocol taken for offline analysis before SE.[5]

Plaque Quantification (Figure 2)

- Atherosclerotic plaque outlined: focal structure height ≥1.5mm or 50% greater vs surrounding intima-media thickness encroaching into arterial lumen.[4]
- Carotid intima media thickness, maximum plaque height and total plaque area data collected.

PDA Analysis via IntelliPlaque software (CINQ proprietary, Ferko Liblik Inc) (Figure 2)

- Atherosclerotic plaque areas outlined based on previous plaque quantification analysis; % pixels in each tissue greyscale value range calculated to determine plaque composition:

Major Adverse Cardiac Event (MACE) Outcome Follow Up

- MACE recorded via follow up telephone interview at 30 days/ 6 months
- Medical health records reviewed for event confirmation.

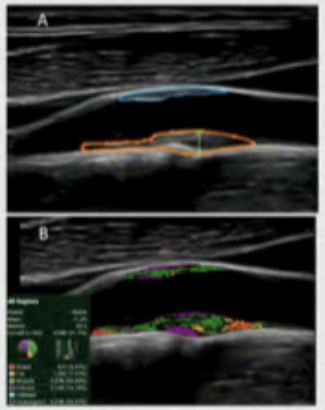

Figure 2: Carotid Ultrasound Plaque Quantification (A) and PDA (B) Analysis of Left Carotid Bulb. (A) Atherosclerotic plaque 1 is outlined in blue, atherosclerotic plaque 2 is outlined in orange. Maximum plaque height is shown in green. (B) Intelliplaque completed semi-automatic identification of the percentage of the plaques taken up by blood, fat, muscle, fibrous and calcified tissues shown in legend on the left bottom corner.

RESULTS

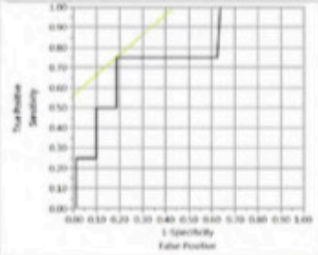

Figure 3: Receiver Operating Curve to Assess Carotid MPH as a Predictor for MACE. A maximum plaque height of ≥ 3.02mm was determined to be the threshold for predicting MACE. The AUC value is 0.762; p=0.04.

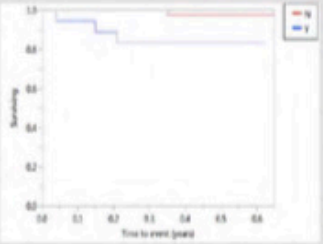

Figure 4: Kaplan-Meier Analysis. Survival from MACE for patients with a MPH ≥ 3.02mm (Blue) was significantly lower than patients who had a MPH < 3.02mm (Red). (p = 0.002.)

Table 1. Baseline population characteristics.

Variable, n (%)	All (n=84)	Stress Echo (+) Yes (n=12)	Stress Echo (+) No (n=72)	P-value	
Caucasian	79 (94)	11 (92)	68 (94)	1	
Sex Male	28 (33)	4 (33)	24 (33)	1	
Age, mean ± SD	62.2±11.0	61.9±8.54	62.3±11.5	0.74	
Hyperlipidemia	35 (42)	5 (42)	30 (42)	1	
Hypertension	38 (45)	5 (42)	33 (46)	1	
Diabetes	17 (20)	3 (25)	14 (19)	0.7	
Current Smoker	10 (12)	4 (33)	6 (8)	0.02	*
Obesity (BMI >30)	30 (43)	6 (50)	30 (42)	0.76	

* Fisher's Exact Test, 2-tail, p=0.05 ;There were no significant differences in medication types between groups.

Table 2. Carotid plaque quantification and PDA variables between stress echo results.

Variable, mean ± SD	All	Stress Echo (+) Yes	Stress Echo (+) No	P-value
CIMT, mm	0.65±0.16	0.64±0.12	0.65±0.16	0.86
MPH, mm	1.90±1.44	2.31±1.57	1.83±1.42	0.25
TPA, mm²	29.9±34.3	38.1±36.8	26.5±33.9	0.32
GSM	51.8±16.0	57.2±20.5	50.8±15.1	0.21
Blood (0-4) %	4.48±6.66	5.19±6.86	4.35±6.66	0.88
Fat (8-26) %	15.8±9.56	13.6±9.68	16.2±9.57	0.40
Muscle (41-76) %	36.8±10.1	33.2±8.81	37.5±10.2	0.12
Fibrous (112-196) %	8.56±7.59	13.3±8.63	7.70±7.14	0.06
Calcium (211-255) %	0.33±0.84	0.28±0.47	0.34±0.90	0.37

Non-parametric Wilcoxon. CIMT, carotid intima media thickness, MPH, maximum plaque area, TPA, total plaque height, GSM, grey scale median.

Table 3: Ultrasound Assessments Identified as Useful for Predicting MACE.

Test (N=84)	Result Type	(+) MACE		(-) MACE		PPV	NPV	Sens.	Spec.	LR+	LR-
	*	TP	3	FP	15						
MPH (3.02 mm)	-	FN	1	TN	65	17%	98%	75%	81%	4.00	0.31

MPH, Maximum plaque height, SE, stress echocardiogram, MACE, major adverse cardiac event, TP, true positive, FP, false positive, FN, false negative, TN, true negative, PPV, positive predictive value, NPV, negative predictive value, LR+, positive likelihood ratio, LR-, negative likelihood ratio.

RESULTS

- Current smokers were significantly more likely to have a positive stress test than non-current smokers (Table 1)
- PDA trend showing a greater % fibrous tissue plaque composition increased the risk of testing positive during SE (Table 2)
- No significant PDA data at this time (Table 2)
- Only MPH had a receiver operating characteristic (ROC) curve significant for predicting MACE. (Figure 3)
- The optimal threshold for predicting MACE was 3.02 mm (Figure 3) with a sensitivity of 75% and a specificity of 81% (Table 3)
- Kaplan-Meier curve analysis: survival was significantly lower for patients with an MPH ≥ 3.02mm vs those with an MPH < 3.02mm (Figure 4)

CONCLUSION

- Overall, this protocol was successful in establishing the necessary team, recruitment methods, patent flow model, and analysis for further continuation of this study.
- Unfortunately, there was not enough data to determine if PDA techniques would enhance prognostic performance over SE alone, although a trend is still present.
- Although a MPH of ≥ 3.02mm was a predictive value for MACE, overall addition of MPH to the SE did not enhance the standard SE sensitivity or specificity vs standard SE alone

Study Limitations

- Small sample size: 84 patients
- Small duration of follow up for MACE collection
- Not all 6 month follow up data collected

Future Directions

- Consent greater number of participants into the study for a larger population size
- Continue to collect MACE over 2 years
- Greater population size and larger duration of follow up time to determine if significant data exists for the addition of PDA to the standard SE

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ACKNOWLEDGEMENTS

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Prediction of Hospitalization and ICU admission for Ontario COVID-19 Patients with Cardiac Comorbidities

Abigail Kearney (BSc, MBI) [a, b], Maddy Hanzlik-Meech (BCPH) [a], Cameron MacKay (BCPH) [a], Liana Evans (BCPH) [a], Alexandra Robins (BSc, MBI) [a, b], Amber L. Simpson (PhD) [a, b, c], Wael Abuzeid (MSc, MD) [b, c]

[a] School of Computing, Queen's University, Kingston, Ontario, Canada;
[b] Department of Biomedical & Molecular Sciences, Queen's University, Kingston, Ontario, Canada; and
[c] Department of Medicine, Queen's University, Kingston, Ontario, Canada;

BACKGROUND

Given limitations on hospital resources as COVID-19 continues to spread, there is a growing interest in how machine learning (ML) can be applied to predict hospitalization and/or ICU admission, especially in patients with cardiac comorbidities.

METHODS

- Supervised (logistic regression) classification models were created based on patient demographic and health data sourced from the Ontario Health Data Platform (OHDP).
- Patients with cardiac comorbidities and a positive COVID-19 test in Ontario between March 2020 and June 2021 were identified.
- Patients with an invalid COVID-19 test, invalid or non-OHIP card number or unlisted outcomes were excluded.
- Outcomes of interest were cardiac comorbidities that can predict 24-hour and 30-day hospitalization or ICU admission.

RESULTS

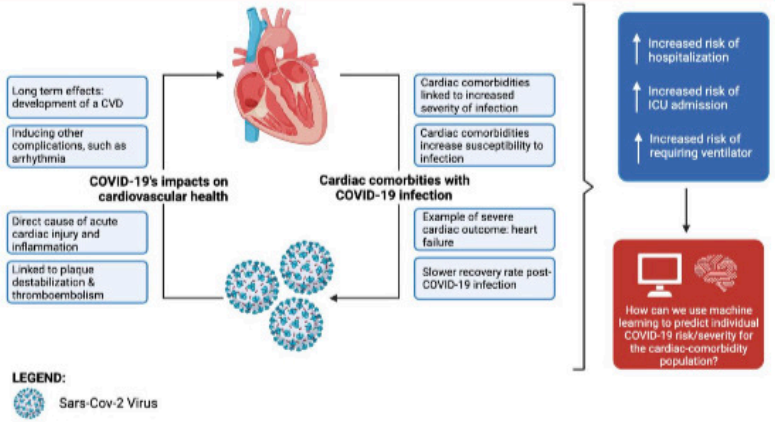
- 72,148 patients were included in our cohort, with 21,912 in the case group (Positive COVID-19 test) and 50,236 patients in the control group (Negative COVID-19 test).
- Presence of Congestive heart failure (CHF), hypertension, diabetes, ischemic heart disease, angina, history of PCI or CABG and bleeding events predicted 24-hour and 30-day hospitalization or ICU admission ($p<0.05$).
- Within 24-hour and 30-day look-back periods, hospitalization or ICU admission was correctly predicted for the cohort at approximately 90% accuracy, using logistic regression models.
- The results were validated by data reserved for model testing and associated analysis of receiver operating characteristic (ROC) plots.

CONCLUSION

Our proposed ML model can predict hospitalization or ICU admission with high accuracy in this large patient cohort with cardiac comorbidities. This model has potential to assist clinicians in classifying patients who may be at risk for a severe COVID-19 outcome, and to further inform public health officials on vulnerable populations. In this way, the project will help to categorize high-risk patients so that more effective intervention strategies can be implemented for treatment of COVID-19.

Cardiovascular disease increases risk of **severe COVID-19** manifestations.

Congestive heart failure, hypertension, diabetes, ischemic heart disease, angina, and history of a major cardiac surgery **predict** COVID-19 based **Hospitalization** and **ICU admission.**



CENTRAL ILLUSTRATION:
Relationship between COVID-19 infection, pre-existing adverse CVD, and severe patient outcomes.

DISCUSSION

- Seven cardiac comorbidities strongly predicted 24-hour and 30-day Hospitalization or ICU admission in patients with COVID-19 in Ontario: CHF, hypertension, diabetes, ischemic heart disease, angina, history of CABG or PCI, and bleeding events.
- This model is one of the first of its kind being produced through the OHDP, making it an important development of the platform and its initiatives.
- Current limitations include lack of vaccination data during the timeframe of the study and its retrospective nature. Future projects should investigate how COVID-19 may cause cardiac ailments or increase susceptibility to their development.

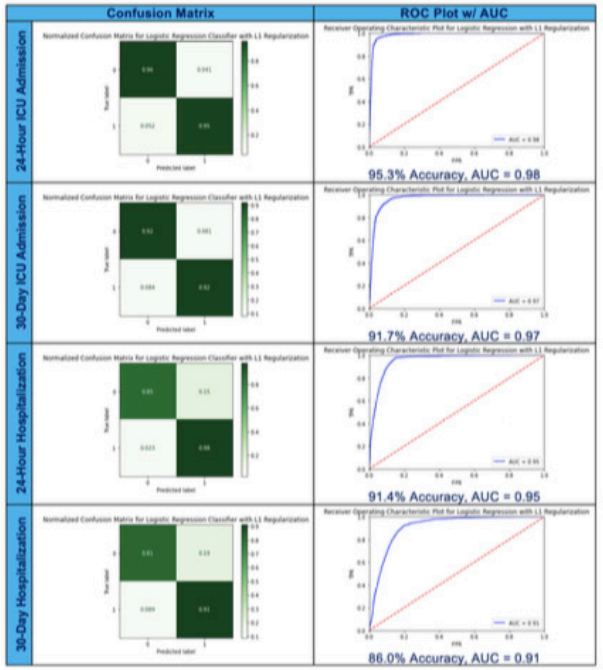


Figure 1. Confusion Matrices and ROC plots with an AUC score were created for each of the four outcome predictions. The AUC value should be taken as the most precise measure of accuracy since the target variable is binary.

DISCLOSURE INFORMATION

- This study was supported by ICES, which is funded by an annual grant from the Ontario Ministry of Health (MOH) and the Ministry of Long-Term Care (MLTC). This study was also supported by the Ontario Health Data Platform (OHDP), a Province of Ontario initiative to support Ontario's ongoing response to COVID-19 and its related impacts. The opinions, results and conclusions reported in this paper are those of the authors and are independent from the funding sources. No endorsement by the OHDP, its partners, or the Province of Ontario is intended or should be inferred.
- Parts of this material are based on data and/or information compiled and provided by CIHI. However, the analyses, conclusions, opinions and statements expressed in the material are those of the author(s), and not necessarily those of CIHI. Further, the authors acknowledge that the clinical registry data used in this Publication is from participating hospitals through CorHealth Ontario, which serves as an advisory body to the Minister of Health and Long-Term Care (MOHLTC), is funded by the MOHLTC, and is dedicated to improving the quality, efficiency, access and equity in the delivery of the continuum of adult cardiac, vascular and stroke services in Ontario, Canada.

Incidence of Left Ventricular Thrombus following STEMI in the Modern Era via Multimodality Imaging:

A Systematic Review and Meta-Analysis

Prasham Dave, Bryce Alexander, Adham El Sherbini, Andrew Day, Patrick Norman, Joseph Abunassar, Wael Abuzeid

Queen's University, Kingston, Ontario, Canada

INTRODUCTION

- LV Thrombus (LVT) is a significant complication in STEMI.
- Previous studies were conducted prior to modern timely percutaneous reperfusion networks. Current expert opinion suggests incidence in the current era has decreased.
- We conducted a systematic review and meta-analysis to better understand the incidence of LVT in patients with STEMI treated with contemporary timely percutaneous techniques as assessed by multimodality imaging.

METHODS

- Cochrane, EMBASE, LILACS, and MEDLINE were searched over the last 10 years only including studies using contemporary techniques.
- The primary outcome was detection of LVT in patients via echocardiogram with or without contrast or Cardiac MRI (cMRI) following STEMI (both anterior and any territory) treated with PCI.
- Data was pooled across studies and statistical analysis was conducted via random effects model. .

RESULTS

- 31 studies were included. 17 studies were included in analysis for anterior STEMI, totaling 7171 patients and incidence of 12.2% (95%CI 8.8-15.5), Fig 1A.
- 18 studies included data on any territory STEMI, totaling 14172 patients, and incidence of 5.7% (95% CI 4.3-7.3), Fig 1B.

CONCLUSION

- Incidence of LV thrombus in STEMI patients treated with contemporary timely percutaneous revascularization is in keeping with historical data and remains significant, suggesting this remains an ongoing issue for further investigation.
- Numerically, both cMRI and contrast echo detected more LVT compared to non-contrast echo in all STEMI patients.

Queen's UNIVERSITY

LV Thrombus remains a relevant complication post STEMI **despite** modern therapy including **PCI**.

Cardiac MRI and Echocardiography with contrast were numerically superior to standard echocardiography in detection of LVT.

For more information or to contact our team, please scan the QR code

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DISCUSSION

- LV Thrombus remains a concern in the modern era for clinicians, with incidence rates in anterior STEMI over 1/10 cases. It is less common amongst patients with any territory STEMI.
- This is despite modern therapies, including timely PCI, which all studies including in this analysis featured.
- Numerical detection of thrombus appears superior in contrast echo and MRI modalities
- There may be benefit in formalizing assessment for this important complication post ACS, however there is limited data on if high sensitivity detection improves outcomes.
- Challenges include technical limitations across centres, including access to cardiac MRI and use of echocardiographic contrast.

FIGURE 1A/B

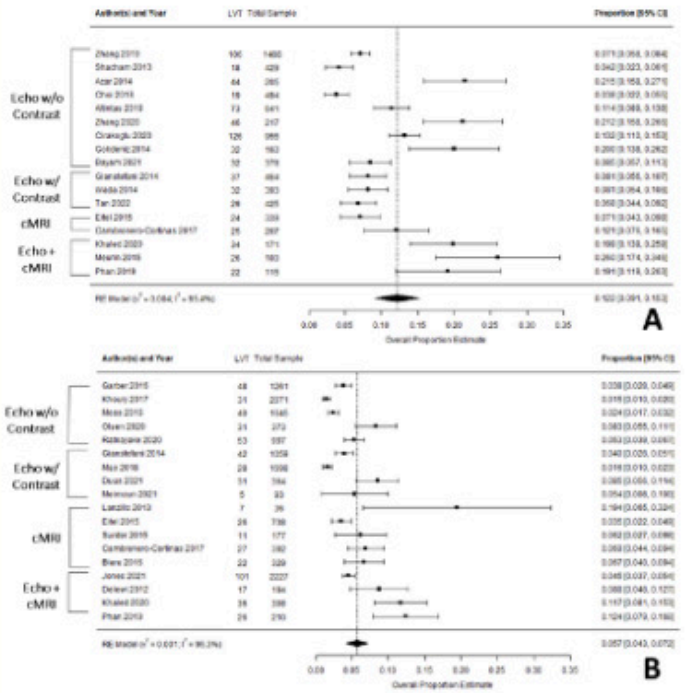

Figure 1. Forest Plot describing incidence of LVT in each study for Anterior STEMI population (A), and all-territory STEMI (B)

DISCLOSURES

There are no disclosures or conflict of interest to report.

Contents lists available at ScienceDirect

Trends in Cardiovascular Medicine

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MY APPROACH

MY APPROACH to cybersecurity for cardiac implantable electronic devices☆

Adrian Baranchuk, MD, FACC, FRCPC, FCCS

Bryce Alexander, MD

Sohaib Haseeb

focused not only on pacemakers but have included the entire spectrum of medical devices. Recently, in August of 2016, St. Jude Medical (now Abbott) was put in the public spotlight following the release of short-sell report by Muddy Waters LLC outlining two methods by which their pacemaker cybersecurity could be breached in what was termed a "crash attack" and a "battery drain attack." However, an effort by a group of researchers to replicate the attack conditions failed to reproduce any clinically significant harm. The United States Food and Drug Administration became involved and issued a warning letter to Abbott. In response, Abbott issued a firmware upgrade for several of its pacemaker models to fix the vulnerability. Implantation of the firmware upgrade is noninvasive and takes only several minutes to complete. During the upgrade, the pacemaker may temporarily change its mode of pacing, leaving open the potential for patients to become symptomatic. The device upgrade itself is not without risks. Abbot has quoted the following small, but not insignificant, risk of adverse events: complete loss of function (0.003%), loss of device settings (0.023%), and failure of the update (0.161%). Due to these risks, it has been recommended that the upgrade take place in a center with the ability to perform urgent temporary pacing. Importantly, these risks have been derived from other clinical settings, and the true adverse event rate of the upgrade may not be known until many upgrades have been completed.

Physicians are responsible for identifying patients who may be at risk and offering the firmware upgrade. Soon, an additional firmware upgrade for Abbot implantable cardioverter-defibrillators will be released in Canada, which will increase the number of patients affected by this issue. Patients have the right to decide if they wish to proceed with the upgrade and must weigh the theoretical risks of a cybersecurity attack against the small, but very real, risk of adverse events during the upgrade. A systematic method of explaining the risks and benefits of the upgrade is a valuable tool for clinicians in this scenario. In our center, we use recommendations devised by Abbott and endorsed by the Canadian Heart Rhythm Society, Ou-

Table 1
Abbott laboratories pacemaker models affected.

Pacemaker models affected
United States
Accent DR RF
Accent MRI
Accent SR RF
Allure RF
Allure Quadra RF
Anthem RF
Assurity
Assurity MRI
Quadra Allure MP RF
Outside United States
Accent DR RF
Accent MRI
Accent SR RF
Accent ST
Accent ST MRI
Allure RF
Allure Quadra RF
Anthem RF
Assurity
Assurity +
Assurity MRI
Quadra Allure
Quadra Allure MP
Quadra Allure MP RF

Table 2
Abbott laboratories cardioverter defibrillator (ICD) and cardiac resynchronization therapy defibrillators (CRT-D) models affected.

ICD and CRT-D models affected
Current
Ellipse
Fortify
Fortify Assura
Promote
Promote Quadra
Quadra Assura
Quadra Assura MP
Unify
Unify Assura
Unify Quadra

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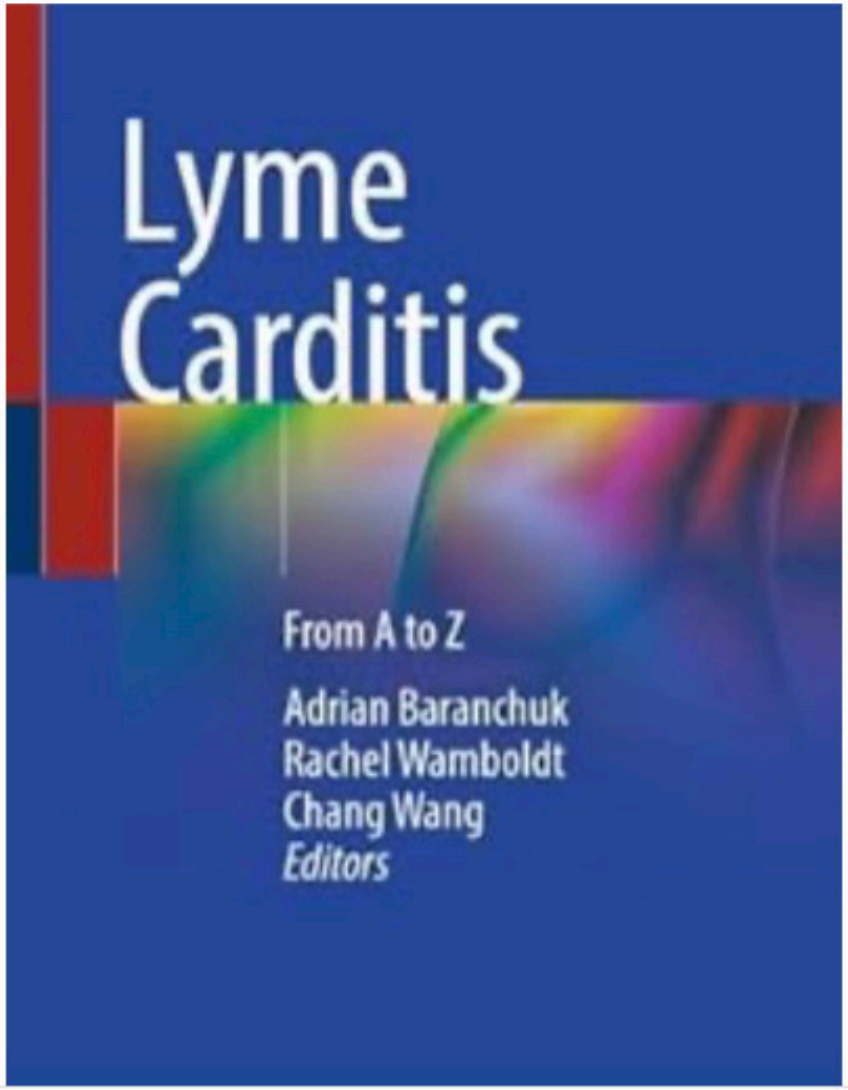
Are implanted electronic devices hackable?☆

Bryce Alexander, Sohaib Haseeb, Adrian Baranchuk*

Division of Cardiology, Queen's University, Kingston, Ontario, Canada



"This book could never be finished without the work of Dr. Wamboldt…"

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EDITORIAL | ARTICLES IN PRESS

Chronic Diseases and QTc in First Nations Women

Melissa Tso, MD FRCPC • Nafisa Abcher, MD • Adrian Baranchuk, MD FACC FRCPC FCCS FSIAC

Published: September 02, 2023 • DOI: https://doi.org/10.1016/j.cjca.2023.08.029

References

Article info

Linked Article

Related Articles

Over the last decade, there have been increasing efforts to enhance our understanding of cardiovascular disease (CVD) among women, particularly Indigenous women. Indigenous women suffer from CVD disproportionately than their non-Indigenous counterparts. Furthermore, CVD is the leading cause of death amongst this group [1]. In Canada, the Indigenous female population is one of the fastest growing populations, with a 20% rise from 2006 to 2011, surpassing the rate of non-Indigenous female population [2]. Despite the ongoing demographic growth of Indigenous people, research on the health of Indigenous women is low compared with Indigenous men, leading to gaps in diagnosis, treatment and prevention of CVD among this population [3].

Out of the Oven!!!

Dermatology

Dr. Sonja Molin
Division Chair

Dr. Yuka Asai
Research Lead

Summary

- *Previous case studies included: treatment side-effects and documenting rare diseases*
- *Investigations into pandemic-related delays in melanoma diagnosis resulting in significant fall in reported cases*
- *Effect of declining of dermatology education of physicians and trainees*
- *Therapeutic treatments for basal cell carcinoma*
- *Patient education in prevention and risk of skin disease*
- *Database creation and analysis of the metrics of dermatology admissions and outpatient appointments*
- *Clinical trial studies of various therapeutics for chronic hand eczema*

Dermatology Research Team Members

Dr. Yuka Asai **Dr. Sonja Molin** **Dr. Thomas Herzinger** **Dr. Erin Dahlke**

Current Studies

Case Reports	Summary
***Cryptococcus uniguttulatus* of the nails in a patient on secukinumab: A case report** **Team:** Dr. Yuka Asai (Dermatology), Dr. Lewis Tomalty (Clinical Microbiology), Andrew Nguyen, Brie Fraser (Research coordinator)	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), Dr. Meghan McPhie (Resident), Andrew Nguyen, Brie Fraser (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.
Porokeratosis post radiation therapy: A case report **Team:** Dr. Yuka Asai (Dermatology), Matthew Hynes (Medical Student), Brie Fraser, Andrew Nguyen (Research Coordinators)	This case report describes a patient who developed unilateral segmental porokeratosis after radiation therapy for rectal carcinoma. This is a rare association described in the literature
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 resulting publications will aid healthcare providers in diagnosing and managing immune mediating conditions of the skin.

Team: Dr. Yuka Asai (Dermatology), Joshua Lowe (Student), Brie Fraser (Research Coordinator)	
Erythematous and boggy nodular eruption on right shin **Team:** Dr. Yuka Asai (Dermatology), Nicholas Lao (Research Assistant), Brie Fraser, Chao Xue, Anna Deriusheva (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.

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), Shirley Li (Data analyst), Brie Fraser, Andrew Nguyen (Research Coordinator)	**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) and during the pandemic period (March-December 2020). 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 3) To examine time trends in the histologic characteristics associated with the melanoma, including Breslow depth, ulceration, mitoses, as well as location
Evaluation of A Punch Biopsy Training Session **Team:** Dr. Yuka Asai (Dermatology), Jessica Ho (Medical Student), Brie Fraser (Research Coordinator)	**Rationale**: Dermatology is an important field for physicians due to the frequency of patients seen with dermatologic problems, and their relationship to multiple other medical conditions. Despite their important role in the diagnosis and treatment of skin conditions, many practicing physicians and graduating trainees report feeling uncomfortable with their knowledge and skill set in dermatology. The shortage of dermatologists not only impacts the number of specialists able to see referrals – it also decreases the number of individuals available to teach dermatology at the undergraduate and post-graduate training levels. Punch biopsies are one technical skill often used in dermatologic diagnosis. We have designed a training session on punch biopsies that aims to increase the knowledge, skills, and comfort levels of non-dermatological medical trainees. A pretest and post-test study is proposed to evaluate the effectiveness of such a training session. The study is to evaluate the effectiveness of punch biopsy training given by a practicing academic dermatologist to non-dermatological

	medical residents and medical students in a southern Ontario University. We hypothesize that a punch biopsy training session will increase the knowledge and comfort levels of non-dermatology medical residents in performing punch biopsies in a real clinical setting. We will ask participants to fill out different surveys at 4 time points: pre-workshop, immediately post-workshop, 6 month follow-up, and 12 month follow-up.
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 (Pathology), Jacob Rullo (Ophthalmology), Dr. Benvon Moran (Mohs Surgery), Brie Fraser, Andrew Nguyen (Research coordinators)	**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. 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.
The Melanoma and Quality of Life Study (MelanQoL Study) **Team:** Dr. Yuka Asai, Dr. Sonja Molin, Dr. Thomas Herzinger (Dermatology), Dr. Timothy Hanna (Radiation Oncology), Tara Baetz (Medical Oncology), Dr. Meghan McPhie (Resident) Brie Fraser (Research Coordinators)	**Rationale**: There is still much debate surrounding the optimal schedule for melanoma follow-up visits. The psychosocial and quality of life impact of routine surveillance is an important consideration; yet, this has largely been unexplored in the literature to date. Benefit from follow-up needs to be balanced with the burden of clinical evaluations on patients and the healthcare system. This is particularly relevant with the recent introduction of new immunotherapies that have drastically changed systemic management of melanoma. These new therapies will affect melanoma survivorship; there is an expectation of greater numbers of individuals surviving melanoma, increasing the numbers of individuals requiring follow-up, separate from increasing rates of melanoma 1 and decreasing numbers of dermatologists 2. These factors are likely to increase demands on the healthcare system. Findings from this study are intended to inform future recommendations regarding the frequency and duration of melanoma follow-up visits. **Objective**: 1. To examine and characterize the influence of follow-up care on the psychosocial outcomes, quality of life, and satisfaction of melanoma patients. 2. To determine which available psychosocial measures best capture the experiences of melanoma patients undergoing routine surveillance.
Effects of Establishment of a dermatology division on hospital admissions, emergency visits and outpatient appointments	**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,

Team: Dr. Yuka Asai (Dermatology), Shirley Li (Data analyst), Brie Fraser (Research Coordinator)	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.
Evaluation of a community-based sun safety program for individuals with recreational sun exposure **Team:** Dr. Yuka Asai (Dermatology), Dr. Meghan McPhie, Dr. Nicole Relke, Alanna Bridgman, Dawn Armstrong (Residents), Brie Fraser (Research Coordinator)	**Rationale**: Skin cancer is highly preventable and yet it is the most common cancer diagnosed in Canada. Ultraviolet (UV) radiation is an important, modifiable risk factor for most skin cancers. Evidence shows that early education regarding sun safety has a positive impact on future attitudes and behaviors related to sun safety and skin cancer awareness. The purpose of this study is to evaluate the effectiveness of a community-based sun safety and skin cancer prevention program for adults with recreational sun exposure. Community-members attending a 1-hour educational presentation about sun safety will be asked to participate in the study. Participants will complete a brief survey pre- and post- presentation that contains questions (multiple choice, Likert scale) about knowledge, attitudes, and behaviours surrounding sun safety. Conclusions will be drawn between pre- and post- presentation surveys to determine the effectiveness of the sun safety program.
Nicotinamide and Outcome of Skin Cancers and Precancers in Leukemia (NO-SCaPL): Feasibility Study **Team:** Dr. Yuka Asai (Dermatology), Dr. Annette Hay (Hematology), Dr. Ami Wang, Dr. Ivan Landego, Dr. Vincent Poon, Dr. Robert Clayden (Residents/Fellows), Shirley Li (Data Analyst)	**Rationale**: Chronic lymphocytic leukemia (CLL) has an estimated prevalence of 8 per 100,000. Similar to other immunosuppressed Individuals, those with CLL are known to develop additional neoplasias. The most frequent tumors include cutaneous basal cell carcinoma (BCC) and squamous cell carcinoma (SCC); which occur in great number. Additionally, these normally indolent tumors may be more aggressive in patients with CLL, and are located in cosmetically and functionally sensitive areas. Epidemiological data regarding the prevalence of these malignancies in this setting is lacking, and we aim to determine through local data the frequency of new BCC and SCC in patients with CLL. By comparing with literature values,

	improved patient information can be provided. This data will also help inform future study design in this context with regards to statistical power.
Dermatology Research Database **Team:** Dr. Yuka Asai, Dr. Sonja Molin, Dr. Thomas Herzinger (Dermatology), Shirley Li (Data Analyst), Brie Fraser (Research Coordinator)	**Rationale**: A research database can be used for quality improvement and for clinical research. This project will establish a dermatology research database from the beginning of the academic dermatology unit at Queen's. This database will be a unique resource regarding the types and frequencies of conditions and treatments received by individuals seen by a dermatologist. From this database, individuals can be invited to participate in subsequent studies. **Objective**: To develop and sustain a dermatology patient database, to investigate healthcare utilization and as a valuable resource for future studies.
PEEPS: Patient Eczema Education Pictorial Study **Team:** Dr. Yuka Asai, Dr. Sonja Molin, Dr. Thomas Herzinger, Dr. Robert Bobotsis (Dermatology), Dr. Anne Ellis (Allergy), Bethany Wilken (Graduate Student), Brie Fraser, Anna Deriusheva, Chao Xue (Research Coordinators)	**Rationale:** Atopic dermatitis (AD), also called eczema, is a chronic itchy skin that often begins as an infant or a child. While many may grow out of their skin disease, about one-quarter will still have it as an adult. This condition is itchy, and can causes red rashes and broken skin. Because of this, people with AD may also have infections and difficulty sleeping. This condition also impacts people's ability to work and to go to school. To deal with this condition, people with AD need medicated creams and skin care regimens that may be complicated and confusing. Steroid creams are commonly used to treat AD as treatment, but anxiety about steroid use is well-documented. Virtually all clinical guidelines for AD treatment involve patient education, but there is not much good evidence on how to provide this. Previous research has shown some results with classes, nurse teaching, or videos, but these may be difficult to implement into clinics with fewer resources. We have designed a pictorial eczema education sheet, based on the commonly used analogy of "eczema is a wildfire" which has been deliberately designed as a one-page, low-cost, photocopy-friendly graphic that covers key messages in patient education for AD. We plan to evaluate this in clinics, with a two-phased approach beginning at specialist clinics in Kingston Health Sciences Centre, followed by additional clinics in primary care and community specialist clinics. **Objective**: To evaluate the "Eczema as a wildfire" patient education tool for clinical use. ***Aim 1:*** Assess baseline AD knowledge and attitudes towards treatment and clinical status. ***Aim 2:*** Determine outcomes immediately after the education tool is implemented. ***Aim 3:*** Determine long-term outcomes of the education tool. ***Aim 4:*** Determine baseline need for patient education tool for eczema among health care workers treating. ***Aim 5:*** Obtain feedback on the patient education tool for eczema from pilot Phase I health care providers.
SCARS: Skin Cancer and Atopy Research Study **Team:** Dr. Yuka Asai (Dermatology),	**Rationale**: Eczema is linked to a higher risk of skin cancer, particularly for BCC and SCC. Filaggrin could mediate this risk in several ways: 1) lack of natural sunscreen leading to increased UV damage, 2) impaired barrier leading to infection with oncogenic viruses, 3) modulation of downstream

Dr. Ami Wang, Dr. Tao Wang, Dr. Kaitlin Vanderbeck, Dr. Christine E. Orr (Pathology)	immunosuppressive products and 4) decreased epidermal thickness leading to higher penetration of UV rays. **Objectives:** ***PHASE I: FUNDING OBTAINED*** 1) Investigate immunohistochemical (IHC) staining of filaggrin in formalin-fixed paraffin embedded (FFPE) BCC and SCC tissue samples vs melanoma tissue samples, examining both the tumor and normal surrounding skin, and normal skin as a control 2) Measure epidermal thickness of skin in BCC, SCC, melanoma, and normal skin 3) Correlate IHC staining of filaggrin with HPV staining for oncogenic strains 16 and 18 in BCC, SCC, melanoma and normal skin FFPE samples ***PHASE II: FUNDING PENDING*** 1) Correlate IHC staining using quantitative RT-PCR (qRT-PCR) of filaggrin from fresh BCC, SCC, melanoma and normal skin specimens 2) Conduct high performance liquid chromatography (HPLC) for cUCA and tUCA from fresh BCC, SCC, melanoma and normal skin specimens
The hand eczema proteome / proteomics in allergic and irritant contact dermatitis **Team: Dr. Sonja Molin, Dr. Juliane Merl, Dr. Thomas Herzinger, Angelika Hoffmann (resident), Jessica Ho (medical student)**	**Rationale:** Hand eczema is a frequent skin disease with high socioeconomic impact. Important pathogenetic factors are irritant skin damage and contact sensitization. **Objective**: To understand the protein expression profile of chronic hand eczema as well as the differences in protein expression between allergic and irritant contact dermatitis.

Dermatology Clinical Trials	Summary
A phase 3 clinical trial to confirm efficacy and evaluate safety of twice-daily delgocitinib cream 20 mg/g compared with cream vehicle for a 16-week treatment period in adult subjects with moderate to severe chronic hand eczema (DELTA 1) **Team:** Dr. Sonja Molin, Dr. Yuka Asai, Dr. Thomas Herzinger (Dermatology), Chao Xue, Andrew Nguyen (Research Coordinators)	The purpose of this phase 3 trial is to confirm the efficacy and evaluate the safety of twice-daily applications of delgocitinib cream 20 mg/g for 16 weeks compared with cream vehicle in the treatment of adult subjects with moderate to severe chronic hand eczema (CHE). This trial aims to recruit 6-15 patients per site. Moderate to severe CHE is common and this study is very pivotal in understanding the treatment as well as improving many patients' quality of life. There is a clear unmet need for new long-term treatment options in the treatment of patients suffering from moderate to severe CHE. Based on the available nonclinical and clinical data, delgocitinib cream has the potential to become an effective, well-tolerated, and user-friendly treatment for CHE and thereby improve the everyday lives of affected patients. **Primary objective:**

	To confirm the efficacy of twice-daily applications of delgocitinib cream 20 mg/g compared with cream vehicle in the treatment of adult subjects with moderate to severe CHE. **Secondary objective:** To confirm the health-related quality of life and efficacy of twice-daily applications of delgocitinib cream 20 mg/g compared with cream vehicle in the treatment of adult subjects with moderate to severe CHE. To evaluate the safety of twice-daily applications of delgocitinib cream 20 mg/g compared with cream vehicle in the treatment of adult subjects with moderate to severe CHE.
A phase 3 extension trial of DELTA 1 and DELTA 2 to evaluate the long-term safety of a twice-daily treatment with delgocitinib cream 20 mg/g as needed for up to 36 weeks in adult subjects with chronic hand eczema (DELTA 3) **Team:** Dr. Sonja Molin, Dr. Yuka Asai, Dr. Thomas Herzinger (Dermatology), Brie Fraser, Andrew Nguyen (Research Coordinators)	This is a long-term extension trial to evaluate the long-term safety of an as-needed treatment with twice-daily applications of delgocitinib cream 20 mg/g in accordance with the ICH E1 guideline. Subjects eligible for this trial will have received blinded treatment with either twice-daily delgocitinib cream 20 mg/g or cream vehicle and will have completed the 16-week treatment period in one of the 2 parent trials: DELTA 1 or DELTA 2. The purpose of the parent trials is to confirm efficacy and evaluate safety of twice-daily delgocitinib cream 20 mg/g compared with cream vehicle for a treatment period of 16 weeks in adult subjects with moderate to severe CHE. Subjects transferring from the blinded parent trials will enter this extension trial without their individual treatment allocation being revealed, in order to maintain the blinding of the ongoing parent trial. An open-label trial design is chosen as the aim of this trial is to evaluate the long-term safety of an as-needed treatment with twice-daily applications of delgocitinib cream 20 mg/g to mimic the anticipated use of delgocitinib cream in clinical practice. Further, a vehicle arm is not included since vehicle treatment beyond 16 weeks is not considered ethical. Based on the available nonclinical and clinical data, delgocitinib cream has the potential to become an effective and well tolerated treatment for CHE and thereby improve HRQoL of affected patients.

DELTA TEEN: A phase 3 clinical trial to evaluate efficacy and safety of twice-daily applications of delgocitinib cream 20 mg/g compared with cream vehicle for a 16 week treatment period in adolescents 12-17 years of age with moderate to severe chronic hand eczema **Team:** Dr. Sonja Molin, Dr. Yuka Asai, Dr. Thomas Herzinger (Dermatology), Brie Fraser, Anna Deriusheva (Coordinators)	The trial is a phase 3 randomised, double-blind, vehicle-controlled, parallel-group, multi-site trial in which adolescents 12-17 years of age with moderate to severe CHE will be treated with delgocitinib cream 20 mg/g or cream vehicle for 16 weeks. **Primary objective:** To evaluate the efficacy of twice-daily applications of delgocitinib cream 20 mg/g compared with cream vehicle in the treatment of adolescents with moderate to severe CHE. **Secondary objective:** To evaluate the health-related quality of life and efficacy of twice-daily applications of delgocitinib cream 20 mg/g compared with cream vehicle in the treatment of adolescents with moderate to severe CHE. To evaluate the safety of twice-daily applications of delgocitinib cream 20 mg/g in the treatment of adolescents with moderate to severe CHE.

PURE: A registry of Patients with moderate to severe chronic plaqUe psoRiasis in Canada and Latin AmErica (LACan)

Team: Dr. Yuka Asai, Dr. Sonja Molin, Dr. Thomas Herzinger (Dermatology), Brie Fraser, Anna Deriusheva (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).

Upcoming Studies

Dermatology Studies	Summary
ADHAND: A phase 3b, interventional, clinical trial to evaluate the efficacy and safety of tralokinumab 300 mg every second week monotherapy compared with placebo in adult and adolescent subjects with atopic dermatitis and moderate-to-severe atopic hand eczema who are candidates for systemic therapy. **Team: Dr. Sonja Molin, Dr. Yuka Asai, Dr. Thomas Herzinger (Dermatology), Brie Fraser, Anna Deriusheva (Research Coordinator)**	**Rationale:** As the currently available treatment options either lack documented treatment effect or are limited by restrictions of long-term use due to safety concerns, there is a high unmet medical need for new treatments of AD with moderate-to-severe involvement of the hands and wrists that have high efficacy in combination with a good safety profile, especially for long-term use. New and better treatments would potentially improve HRQoL of patients with moderate-to-severe atopic hand eczema. **Primary Objective:** To evaluate the efficacy of tralokinumab on severity and extent of atopic hand eczema compared with placebo in treatment of subjects with moderate-to-severe atopic hand eczema. **Secondary Objective:** To evaluate the efficacy of tralokinumab on severity, extent, itch, pain, sleep, and health-related quality of life compared with placebo in treatment of subjects with moderate-to-severe atopic hand eczema. To evaluate the safety and tolerability of tralokinumab in subjects with moderate-to-severe atopic hand eczema. **Other Objective:** To evaluate the efficacy on severity, extent, itch, pain, sleep, and health-related quality of life and the safety and tolerability of continued tralokinumab treatment in subjects with moderate-to-severe atopic hand eczema in the open-label treatment period (up to 32 weeks).

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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

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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

October 2021
ILD clinic- differential diagnosis of hypersensitivity pneumonitis

Differential diagnosis: Hypersensitivity pneumonitis (HP)

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

Differential diagnosis: Foam-related HP

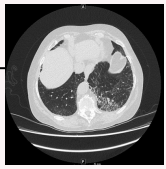
- Mold in foam pillows has been associated with ILD (2).
- Patient switches pillows from foam to polyester
- Incased pillows and mattress with anti-allergic waterproof casings.

Expect resolution of symptoms almost immediately (2).

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

January 2022
Differential diagnosis of drug induced interstitial lung disease

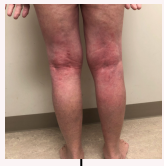
Differential diagnosis: Drug induced interstitial lung disease



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).

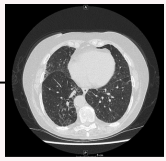
March 2022
Patient discontinues dupilumab



April 2022
Patient erythrodermic

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

June 2022
Patient started tralokinumab



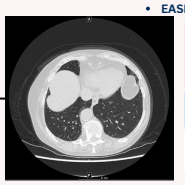
Significant improvements in the ground glass appearance and reticulations in the left lower lobe yet, the right middle lobe had progressive fibrosis.

Decline in pulmonary function

September 2022
AD controlled on tralokinumab

- **EASI - 0**

March 2023
Resolution of ILD



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)

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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.

Dermatology
beyond the skin

Do you suffer from atopic dermatitis and moderate to severe atopic hand eczema?

Participating in a clinical trial could be a possibility

Inclusion
You may qualify to the clinical trial if you have atopic dermatitis and moderate-to-severe atopic hand eczema and are a candidate for systemic therapy. The duration of your atopic dermatitis should be at least 1 year and the presence of atopic hand eczema should have persisted for at least 3 months.

Duration
The trial may have a duration up to 40 weeks for each trial participant. This includes a screening period of up to 4 weeks, a double-blinded treatment period of 16 weeks, an open label treatment period of 16 weeks and a safety follow-up period of 4 weeks.

Cost
There is no cost for you related to trial participation and reasonable travel cost will be reimbursed.

Do you want to know more?
Please reach out to the trial personnel about the possibility for you to participate in the trial.

ADHAND **LP0162 2328** VERSION: 1.0, 08-Mar-2023

Do you suffer with Chronic Plaque Psoriasis?

Do you want to contribute to research on an international scale?

The medical information collected from patients participating in this study might be of future benefit to you and other patients suffering from moderate to severe chronic plaque psoriasis

You may be eligible to participate if you are:

- 18 years of age or older
- Diagnosed with chronic plaque psoriasis
- Starting or changing treatment for psoriasis

The PURE study will observe patients with moderate to severe chronic plaque psoriasis in Canada and Latin America

This study will research the long term effects of treatment licensed for chronic plaque psoriasis using questionnaires and assessments

For more information, please contact the PURE study at:

Email:
DermResearch@Queensu.ca
Phone:
613-544-3400 x3415
Principal Investigator/Address:
Dr. Yuka Asai
Centenary 3-027
Hotel Dieu Hopsital
166 Brock Street
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PURE Poster Version 1.0 dated 28Sep2018

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

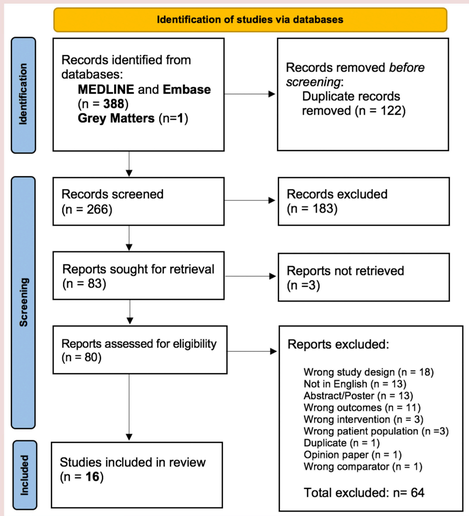


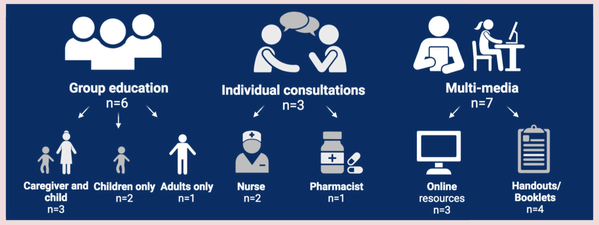
Figure 1. PRISMA flow chart of the screening process. **16** studies were included in the review.

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	✓✓✓✓✗✗✗✗✗	N=9
Disease Severity	✓✓✓✓✓✓✗✗✗	N=9
Self-efficacy	✓	N=1
Knowledge	✓✓✓✓✓✓	N=6
Comfort	✗	N=1
Family Impact	✓✗✗✗	N=4
Anxiety	✓✗✗	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*

Research Projects

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

Current research opportunity

Predictors of Thyroglobulin Antibody Development in Thyroid Cancer Patients

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

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

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

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

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[1]Department of Medicine, Division of Endocrinology, [2]Queen's University School of Medicine, Queen's University, Kingston, Ontario, Canada

Introduction

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

Method

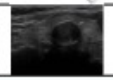
- Conducted literature searches on EMBASE, MEDLINE, CINAHL, Cochrane databases
- Identify studies which assessed factors associated with pain following FNAB
- 2244 studies were screened
- 22 studies were identified

Results

Author, Year	Study Type	Patients (M/F)	Pain Scales Used
Patient Related Factors			
Toman, 2016	Cohort study	98 (17/81)	VAS[1]
Leboulleux, 2013	Cohort study	218 (55/163)	VAS
Stangierski, 2012	Cohort study	75 (20/55)	VAS
Procedure Related Factors			
Ay, 2021	RCT[2]	50 (14/36)	VAS
Lee, 2019	RCT	99 (20/79)	NRS[4]
Tanaka, 2019	CCT[3]	200 (unknown)	Original Scale
Kim, 2019	Cohort study	167 (30/137)	VAS
Jeong, 2018	Cohort study	200 (30/170)	VAS
Jung, 2017	RCT	88 (75/13)	NRS
Yuce, 2016	CCT	58 (23/35)	VAS, NRS, VRS[5]
Nasrollah, 2014	Cohort study	61 (unknown)	Original Scale
Carpi, 2013	Cohort study	126 (16/110)	VRS
Lee, 2013	Cohort study	157 (17/140)	NRS
Sibbitt, 2011	Cohort study	110 (unknown)	VAS
Kumarasinghe, 1995	Cohort study	410 thyroid nodules (unknown)	VRS
Analgesia Related Factors			
Cao, 2020	Cohort study	585 (157/428)	Likert pain scale
Liao, 2018	Cohort study	183 (45/138)	VRS
Demirci, 2010	RCT	50 (0/50)	VAS
Kim, 2009	CCT	50 (unknown)	VAS, NRS, VRS
Gursoy, 2009[15]	RCT	138 (25/113)	VAS, NRS, VRS
Gursoy, 2007[32]	RCT	107 (90/17)	VAS, NRS, VRS
Gursoy, 2007[33]	CCT	99 (14/85)	VAS, NRS, VRS

Results

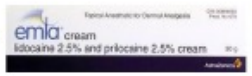
Patient Related Factors

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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[1]Department of Medicine, Division of Endocrinology, [2]Department of Pathology and Molecular Medicine, [3]Queen's University School of Medicine, Queen's University, Kingston, Ontario, Canada

Introduction

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

Case Presentation

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

References

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Case Presentation

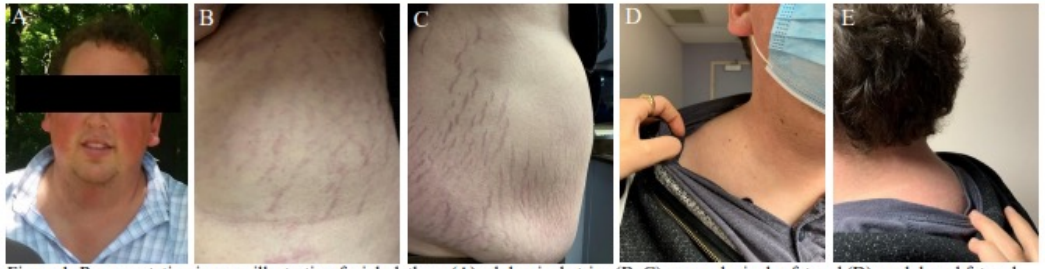

Figure 1. Representative images illustrating facial plethora (A); abdominal striae (B, C); supraclavicular fat pad (D); and dorsal fat pad (E)

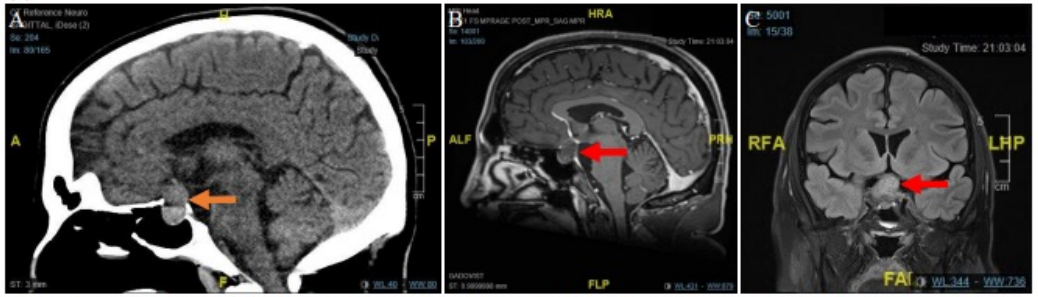

Figure 2. Hyperattenuating 2.0 cm x 2.8 cm x 1.5 cm mass (orange arrow) at the sella turcica on unenhanced CT (A); 1.9 cm x 3.2 cm x 2.4 cm heterogeneous mass (red arrow) on T1 (B); and T2-weighted imaging with flattening of the optic chiasm, remodeling/dehiscence of the floor of the sella and extending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

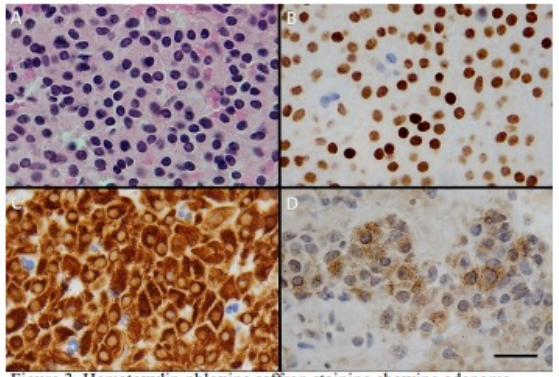

Figure 3. Hematoxylin phloxine saffron staining showing adenoma with solid growth pattern (Figure 3A); immunohistochemical staining showing T-pit reactivity of tumor nuclei (Figure 3B); diffuse cytoplasmic staining for cytokeratin CAM5.2 (Figure 3C); and regional moderately intense granular cytoplasmic 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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Kingston Health Sciences Centre[1], Department of Medicine[2], Division of Endocrinology and Metabolism,[3] Queen's University, Kingston, Ontario

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 (DTSQs)

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

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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.

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

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Introduction

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

Methods

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

Results

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

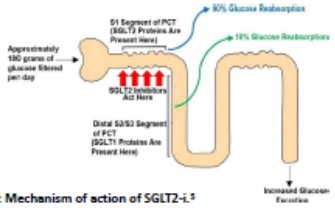

Figure 1: Mechanism of action of SGLT2-i.[5]

Study	Alkindi et al. 2020[6]	Mahling et al. 2019[7]	Shah et al. 2019[8]	Attallah et al. 2019[9]	Halden et al. 2019[10]	Schwaiger et al. 2019[11]	Beshyah et al. 2018[12]	Kwon et al. 2017[13]	Rajasekaran et al. 2017[14]
Type	Retro-spective Case Series	Prospective cohort	Pros-pective cohort	Retro-spective Case Series	Pros-pective RCT (Empa: Placebo)	Prospective cohort	Case report	Pros-pective Case Series	Retrospective Case Series
Center	UAE	Germany	India	UAE	Norway	Austria	UAE	South Korea	Canada
# of patients	8	10	24	8	44	14	1	25	10
Mean Age (yr)	56.8±13.7	66 (56-73)	53.8±7.1	45.9±7.1	63 (31-72);59 (21-75)	56.5±7.9	58	-	KT: 61.6±12.6, PKT: 49.4±8.9
Gender (M:F)	6:2	8:2	23:1	4:4	17:5, 17:5	7:7	1:0	-	KT: 5:1, PKT: 2:2
Duration	24 months	12 months	6 months	12 months	6 months	12 months	30 months	12 months	22 months
Type of Kidney Transplant	LKD: 8	LKD: 8	-	-	LKD: 9:7	-	LKD: 1	-	-
	DKD: 0	DKD: 2	-	-	DKD: 13:15	-	-	-	KT: 6, PKT: 4
Type of Diabetes	DM II:2	DM II: 6	DM II: 20	DM II: 4	DM II: 0	DM II: 0	DM II: 1	DM I: 3, DM II: 15	DM II: 2
	NODAT: 6	NODAT: 4	NODAT: 5	NODAT: 4	NODAT: 44	NODAT: 14	-	NODAT: 7	NODAT: 8
eGFR	75.75±13.38	57 (47-73) (> 45)	86±20 (> 60)	NR	66 (57-68);59 (52-72)	54±23.8 (> 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	6.9 (6.5-8.2);6.8 (6.1-7.2)	6.7±0.7	8.8	7.9±1.3	KT:8.6±1.4, PKT:7.4±1.1
SGLT2 Inhibitor / Dose (# patients)	Empa-gliflozin (8) 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 infections: 1	-UTI: 3	NR	-Cystitis: 2	-Low BS: 1
		-AKI stage 1: 1 -Small lower limb ulcer: 1			-Dizziness: 2 -Facial swelling: 1 -Hematuria: 1	-Balanitis: 1 -Pneumonia: 1 -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.

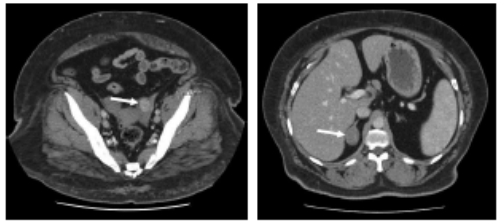

Figure 1: 2.1-cm left ovarian tumour (left, see arrow); 3.2-cm right adrenal tumour (right, see arrow).

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.

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

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

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INTRODUCTION

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

CASE

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

INVESTIGATIONS

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

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

DISCUSSION

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

CONCLUSION

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

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

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

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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

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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

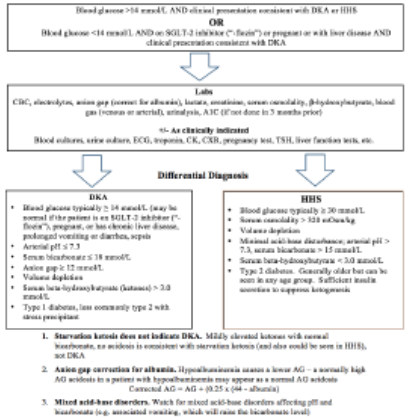
- This study demonstrates variability in the diagnosis and management of HHS at our centre, and identifies a need to standardize the work-up and management of patients presenting with HHS.

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.

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

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

1. Queen's University, Faculty of Health Sciences.

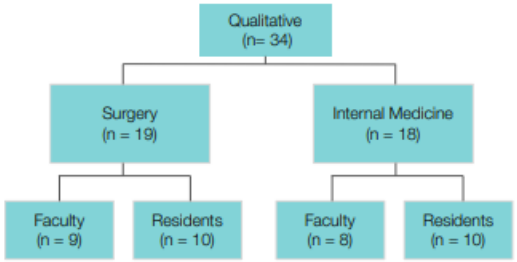
Introduction

- 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

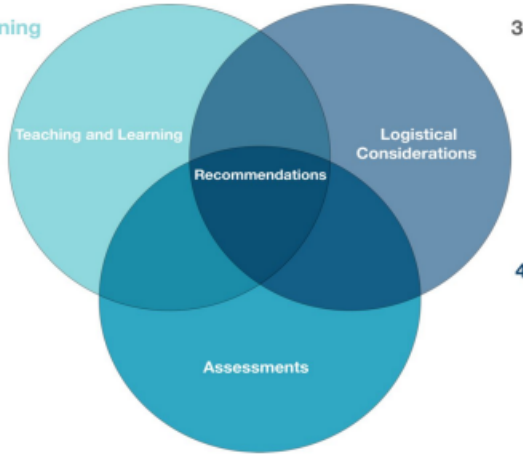


Results

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

1. Teaching and Learning
a) Evolution
b) Strategies
c) Facilitators
d) Barriers

2. Assessments
a) Feedback
b) EPAs
c) CanMEDS
d) Facilitators
e) Barriers



3. Logistical Considerations
a) Limitations of virtual care
b) Infrastructure of virtual care
c) Modality of virtual care

4. Recommendations
a) Preparation
b) Resources
c) Technology
d) Education and Support
e) Clinic Efficiency
f) Next steps

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

Conclusion

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

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

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

Study objectives

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

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

Methods – STUDY DESIGN

Selection Period:

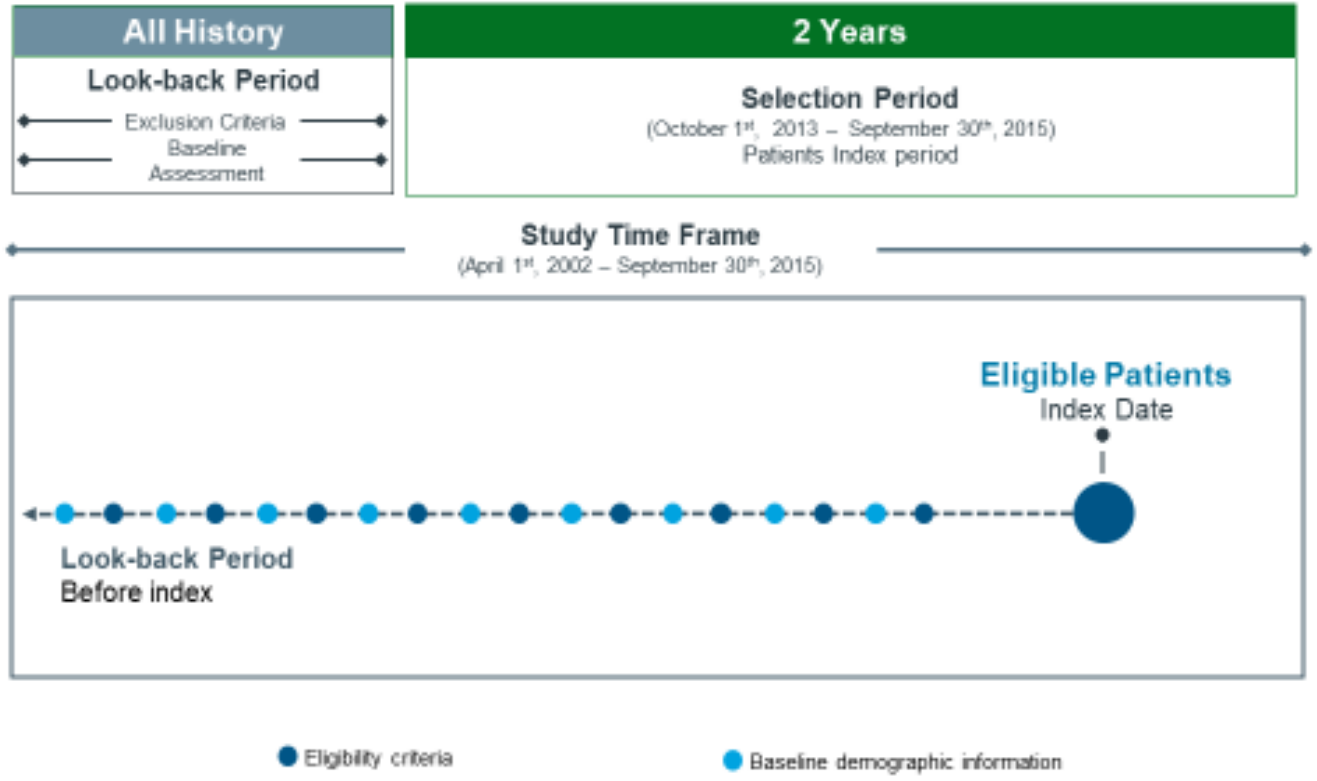
- A 2-year period from Oct 1st, 2013 to Sept 30th, 2015 will be used to select patients that have met the inclusion and exclusion criteria

Index Date:

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

Look-back Period:

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



Methods – Data source

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

Methods – study population

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

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

Methods – analysis

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

Results

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

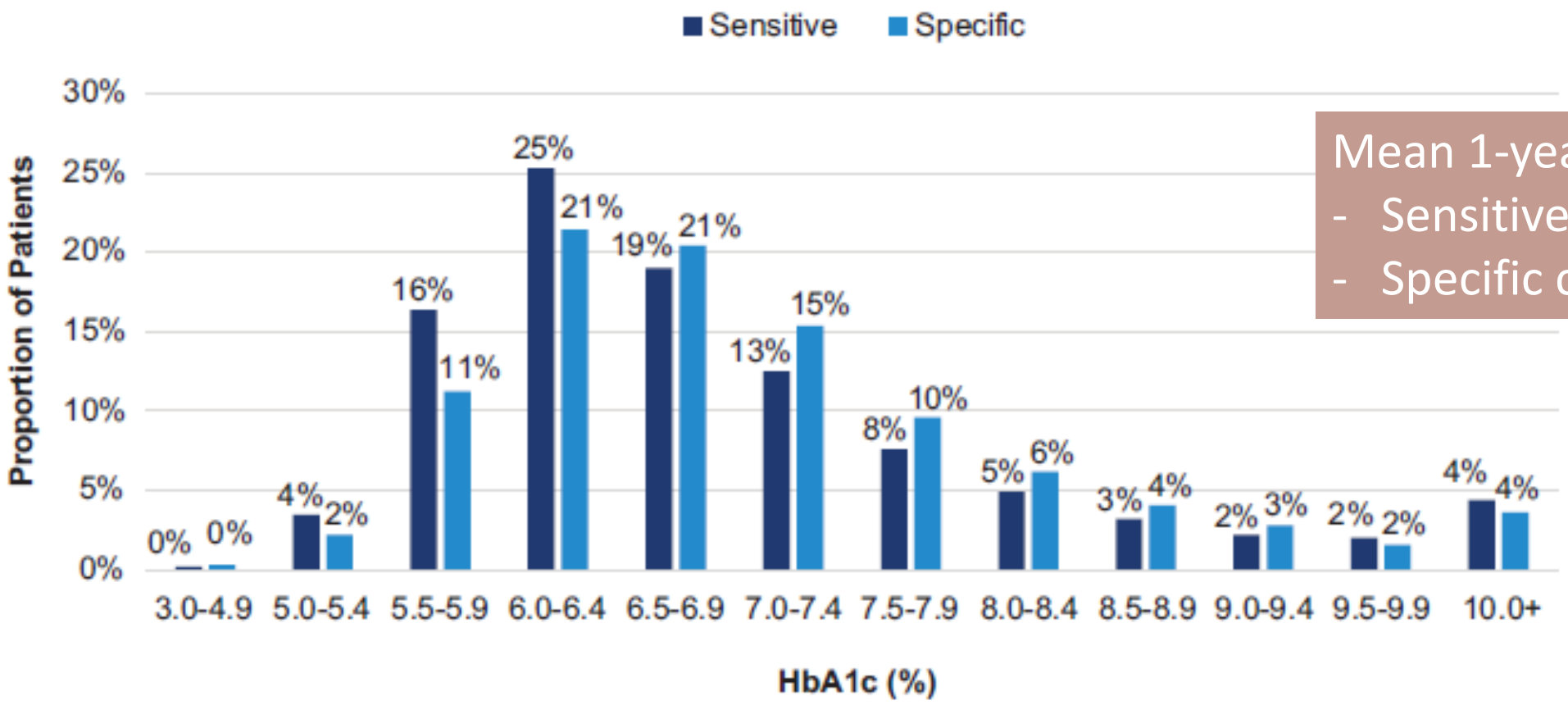
Results

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

Results

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

Results – HbA1c

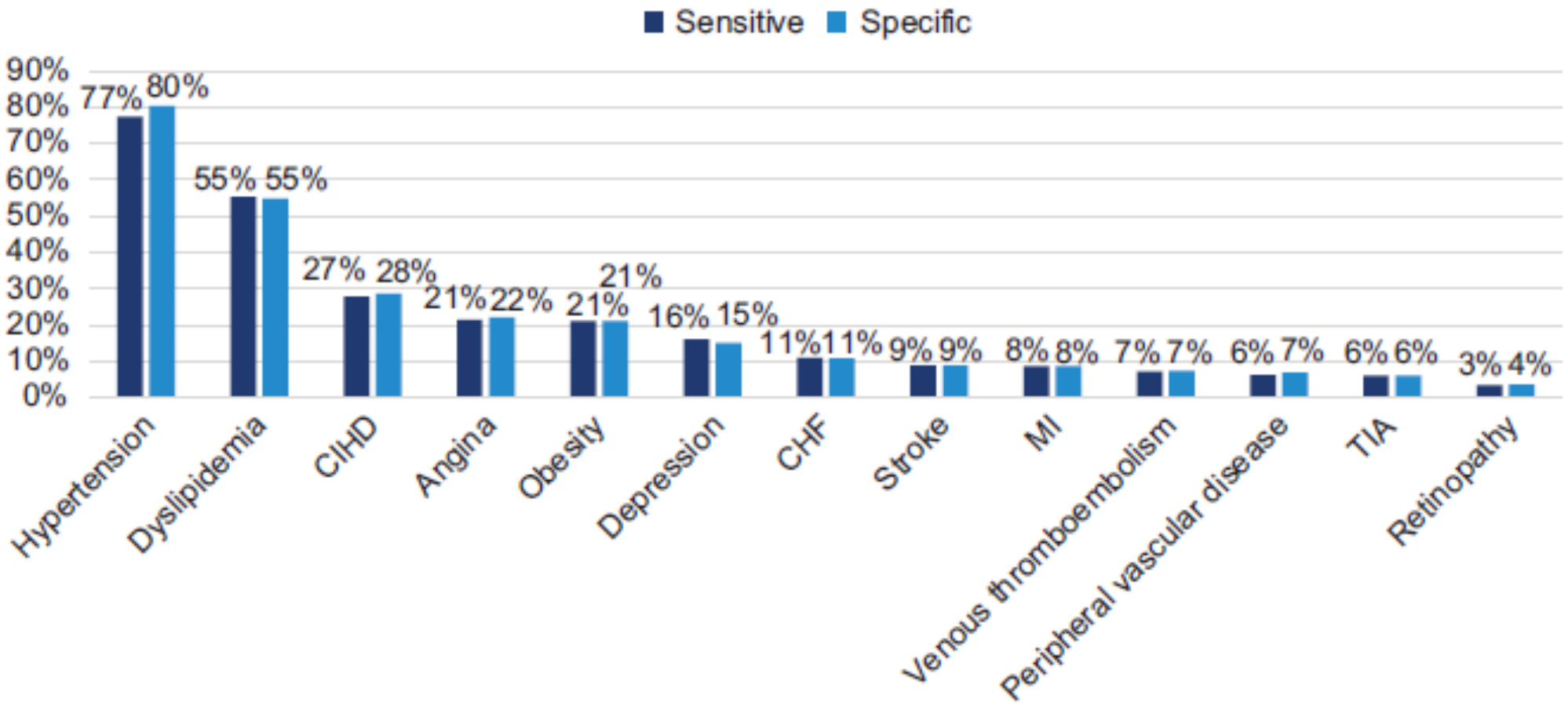


Mean 1-year HbA1c
- Sensitive cohort: 6.9%
- Specific cohort: 7.4%

Discussion - HbA1c

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

Results - comorbidities



Discussion - comorbidities

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

CONCLUSION - SUMMARY

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

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

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

Conclusion – NEXT STEPS

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

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

Gastroenterology

Dr. Lawrence Hookey
Division Chair

Dr. Jennifer Flemming
Research Lead

Summary

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

Division of Gastroenterology

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

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

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

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

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

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

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

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

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

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

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

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

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

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

BACKGROUND

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

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

METHODS

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

Table 1: ON-MARG DIMENSIONS

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

RESULTS

Table 1: Baseline demographics of study population

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

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

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

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

RESULTS

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

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

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

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

CONCLUSION

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

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

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General Internal Medicine

Dr. Lauren Marcotte
Division Chair

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Summary

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

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Systematic or Meta-analysis Studies

A systematic review of eHealth technologies for breast cancer supportive care

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ABSTRACT

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

Introduction

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

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

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

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Canadian Medical Education Journal

Black Ice

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

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

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Abstract

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

Résumé

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

Introduction

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

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

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

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

A Proof-of-Concept Study in 2 Canadian Communities

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

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

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

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

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

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Review

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

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Key Messages

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

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ABSTRACT

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

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Mots clés:
diabète
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cancer du sein
pharmacothérapie

RÉSUMÉ

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

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RESEARCH/Original Article

Videoconferencing interventions and COPD patient outcomes: A systematic review

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

Abstract

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

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

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

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

Keywords

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

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Introduction

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

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

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SPECIAL SERIES: CANCER CARE IN THE ASIA PACIFIC

original reports

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

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abstract

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

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

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

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

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INTRODUCTION

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

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

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

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

ASSOCIATED CONTENT

Data Supplement

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

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Research Article

Rising Healthcare Costs and Utilization among Young Adults with Cirrhosis in Ontario: A Population-Based Study

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Objectives. Chronic diseases account for the majority of healthcare spending. Cirrhosis is a chronic disease whose burden is rising, especially in young adults. This study aimed at describing the direct healthcare costs and utilization in young adults with cirrhosis compared to other chronic diseases common to this age group. *Methods*. Retrospective population-based study of routinely collected healthcare data from Ontario for the fiscal years 2007–2016 and housed at ICES. Young adults (aged 18–40 years) with cirrhosis, inflammatory bowel disease (IBD), and asthma were identified based on validated case definitions. Total and annual direct healthcare costs and utilization were calculated per individual across multiple healthcare settings and compared based on the type of chronic disease. For cirrhosis, the results were further stratified by etiology and decompensation status. *Results*. Total direct healthcare spending from 2007 to 2016 increased by 84% for cirrhosis, 50% for IBD, and 41% for asthma. On a per-patient basis, annual costs were the highest for cirrhosis ($6,581/year) compared to IBD ($5,260/year), and asthma ($2,934/year) driven by acute care in cirrhosis and asthma, and drug costs in IBD. Annual costs were four-fold higher in patients with decompensated versus compensated cirrhosis ($20,651/year vs. $5,280/year). Patients with cirrhosis had greater use of both ICU and mental health services. *Conclusion*. Healthcare costs in young adults with cirrhosis are rising and driven by the use of acute care. Strategies to prevent the development of cirrhosis and to coordinate healthcare in this population through the development of chronic disease prevention and management strategies are urgently needed.

1. Introduction

Collectively, chronic diseases account for two-thirds of deaths in Canadians, are responsible for 58% of total direct healthcare costs, [1] and, in Ontario, are estimated to account for 55% of total direct and indirect healthcare costs [2]. In response to this, Canada has developed the Chronic Disease Prevention and Management (CDPM) framework, which has been successfully applied to a number of chronic diseases including heart failure [3], diabetes, [4] chronic obstructive pulmonary disease (COPD), [2, 5, 6] and asthma [7]. These programs have successfully reduced hospitalization rates, and improved both quality of life and mortality [5, 8–11].

Cirrhosis refers to an advanced stage of hepatic fibrosis and represents the final common pathway of multiple chronic liver diseases (CLD) with a median survival of <3 years once decompensation occurs [12]. Over the past two decades, the burden of cirrhosis has increased substantially with prevalence reaching almost 1% of the Ontario population in 2016 [13]. Of most concern, however, the highest increase in new diagnoses of cirrhosis has been observed in young adults driven mostly by alcohol-associated disease (ALD) and nonalcoholic fatty liver disease (NAFLD) [14, 15]. Furthermore, in Canadian adults aged 35–64 years, CLD and cirrhosis were the fifth leading causes of death in 2018 behind only cancer, heart disease, accidents, and suicide with mortality rates in this age group increasing by 25% between 2000 and 2018 [16].

Geriatric Medicine

Dr. John Puxty
Division Chair

Dr. Sudeep Gill
Research Lead

Summary

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

Division of Geriatrics
Department of Medicine, Queen's University

Geriatric Medicine Faculty Available to Mentor Resident Research Projects

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

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

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

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

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

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

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

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

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

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

Problem-based deprescribing

Using your patients' clinical concerns to guide medication review

Frank Molnar MSc MD CM FRCPC Chris Frank MD CCFP(COE) FCFP

Clinical question

How can I best approach deprescribing for my medically complex frail seniors?

Bottom line

A recently published article in the *Canadian Geriatrics Society Journal of CME* provides a practical approach to deprescribing with older patients who have complex health issues.[1] Many FPs take a problem-based approach to optimizing medications rather than doing medication reviews as a stand-alone activity.

Evidence

- Polypharmacy, defined as using more medications or a higher dose than clinically indicated, is more common in the geriatric population and increases the risk of adverse drug events (ADEs).[2]
- Older patients are at greater risk of ADEs owing to body composition and physiology changes that result in altered pharmacokinetic and pharmacodynamic properties of medications, as well as owing to interactions with other medications.[3]
- These risks are sometimes not fully appreciated by clinicians, which is supported by the fact that ADEs contribute to up to 20% of hospitalizations in the elderly.[4-6]

Approach

Seniors typically present to FPs for specific clinical or functional problems (eg, falls, incontinence, cognitive changes, weight loss) rather than to seek a general review of medications. With older patients, FPs should always consider medications as a primary or contributing factor in any clinical presentation and review the patient's medication list as a key part of care. Any new symptom a patient experiences should be screened as a possible ADE and as a potential opportunity to deprescribe.

While resources such as the Beers criteria[7] and the STOPP/START[8] (Screening Tool of Older People's Prescriptions and Screening Tool to Alert to Right Treatment) criteria promote a deprescribing approach, their focus is on the medications themselves and their appropriateness in the geriatric population in general terms. Problem-based deprescribing is a complementary strategy to enhance the use of these "optimal prescribing" criteria and help prioritize a deprescribing focus. **Box 1**[9] outlines the steps to promoting problem-based deprescribing.

Box 1. Steps to problem-based deprescribing

1. Routinely include ADEs in the differential diagnosis when a patient presents with a new symptom; this helps to recognize ADEs, as well as to avoid prescribing cascades
2. Prioritize clinical issues according to risk; start problem-based deprescribing by focusing on the highest-risk clinical issues (eg, delirium and falls)
3. When assessing concerning medications for deprescribing, weigh risk versus benefit of deprescribing and use evidence-based guidelines where available[9]
4. Forge a working partnership between the patient, caregiver, other physicians, and pharmacist to determine a plan for deprescribing and for monitoring outcomes

ADE—adverse drug event.

Implementation

The most important step is to consider the role of medications in all concerns brought by your older patients (and younger ones, too!). For additional resources on problem-based deprescribing for common issues like incontinence, anorexia and weight loss, postural hypotension, and falls and delirium, visit **canadiangeriatrics.ca/wp-content/uploads/2018/10/5_Frank-Molnar-Article-Formatted-Final.pdf**.[1] Clinical practice guidelines for deprescribing benzodiazepines, proton pump inhibitors, and antipsychotics can be found at **deprescribing.org/resources/deprescribing-guidelines-algorithms**.[10-12]

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Competing interests
None declared

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Mortality of hospitalised internal medicine patients bedspaced to non-internal medicine inpatient units: retrospective cohort study

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ABSTRACT

Objective To compare inhospital mortality of general internal medicine (GIM) patients bedspaced to off-service wards with GIM inpatients admitted to assigned GIM wards.

Method A retrospective cohort study of consecutive GIM admissions between 1 January 2015 and 1 January 2016 was conducted at a large tertiary care hospital in Canada. Inhospital mortality was compared between patients admitted to off-service wards (bedspaced) and assigned GIM wards using a Cox proportional hazards model and a competing risk model. Sensitivity analyses included propensity score and pair matching based on GIM service team, workload, demographics, time of admission, reasons for admission and comorbidities.

Results Among 3243 consecutive GIM admissions, more than a third (1125, 35%) were bedspaced to off-service wards with the rest (2118, 65%) admitted to assigned GIM wards. In hospital, 176 (5%) patients died: 88/1125 (8%) bedspaced patients and 88/2118 (4%) assigned GIM ward patients. Compared with assigned GIM wards patients, bedspaced patients had an HR of 3.42 (95% CI 2.23 to 5.26; P<0.0001) for inhospital mortality at admission, which then decreased by HR of 0.97 (95% CI 0.94 to 0.99; P=0.0133) per day in hospital. Competing risk models and sensitivity analyses using propensity scores and pair matching yielded similar results.

Conclusions Bedspaced patients had significantly higher inhospital mortality than patients admitted to assigned GIM wards. The risk was highest at admission and subsequently declined. The results of this single centre study may not be generalisable to other hospitals and may be influenced by residual confounding. Despite these limitations, the relationship between bedspacing and patient outcomes requires investigation at other institutions to determine if this common practice represents a modifiable patient safety indicator.

INTRODUCTION

Hospital capacity strain negatively impacts quality of care.[1] Overcrowding creates many challenges to efficient patient navigation of the hospital system from initial assessment in the emergency department (ED), to admission onto inpatient wards, and ultimately to patient discharge. Beginning in the ED, overcrowding is associated with delayed care and reduced survival.[2] After admission, patients may then become 'boarders', who remain in EDs after admission while awaiting inpatient beds. ED boarding delays medical care, prolongs length of stay and may increase mortality.[3–6]

When assigned general internal medicine (GIM) ward beds become fully occupied, new patients are often 'bedspaced', meaning they are admitted to off-service inpatient units to free up ED beds.[7 8] This is a common occurrence across hospitals.[8] Bedspaced patients reside in areas of the hospital away from assigned GIM wards where medical team members responsible for their care are usually located. Allied health services (eg, nursing, physiotherapy) for bedspaced patients are typically delivered by the 'host service',and they may have limited contact and communication with the GIM team responsible for patient care.[8]

Little research exists to assess whether bedspacing compromises quality of care or patient outcomes. In other areas of medicine, patients who are not cared for in the appropriate specialised setting may have worse quality of care and outcomes; for example, stroke patients not on specialised stroke services[9] and haemodialysis patients on surgical services.[10] Similar issues may apply to bedspaced GIM patients.

This study aimed to evaluate the relationship between bedspacing of GIM patients and inhospital mortality.

METHODS

Design

We conducted a retrospective cohort study using data collected during 2015

Approach to inappropriate sexual behaviour in people with dementia

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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.

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Promoting Quality Improvement in Long-Term Care

A multi-site collaboration to improve outcomes with pneumonia, falls, bacteriuria and behavioural issues in dementia

John Puxty, Rosemary A. Brander, Susanne Murphy and Vaughan Byrnes

Abstract

The Bridges to Care for Long-Term Care research project aimed to facilitate improvements in outcomes for long-term care residents through the provision of knowledge-to-practice and quality improvement resources by trained facilitators. Point-of-care staff reported improved communication and collaboration, improved use of scope of practice and implementation of best practice knowledge. Overall, participating long-term care homes demonstrated an enhanced capacity for common care issues of the elderly (pneumonia, falls, bacteriuria and behavioural and psychological symptoms of dementia) and the ability to effectively engage in quality improvement processes with efficient and effective use of healthcare resources.

The long-term care (LTC) sector is a crucial component of our healthcare system and has distinct challenges. Physicians and LTC health professionals are increasingly challenged in responding to higher-acuity and more advanced disease processes. An additional concern is how to best minimize the occurrence of common safety issues and risks, such as nosocomial infections (Wagnar and Rust 2008). Research has revealed that the context of LTC homes in Ontario may include stagnant approaches to care, a lack of teaching resources, suboptimal quality of resident life and a lack of positive nursing role models (Gates et al. 2009).

A review of the literature combining the major headings of LTC, nursing homes and quality improvement (QI) revealed 140 scholarly publications. The search was refined to focus on research that had targeted issues such as professional roles, general methodologies for QI in LTC and reducing the potentially avoidable use of emergency rooms and acute care hospitals. Despite variability in topic areas and methodologies for implementation, there were common themes that influenced the design and implementation of the Bridges to Care initiative:

- There is an opportunity and willingness for process and practice improvement within LTC (Ouslander et al. 2009).
- The uptake of comprehensive evidence-based tools and multiple risk-based processes may be problematic (Colon-Emeric et al. 2006; Ouslander et al. 2009).
- Change must be supported and endorsed at all levels of care within facilities (Capezuti et al. 2007).
- LTC staff and practitioners need additional supports in both initiating and incorporating new QI strategies into their normal work processes for sustainable change (Davies and Cripacc 2008).

The Centre for Studies in Aging and Health (CSAH) at Providence Care provided project leadership. This project was designed to foster improved care within LTC through facilitated introduction of evidence-based resources within a resident-centred collaborative care model linked to a QI framework. The project research question was, what is the effectiveness of a QI model for

knowledge-to-practice resource delivery on collaborative practice, staff satisfaction, knowledge translation and resident outcomes?

Ethics Approval

The Queen's University Research Ethics Board, Providence Care Research Review Committee, Kingston, Ontario, and Research Ethics Boards of Lakehead University, Thunder Bay, and the University of Ottawa approved the project.

Methods

The research project was divided into five broad phases: (1) the recruitment of LTC homes, (2) the preparation of knowledge-to-practice resources (preliminary phase), (3) the learning collaborative (first workshop), (4) the initiation of the change process (action) and (5) the sharing of results (second workshop). Six LTC homes were recruited within three LHINs: South East, Champlain and North West, Ontario. Each site identified its internal QI team: a point-of-care staff caregiver (non-regulated), a regulated staff member and a manager. Each site also identified external facilitators to its QI initiative. Funds were supplied for appointment of a local resource consultant to facilitate the improvement initiative at the LTC home level and to liaise and coordinate interactions between local teams and CSAH.

The QI projects were defined for each home, and plans evolved to create resource tool kits for each topic (**preliminary phase**; topics included pneumonia, falls, bacteriuria and behavioural and psychological symptoms of dementia [BPSD]). Resource tool kits included recommended assessment and decision support tools, best practice guidelines, evidence summaries, fact sheets and electronic informational links to other resources. The tool kits were created in both electronic and hard copy formats, with selected resources translated into French, with this need determined by the homes that would use them.

The **first workshop** was held in Kingston over two days in November 2009, and all invited LTC home teams participated. The focus was to share information and training in best practices for the core topic areas and in QI methodologies, and to begin a process of a creating a learning collaborative network for the project.

Over a three-month period (**action phase**), LTC home teams applied the QI strategies designed for their topics. Each team refined aim statements for their QI projects, outcome targets, processes to achieve these outcomes and metrics to monitor progress to targets (Table 1). They applied rapid-cycle improvement methodology using the Plan-Do-Study-Act cycle. Feedback and discussion occurred between participating LTC homes, facilitators, resource consultants and the CSAH team through monthly videoconferences, webcasts and teleconferences.

The **second workshop** was held in March 2010 in Kingston, with representatives from all participating LTC homes. Homes demonstrated QI in action by presenting highlights, challenges and successes for their individual projects.

Results

The Collaborative Practice Assessment Tool (CPAT) is a standardized and validated tool (Schroder et al. 2010) that measures levels of collaboration between members of a healthcare team. The CPAT results showed increases in six of the eight domains of collaborative practice, with a statistically significant increase in the area of "goals, mission and meaningful purpose" (Table 2).

TABLE 1.
Quality indicators as selected by long-term care homes for individual projects

Pneumonia
Hospitalization rates of residents with pneumonia
Time from identification to treatment of pneumonia
Staff and family satisfaction surveys
Behaviours and psychological symptoms of dementia
Quality and content of communication and collaboration among staff around behaviours associated with dementia
Staff and family satisfaction surveys
Frequency of occurrence and type of undesired behaviours associated with dementia
Falls
Compliance with a post-falls assessment tool and implementation of physiotherapy assessment and treatment after a fall
Falls rate over a three-month period, from January to March 2010

For all four topics combined, there were overall improvements for all three domains of knowledge: general knowledge, ability to identify and application to practice (Table 3). However, when each topic area was considered separately, differences were noted. Statistically significant increases were seen in all three domains for pneumonia, for two domains (knowledge and application to practice) for falls and a single domain (application to practice) for bacteriuria. Although there were trends to improvement in BPSD, they did not reach statistical significance.

Project participants reported significantly better knowledge of the QI process, as would be expected, but no increased

TABLE 2.
Average Collaborative Practice Assessment Tool scores

	Workshop 1 ($n = 35$)	Workshop 2 ($n = 21$)	Difference	p Value
Goals, mission	5.7	6.1	+0.4	.020*
Relations	6.0	6.3	+0.3	.343
Leadership	5.7	6.0	+0.3	.185
Roles and responsibility	5.4	5.2	–0.2	.154
Communication	5.7	5.8	+0.1	.516
Community linkages	5.4	5.6	+0.2	.554
Decision-making	5.1	5.1	0.0	.964
Patient involvement	6.3	6.2	–0.1	.564

*Statistically significant at $p < .05$ level.

TABLE 3.
Average scores from the Bridges to Care workshop evaluation

	First Workshop ($n = 27$)	Second Workshop ($n = 18$)	p Value
Average combined score for knowledge, ability to identify and application to practice for topic			
Falls	7.1	8.0	.019*
Pneumonia	6.2	7.4	.006*
Bacteriuria	6.3	7.1	.161
BPSD	7.0	7.6	.290
Average combined score for all topics			
Knowledge	6.7	7.5	.038*
Ability to identify	6.5	7.5	.016*
Application to practice	6.5	7.5	.030*

BPSD = behavioural and psychological symptoms of dementia.
*Statistically significant at $p < .05$ level.

confidence. There was also a significant increase in participants' likelihood of recommending LTC to others as a place of work, and significance (p = .061) in their own increased workplace satisfaction.

Five of six participating LTC homes reported on the process and outcomes at the second workshop (Table 4). One LTC home was unable to report due to a number of staff changes, resulting in a disruption of the original QI team. Each of the five reporting LTC homes met or exceeded its QI target. All LTC homes reported ongoing sustainable activities.

Qualitative data from focus groups supported that the roles and responsibilities of team members as adopted in the QI change processes were effective in ensuring success. There were three key themes from the LTC home teams:

1. The fact that they worked in "real teams on real issues," as opposed to using "fictitious" case studies, was very pertinent to their ability to apply their knowledge in their own working environments.
2. Project processes enabled a safe environment where there was

TABLE 4.
QI strategies and outcomes

Site Area of QI Focus	Aim Statement	Process	Outcome at Three Months
Pneumonia	Reduce hospitalization with pneumonia by 30% within three months	Implement Alberta Care Plan and Assessment Tool Educate registered staff, PSWs, family, residents and staff	No hospitalizations with pneumonia despite five diagnosed cases
BPSD	Educate 100% in use of three question template	Educate staff and implement use of three question template at daily reports	Stream-lined communication at daily reports Increased staff satisfaction Established secondary QI initiative at mealtime
BPSD	Improve atmosphere in dining room at meal times	Turn off the radio during mealtimes Repaint the dining room Nutrition and dementia information/staff training delivered to resident care and dining room staff Eliminate stress factors such as drug trolley	Improvement in dining room atmosphere by 75% Improved awareness of resident-specific needs by 60% Reduction of stress level in dining room by 75%
Falls	Reduce number of harmful falls in one year	Introduce PFAT Improve post-fall documentation and care plan	100% completion of PFAT at 3/12 months PT assessment and treatment linked to PFAT
Falls	Reduce number of harmful falls by 6% in three months	Implement PFAT and PFOT with post-fall medication and PT assessment	100% completion of PFAT and PFOT at 3/12 months 55% reduction of harmful falls

BPSD = behavioural and psychological symptoms of dementia; PFAT = post-fall assessment tool; PFOT = post-fall observation tool; PSW = personal support worker; PT = physiotherapy; QI = quality improvement.

a "meeting of equals" to share ideas and design team-built strategies in a spirit of mutual respect.

3. Group facilitators were highly credible, and physician engagement augmented the team's ability to move forward in their local QI processes.

Finally, staff satisfaction surveys were completed by two of the LTC home teams. The results showed that most staff members on each of the teams were highly satisfied with knowledge of their team's projects, the usefulness of the tools they chose and the implementation of those tools, and the levels of education and communication surrounding changes made as part of the project. Open-ended comments from staff showed a belief that the changes made led to improved communication and early identification and treatment of patients with particular need.

Discussion

At the end of three months, all participating LTC homes reported significant improvements in sustainable collaborative resident-centred care processes within the focus of their QI initiatives. These improvements were associated with improved resident care outcomes in terms of reductions in hospitalization with pneumonia, serious falls and troublesome behaviours associated with dementia.

These benefits are first attributable to the homes being strongly engaged in the development of their QI learning and applications from onset. They identified their own projects, their own teams, many of their own resources and the way and means of implementing best practices that would work within their own environments. They also identified and refined the measures and targets to determine their own successes. They worked with their teams on real issues and expressed feelings of ownership concerning their project.

Benefits are also attributable to the provision of combining facilitated knowledge-to-practice and QI processes through the use of internal champions, resource consultants and external facilitators. Home participants repeatedly stated that this personal contact and support were key to their success in moving resources from a "shiny tool kit gathering dust on a shelf" to successful changes in collaborative care practices.

A number of complementary improvements in both collaborative care processes and the working environment were demonstrated:

- Increased knowledge, attitudes and skills of the participating individuals were confirmed in common care issues of the elderly in LTC and in QI processes.
- All homes reported that participants were empowered to use their new skills and to act as a both a resource and support to other staff members in improved collaborative care practices. The unregulated staff reported feelings of empowerment and being active contributors to the QI processes.
- There was evidence of an increased inter-professional approach to resident care in terms of clarification of scopes of practice and in both team and improved inter-organizational communication and collaboration. Respective roles and scopes of practice of champions within the process appear to have been enhanced beyond the team members' usual respective areas of influence.
- Improved health and safety outcomes for residents resulted within the three QI topic areas. This was likely a result of both access to and the expanded use of evidence-based, resident-centred, collaborative practice resources offered through the project. Participants accessed these resources through a variety of formats, including a web-based repository.
- There was evidence of efficient and effective use of both onsite and external health human resources through the transfer of evidence into relevant care plans that optimize clinical decision-making and care delivery skills of a variety of healthcare providers.
- Sites that collected data reported that staff, family and resident satisfaction improved concerning the quality of care within LTC. This included an increased appreciation by staff that LTC homes are desirable places in which to work.

The Bridges to Care initiative was conceptualized and designed as a pilot project; this limits some of the generalizability of the results. The small sample of LTC homes limits the analysis and generalizability of the findings, although three distinct geographical communities were included. In addition to this, the relative contributions of the various components of the process have not been examined as independent variables. Future research might examine the relationships between the different components and levels of support provided and the outcomes examined through this initiative.

Conclusions

The participating LTC homes were positively influenced in the education and training of staff, with commitments for sustainability and spread within their sites and throughout their regions. All participating LTC homes reported success in achieving their primary QI outcomes. HQ

Acknowledgements

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ORIGINAL RESEARCH

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

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ABSTRACT

Background

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

Methods

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

Results

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

Conclusion

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

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

INTRODUCTION

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

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

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

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ORIGINAL RESEARCH

Pre-Clerkship Observerships to Increase Early Exposure to Geriatric Medicine

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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.

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Canadian Medical Education Journal

Brief Reports

Prescribing competency assessment for Canadian medical students: a pilot evaluation

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Abstract

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

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

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

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

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Abstract

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

Introduction

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

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

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

Sources and consequences of ageism in healthcare

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

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

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

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

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

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

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

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

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

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

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT03272607

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COMMENTARY

WILEY

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

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COMMENTARY

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

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

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

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

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

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

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

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

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The Timing of Drug Funding Announcements Relative to Elections: A Case Study Involving Dementia Medications

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Abstract

Background: Following initial regulatory approval of prescription drugs, many factors may influence insurers and health systems when they decide whether to add these drugs to their formularies. The role of political pressures on drug funding announcements has received relatively little attention, and elections represent an especially powerful form of political pressure. We examined the temporal relationship between decisions to add one class of drugs to publicly funded formularies in Canada's ten provinces and elections in these jurisdictions.

Methods: Dates of provincial formulary listings for cholinesterase inhibitors, which are drugs used to treat Alzheimer's disease and related dementias, were compared to the dates of provincial elections. Medical journal articles, media reports, and proceedings from provincial legislatures were reviewed to assemble information on the chronology of events. We tested whether there was a statistically significant increase in the probability of drug funding announcements within the 60-day intervals preceding provincial elections.

Results: Decisions to fund the cholinesterase inhibitors were made over a nine-year span from 1999 to 2007 in the ten provinces. In four of ten provinces, the drugs were added to formularies in a time period closely preceding a provincial election ($P = 0.032$); funding announcements in these provinces were made between 2 and 47 days prior to elections. Statements made in provincial legislatures highlight the key role of political pressures in these funding announcements.

Conclusions: Impending elections appeared to affect the timing of drug funding announcements in this case study. Despite an established structure for evidence-based decision-making, drug funding remains a complex process open to influence from many sources. Awareness of such influences is critical to maintain effective drug policy and public health decision-making.

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Competing Interests: SSG is a member of the Committee to Evaluate Drugs, which provides advice to the Ontario Ministry of Health and Long-Term Care on drug-related matters such as drugs to list on the provincial formulary. NG, CMB, PAR, PCA, and AL all declare that they have no competing interests related to this manuscript. This does not alter the authors' adherence to all the PLOS ONE policies on sharing data and materials.

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Introduction

More than two years after the historic passage of the *Patient Protection and Affordable Care Act* (ACA), ongoing debate over US health care reform has reinforced how profoundly politics can shape health policy. The results of the 2012 Presidential election will have a profound impact on the delivery of health care in the US for years to come [1].

Specific elements of health policy, however, are traditionally viewed as being relatively insulated from political influences. For example, insurers and health care systems in many countries provide formulary coverage for prescription medications and must balance rising costs against appropriate access to new treatments [2–4]. A number of agencies help to determine whether new drugs should be listed in drug formularies, and the principles that drive their decisions (such as evidence of effectiveness and safety, evidence of need, and cost implications) have been reviewed [2,3,5]. Although cost-effectiveness criteria are used to guide policy related to drug coverage in many countries, drug reimbursement decisions within publicly funded health care settings in the US largely exclude considerations of cost [4]. For example, the ACA specifically prohibits use of cost effectiveness thresholds to guide coverage decisions [6]. The emergence of very expensive

Hematology

Dr. Annette Hay
Division Chair
Research Lead

Summary

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

Resident Research Projects – Hematology
Current/Past Projects 2023

Potential opportunities

1. Clonal hematopoiesis

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

2. Bleeding Disorders

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

3. Blood Transfusion

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

4. Thrombosis

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

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

5. Inherited red blood cell disorders

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

Current projects

6. Primary care patient management pathways

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

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

Examples of completed projects

7. Refractory Hypercalcemia: Rare Presentation of a Common Disease

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

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

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

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

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

Current practice for many Canadian leukemia and bone marrow transplant centers is a liberal transfusion threshold of 2 units of PRBCs for a hemoglobin < 80 g/L, however there is little evidence assessing optimal transfusion targets, and a restrictive strategy appears feasible. In this study, the objective was to evaluate if a more restrictive (1 unit for Hgb ≤ 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

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

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

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

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

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

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

M. BOTROS[1], M. CHAIGNEAUF[2], J. GRABELL[3], W. HOPMAN[4], P. JAMES[5]

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2. RN, MSc, Queen's University Dept. of Medicine
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5. MD, FRCPC Queen's University Dept. of Medicine

WFH 2022 WORLD CONGRESS

LET'S TALK PERIOD

Queen's UNIVERSITY

KHSC

INTRODUCTION

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

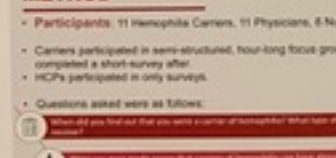
Figure 1. **The Study Purpose.** This project aims to understand gaps in knowledge to improve care for carriers.

AIM

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

METHOD

- **Participants:** 11 Hemophilia Carriers, 11 Physicians, 6 Nurses
- Carriers participated in semi-structured, hour-long focus groups, and completed a short-survey after.
- HCPs participated in only surveys.
- Questions asked were as follows:



Statistical Analyses:

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

RESULTS

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

Psychosocial impacts of abnormal bleeding

Participants described many negative psychosocial impacts associated with abnormal bleeding symptoms, including increased anxiety, low self-esteem, and missed opportunities.

"When I had my period throughout my teens, and experienced symptoms, there was nothing about being a symptomatic carrier. I sort of suffered in silence, and those things at school, anxiety, self-esteem were all certainly affected"

Difficulty determining symptom significance

Participants were often unsure when a given symptom constituted abnormal bleeding and when it was appropriate to seek treatment. They described a tendency to underestimate the severity of their bleeding.

"Even now treatment guidelines for women with bleeding disorders are very vague. It's still very vague, should we be using tranexamic acid or desmopressin... moving forward, I'd like to see some consistency around when I should treat myself."

Need for self-advocacy

Participants having to advocate for themselves and 'prove' the legitimacy of their experiences was frustrating for several of the carrier participants.

"My GP is old fashioned and didn't believe that I could be symptomatic. It took the (HTC) intervening with my GP to tell her, no, (patient name) can have bleeding as well."

Testing concerns

Participants described "inconsistent recommendations" around hemophilia carrier testing. Carriers who learned their carrier status at a young age unanimously found it beneficial.

"I can't imagine my parents not knowing that. If an accident had happened, and you didn't know, it's preventative and proactive to know your medical situation... That idea, we're protecting girls by not getting them tested is more harmful."

Table 7

In your opinion, under what circumstances should genetic testing for a hemophilia carrier UNDER THE AGE OF CONSENT be administered? (Assuming request has been made by the patient/family, and previous factor level assay was normal)

	HC (n=11)	HCP Response: VIRULENT: Carriers (n=28)	HCP Response: POTENTIAL: Carriers (n=28)	Significance
1. At birth	45.5%	10.3%	0%	p = <0.001
2. Patient has upcoming surgical procedure	72.7%	26.3%	10.5%	p = 0.027
3. Patient has symptoms of abnormal bleeding	100%	67.4%	84.2%	p = 0.010
4. Age of menarche is approaching	72.7%	21.1%	21.1%	p = 0.010
5. Patient has symptoms of heavy menstrual bleeding	100%	52.6%	78.9%	p = 0.045
6. No medical indication but request has been made by family	72.7%	21.1%	21.1%	p = 0.039

Survey Results:

- Similar beliefs regarding when factor testing should be done.
- Misalignment in beliefs regarding genetic testing (Table 1). When both study groups were asked about the circumstances under which genetic testing for a hemophilia carrier under the age of consent should be considered, hemophilia carriers were significantly more in favour of genetic testing than health care providers in all scenarios (Table 7).

CONCLUSIONS

- Interventions needed include:

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

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

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BAYER

PP-82

Quality of life/ Outcome research

Monique Botros

Poster presented at

Poster Session Online

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

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INTRODUCTION

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

OBJECTIVE

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

METHODS

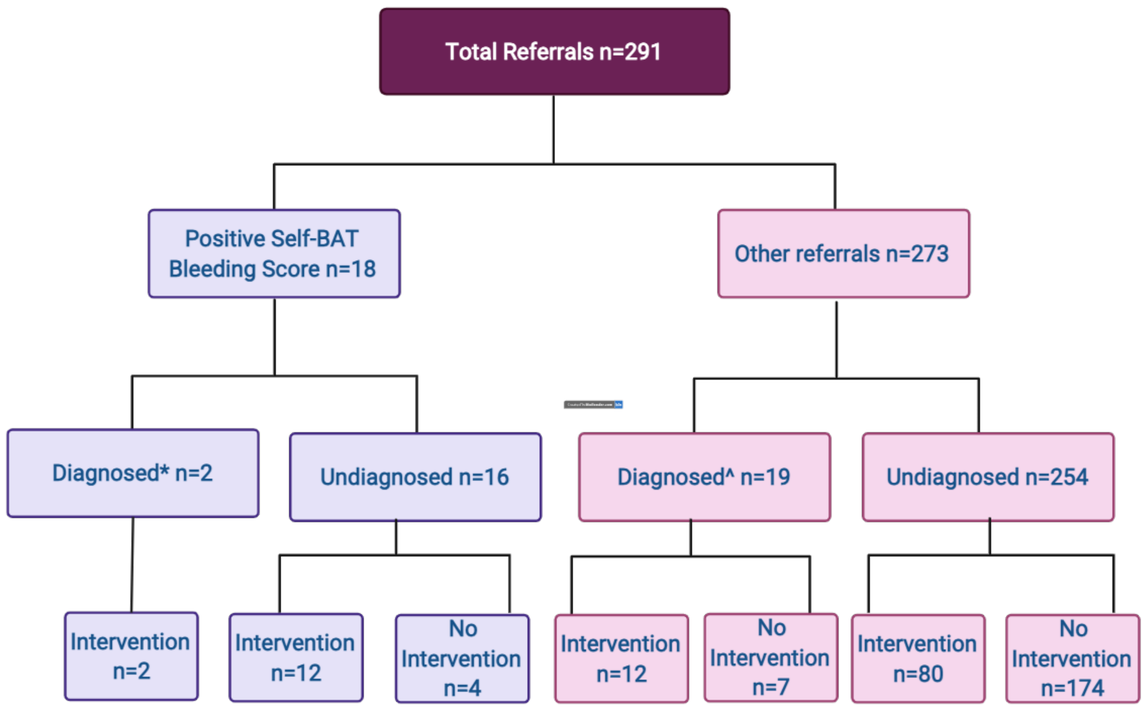
•A retrospective, observational study
•REB approval was obtained
•Chart review of all clinic patients assessed for suspicion of an inherited bleeding disorder during a 5-year period
•Clinical assessment of bleeding symptoms was by expert administered Condensed MCMDM-1VWD Bleeding Score (BS)

•Subjects were divided into two groups: 1: Referred for abnormal Self-BAT BS or 2: Referred for other reasons; mucocutaneous bleeding, abnormal laboratory results or family history of an inherited bleeding disorder
•Further intervention is defined as: referral to other specialist, iron replacement or surgical/procedural management.

Subject Characteristics

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

Flow Diagram of Referrals and Results



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

SUMMARY

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

CONCLUSION

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

ACKNOWLEDGEMENTS

CSL Behring

Created with BioRender Poster Builder

ISTH VIRTUAL CONGRESS 2021 JULY 17–21 ISTH2021.ORG
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SCIENCE CONQUERING DISEASE

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

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[7]Pathology & Molecular Medicine, Queen's University, Canada; [8]Neurosurgery, Washington University School of Medicine, USA; [9]Pediatrics, Washington University School of Medicine, USA

Queen's University
Clinical and Molecular Hemostasis Research Group
Queen's University & Kingston General Hospital

INTRODUCTION

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

AIM

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

METHODS

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

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

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

RESULTS

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

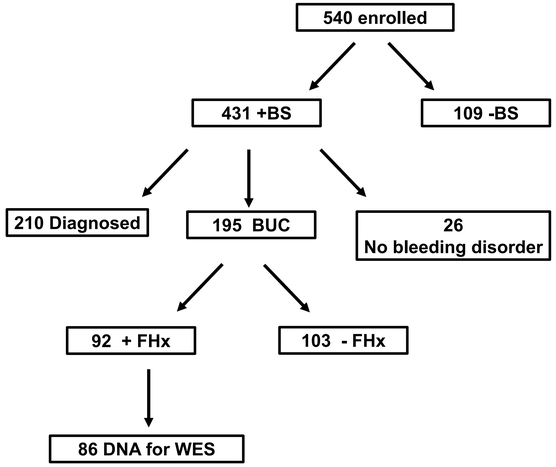

Figure 1: Flow diagram showing the number of patients enrolled in overall study and the prioritization of BUC with +FHx for WES.
BS: bleeding score; BUC: bleeding of unknown cause; FHx: family history of bleeding; WES: whole exome sequencing

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

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

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

Patient ID	Bleeding score	Platelet count ($x10^9$/L)^	Mean platelet volume (fL)#	Platelet aggregation studies	Gene symbol	Gene name	Associated Disease(s)	Inheritance	Amino Acid change	Genotype
GWC-101	4	264	n/a	normal	*HPS1*	HPS1 biogenesis of lysosomal organelles complex 3 subunit 1	Hermansky-Pudlak syndrome	AR	p.Pro324fs	Heterozygous
GWK-023	13	177	11.2	normal	*ITGA2B*	integrin subunit alpha 2b	Platelet-type bleeding disorder 16, Glanzmann thrombasthenia	AD, AR	p.Gln852fs	Heterozygous
GWK-195	4	170	11.5	normal	*ITGA2B*	integrin subunit alpha 2b	Platelet-type bleeding disorder 16, Glanzmann thrombasthenia	AD, AR	p.Arg889fs	Heterozygous
GWK-182	6	146	8.9	normal	*MYH9*	myosin heavy chain 9	May-Hegglin	AD	p.Glu1350del	Heterozygous
GWC-063	9	209	n/a	normal	*NBEAL2*	neurobeachin like 2	Gray platelet syndrome	AR	p.Arg2187fs	Heterozygous

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

CONCLUSIONS

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

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PB0906

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

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INTRODUCTION

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

AIM

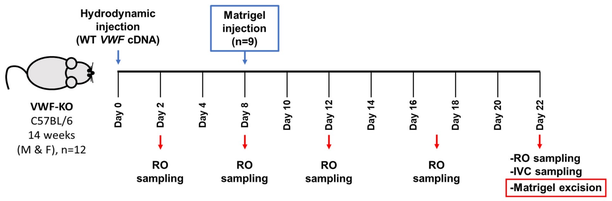
To examine the effect of VWF replacement on *in vivo* angiogenesis in a mouse model of VWF deficiency.

METHODS

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

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

Experimental timeline



RESULTS

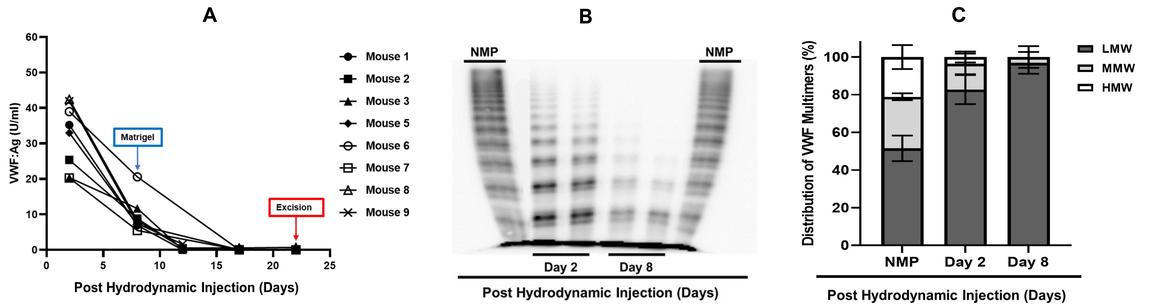


Figure 1 (A) VWF:Ag of each mouse from day 2 to 22 post hydrodynamic injection. (B) Representative multimers are shown for C57Bl/6 normal plasma pool (NMP; lane 1 & 6), day 2 (lane 2 & 3), and day 8 (4 & 5) post-hydrodynamic injection. (C) Densitometric analysis of multimers shown as mean ± SD; N=9 (NMP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

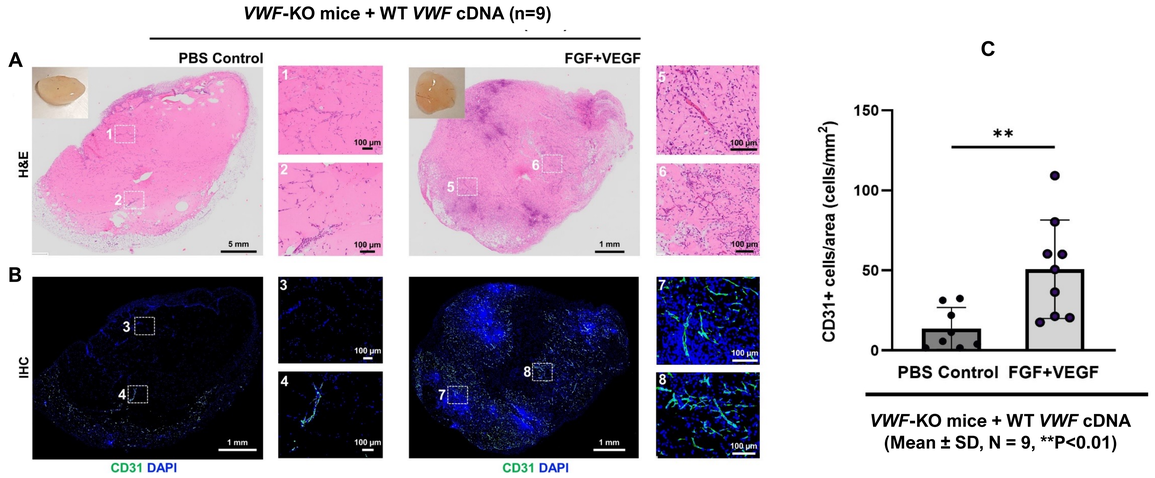


*Figure 2. Sections from FGF + VEGF supplemented plugs and PBS controls were stained for (A) H&E and (B) IHC: DAPI (blue), and CD31 (green). (C) The number of CD31+ cells in the entire area of each plug section were quantified and is shown as mean ± SD; PBS Control: dark gray and FGF + VEGF: light gray.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

CONCLUSIONS

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

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

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ACKNOWLEDGEMENTS

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Infectious Disease

Dr. Gerald Evans
Division Chair

Dr. Tony Bai
Research Lead

Summary

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

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

Queen's University

DIVISION OF INFECTIOUS DISEASES RESEARCH PROJECTS

Internal Medicine Resident Research Fair

Sep 12,2023

FACULTY

Dr Gerald Evans

Dr Santiago Perez-Patrigeon

Dr Evan Wilson

Dr Jorge Martinez-Cajas

Dr Bradley Stoner

Dr Anthony Bai

Dr Kirk Leifso (Pediatric Infectious Diseases)

Dr Prameet Sheth (Microbiology and Immunology)

Topic: HIV

Projects	Period	Methods	Opportunity	Supervisor
Building the HIV database for the IIC clinic	2023-	Make a descriptive analysis of the cohort; participant identification for future trials; collaboration with other cohorts	The role for the resident would be to apply for a PSI grant and head the project in terms of accessing database, doing analysis and writing up a manuscript.	Santiago Perez-Patrigeon
Immunophenotype and reservoir of patients with hyper immune recovery post-ART and patients treated during acute HIV	2023-	After publishing papers about each of the 2 cohorts independently we are performing a comparative analysis of the 2 and working on the next paper.	The role for the resident would be contribution to data analysis and will be a co-author on manuscript.	Santiago Perez-Patrigeon

Topic: HIV pre-exposure prophylaxis

Projects	Period	Methods	Opportunity	Supervisor
Improving PrEP access in suburban/rural Ontario	2022-2024	Mixed methods/implementation research	Design, analysis and publication	Jorge Martinez-Cajas Evan Wilson Bradley Stoner Santiago Perez-Patrigeon
An Assessment of Primary Care Provider's Readiness, Educational Needs and Preferences for PrEP Adoption in Colombia	2022-2024	Mixed Methods/implementation research	Analysis and publication	Jorge Martinez-Cajas Evan Wilson Bradley Stoner Santiago Perez-Patrigeon

Topic: *C. difficile*

Projects	Period	Methods	Opportunity	Supervisor
Initial vancomycin taper for the prevention of recurrent *Clostridium difficile* infection (TAPER-V)	2023-	This is a pragmatic, real-world, investigator-initiated placebo-controlled randomized controlled trial where all patients will initially receive standard oral vancomycin dosing (according to the most recent Canadian guidelines[1]) followed by either a two week low dose tapering continuation phase (intervention) or matched placebo (control).	The role for the resident would be to enroll participants and perform clinical follow up. It will be an opportunity to learn about Good Clinical Practices and participate in a multi-institutional randomized clinical trial.	Santiago Perez-Patrigeon

Topic: COVID-19

Projects	Period	Methods	Opportunity	Supervisor
Serologic Evidence of Covid-19 in Healthcare workers in SE Ontario	2020-	Epidemiology and Infection Control	Conduction, analysis, publication	Jorge Martinez-Cajas

Topic: Outpatient Antimicrobial Treatment

Projects	Period	Methods	Opportunity	Supervisor
Implementation of an OPAT program at KGH Focus on Database development for performance metrics	2017-	Implementation/Quality Improvement methods	Design, conduction, data analysis, publication	Jorge Martinez-Cajas Evan Wilson
Audit on appropriateness of antimicrobial treatment for OPAT patients	2020-	Retrospective/Prospective descriptive studies	Design, conduction, publication	Jorge Martinez-Cajas Evan Wilson

Topic: Bacteremia

Projects	Period	Methods	Opportunity	Supervisor
Mandatory infectious diseases consultation for Staphylococcus aureus bacteraemia: A retrospective cohort study	2022-	Quality Improvement methods. The study will collect information on outcomes for S. aureus bacteremia for 1 year before and after implementation of mandatory S. aureus bacteremia. The study will analyze if mandatory infectious diseases consultation improve patient outcomes.	The role for the resident would be to extract data, perform the analysis and write a manuscript as a first author.	Anthony Bai
Long-term morbidity in bacteremia survivors	2023-	Population-based retrospective cohort study using the ICES database to study the long term morbidity (e.g. cognitive decline, cardiovascular event, need for dialysis, long term care placement) up to 1 year in survivors of bacteremia.	The role for the resident would be to assist with performing a background literature search, forming a statistical analysis plan and writing up of manuscript.	Anthony Bai

Topic: Pneumonia

Projects	Period	Methods	Opportunity	Supervisor
Anaerobe coverage in aspiration pneumonia	2023 -	Retrospective multicentre cohort study using the GEMINI database to compare the effectiveness of no anaerobe coverage versus anaerobe coverage in the treatment of aspiration pneumonia for patients admitted to the internal medicine service across Ontario Hospitals.	Assistance with research of background literature and writing of the manuscript.	Anthony Bai

Topic: Antimicrobial stewardship

Projects	Period	Methods	Opportunity	Supervisor
Evaluation of peritoneal dialysis related peritonitis events at KHSC	2019-	Retrospective cohort, quality improvement	Design, conduction, analysis, publication	Gerald Evans
Targeted Penicillin Allergy Skin Test for Self-reported Penicillin allergic in-patients	2020-	Quality improvement	Design, conduction, analysis, publication	Evan Wilson
Implementation of antimicrobial stewardship IT infrastructure	2020-	Quality improvement, Implementation research	Design, conduction, analysis, publication	Evan Wilson
Global Point Prevalence Survey on Antimicrobial Use	2019-	Observational, point prevalence study	Conduction, data analysis	Evan Wilson

Topic: Lyme disease

Projects	Period	Methods	Opportunity	Supervisor
Evaluation of quality of cited literature by Lyme disease advocacy groups	2018-	Bibliographic search and quality assessment of scientific rigor of literature cited by Lyme guidelines endorsed by Lyme disease advocacy groups	Design, conduction and publication	Gerald Evans
Follow up of confirmed Lyme-disease patients in the SEO area	2017-	Cohort study looking at outcomes in patients with confirmed Lyme disease	Design, conduction, data analysis, publication	Evan Wilson Kirk Leifso
Referrals for Lyme Disease in a highly endemic Canadian region	2020-onwards	Retrospective chart review	Conduction, analysis, publication	Evan Wilson Kirk Leifso

DIVISION OF INFECTIOUS DISEASES- ACTIVE PROJECTS

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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

Anthony D. Bai, MD; Yunbo Jiang, BHSc; David L. Nguyen, BHSc; Carson K. L. Lo, MD; Isabella Stefanova, MD; Kevin Guo, BHSc; Frank Wang, BHSc; Cindy Zhang, BHSc; Kyle Sayeau, BSc; Akhil Garg, MDCM; Mark Loeb, MD, MSc

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.

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Aspiration pneumonia

Vincent Girard MD, Anthony D. Bai MD MSc **[AU1: Please confirm author names and degrees]**

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1 Aspiration pneumonia causes X%–15% [AU2: Please provide the lower end of this range.] 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 of patients with 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 in aspiration pneumonia

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 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 (min to h) 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 an 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: **[AU3: Please confirm Competing interests]** None declared.

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Systematic review

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

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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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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

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,[2,3,4] and Todd C. Lee[13]

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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 effect when applying RCT results to bedside care.

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

To evaluate the effect of interventions on mortality in *Staphylococcus aureus* bacteremia (SAB), there have been increasing efforts to conduct pragmatic randomized controlled trials (RCTs). The 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. This will be amplified 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. This 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. Therefore, 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

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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 definition of attributable deaths.

Results. Twenty-four observational cohort studies were included. The 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. The 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 first 5 days. If the patient dies within the first 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.

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Review

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

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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.

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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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Nephrology

Dr. David Holland
Division Chair

Dr. Rachel Holden
Research Lead

Summary

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

Rachel Holden, MD

Research Interests:

- Phosphate homeostasis and cardiovascular risk
- The role of vitamin K in the inhibition of vascular calcification in chronic kidney disease
- Vitamin D metabolism
- Calcification imaging
- Vascular calcification in experimental CKD – mechanisms and treatments

Current Clinical Projects:

- Development of a novel clinical test for the diagnosis of phosphate intolerance
- The impact of sex on dietary phosphate handling
- The impact of obesity, insulin resistance and diabetes on dietary phosphate handling
- Vitamin D metabolism in CKD
- Randomized controlled trial of vitamin K supplementation to prevent vascular calcification progression in dialysis patients
- The impact of phosphate bioavailability on counter-regulatory hormone response to phosphate exposure
- Dialysis frequency and quality of life in elderly patients
- Novel biomarkers of vascular calcification

Research Project Ideas for a Resident:

- Impact of pre-surgical PTH and dialysis vintage on clinical and laboratory outcomes post-parathyroidectomy.
- Predictors of vitamin D deficiency in dialysis patients
- Recovery of vitamin D metabolome post kidney transplantation

Relationship Between Coronary Artery Calcification and Renal Function Decline, End-Stage Kidney Disease, and Mortality in Stage 3-5 CKD Patients

Michelle C. Lamarche, Wilma M. Hopman, Jocelyn S. Garland, Christine A. White, Rachel M. Holden

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2. Clinical Research Centre, Kingston General Hospital, and Department of Public Health Sciences, Queen's University, Kingston, Canada

INTRODUCTION

• Arterial calcification in chronic kidney disease (CKD) occurs in both the intimal and medial layers. This calcification is driven by both production of hydroxyapatite crystals resulting from an elevated calcium-phosphate product as well as dedifferentiation of the vascular smooth muscle cells (VSMC) to osteoblastic-like cells through an imbalance in activators and inhibitors (Figure 1)[1,2]

• Patients with CKD have higher coronary artery calcification (CAC) scores when compared to age and sex matched control[3-5]

•Elevated CAC score is an independent risk factor of cardiovascular and all-cause mortality in the general population[6,8,9] and in patients with CKD/ESKD[10].

• Patients with ESKD have increased cardiovascular mortality, due in part to increased vascular calcification in addition to the high prevalence of traditional Framingham risk factors[8]

• Increased CAC score is associated with more advanced renal disease[3,4]. However, it has not yet been documented the effect of CAC score on long-term renal function decline or rate of ESKD.

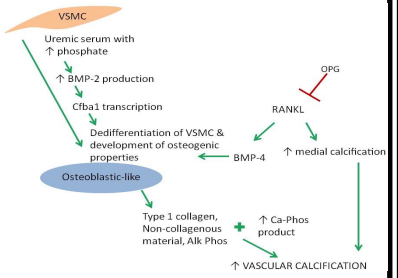

Figure 1: Vascular calcification in CKD

AIM: To assess if CAC is an independent risk factor for renal function decline, ESKD, and/or mortality in pre-dialysis CKD patients

RESULTS

One hundred seventy-eight patients were initially enrolled, of which 39 were lost to follow up at 10 years. The mean age (SD) was 61.2 (13.8) years, with a mean (SD) eGFR of 25.62 (11.7). Seventy-nine (44.4%) had diabetes and 165 (92.7%) had hypertension.

At 5 and 10 years, the rate of mortality was 16.9% and 38.6% and ESKD was 33.3% and 53% respectively for those who made it to the time point. Overall, the mean percent change in eGFR after 5 years of follow-up in those without ESKD was 15.1%.

In a multivariable analysis that controlled for all statistically significant baseline variables, the independent predictors of the ESKD, eGFR and mortality outcomes were:

• ESKD at 5 years:
  • baseline eGFR, urine ACR, PTH, and OPG
• ESKD at 10 years:
  • urine ACR, PTH, and CAC score
• Percent change in eGFR over 5 years:
  • urine ACR, PTH, and CAC score
• Mortality at 5 years:
  • age, diabetes, and baseline eGFR
• Mortality at 10 years:
  • age, diabetes, baseline eGFR, and CAC score

	End-Stage Kidney Disease			
	5 year		10 years	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (years)	0.956 (0.89, 1.026)	0.213	0.924 (0.848, 1.008)	0.074
Baseline eGFR (mL/minute)	0.858 (0.750, 0.982)*	0.026	1.013 (0.932, 1.101)	0.759
Log UACR (mg/mmol)	3.239 (1.144, 9.171)*	0.027	2.343 (1.025, 5.357)*	0.044
Log PTH (pg/mL)	16.74 (1.47, 190.57)*	0.023	21.02 (1.34, 330.21)*	0.03
Ca/P product (mg2/dL2)	0.721 (0.206, 2.526)	0.609	1.666 (0.484, 5.731)	0.418
OPG (pg/mL)	1.001 (1, 1.001)	0.057	1.0 (1.0, 1.001)	0.16
%ucOc	1.016 (0.98, 1.053)	0.379	1.018 (0.983, 1.055)	0.322
Log CAC (AU)	0.809 (0.332, 1.971)	0.641	2.243 (1.040, 4.840)*	0.039

	Mortality			
	5 years		10 years	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (years)	1.085 (1.027, 1.145)*	0.003	1.104 (1.048, 1.163)*	<0.001
Baseline eGFR (mL/minute)	0.938 (0.891, 0.987)	0.014	0.932 (0.891, 0.975)*	0.002
History of CVD	1.167 (0.385, 3.539)	0.785	1.030 (0.318, 3.337)	0.96
Diabetes	2.838 (1.020, 7.897)*	0.046	4.981 (1.84, 13.483)*	0.002
Log CAC (AU)	1.481 (0.88, 2.492)	0.139	2.053 (1.237, 3.407)*	0.005

Table 1: Multivariable analysis for end-stage kidney disease and all cause mortality

		Individual Predictors		95% Confidence Interval for B	
	B	β	p-value	lower bound	upper bound
Age (years)	-0.71	-0.25	0.194	-1.79	0.38
Baseline eGFR (mL/minute)	0.33	0.11	0.592	-0.90	1.55
Log UACR (mg/mmol)	12.98	0.38	0.1	3.32	22.65
Log PTH (pg/mL)	38.05	0.40	0.014	8.13	67.97
Ca/P product (mg2/dL2)	-6.10	-0.13	0.461	-22.75	10.56
OPG (pg/mL)	0.00	0.18	0.313	0.00	0.01
%ucOc	-0.23	-0.17	0.361	-0.74	0.28
Log CAC (AU)	11.99	0.48	0.012	2.78	21.20
Constant	-0.5731				

Table 2: Multivariable analysis for percent change in eGFR

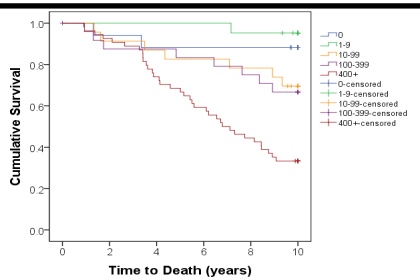

Figure 2: Unadjusted Kaplan-Meier curve for all cause mortality stratified by level of coronary artery calcification
Survival is statistically significant between CAC levels, P <0.001

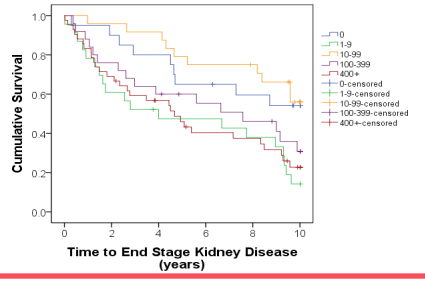

Figure 3: Unadjusted Kaplan-Meier curve for dialysis or transplant stratified by level of coronary artery calcification
Time to ESKD stratified by CAC score is significant, P = 0.003. CAC score does not differ significantly between stages of CKD (P= 0.923)

METHOD

- Prospective cohort study involving 178 Caucasian patients with stage 3-5 CKD enrolled between 2005 and 2007 at the Kingston General Hospital CKD clinic
- Development of ESKD, defined as dialysis initiation or renal transplant, and mortality were determined 5 and 10 years and change in eGFR was determined at 5 years after study enrolment by chart review
- Baseline variables assessed included eGFR, urine ACR, CAC score, age, diabetes, history of CVD, history of PVD, hypertension, dyslipidemia, smoking, BMI, CRP, uric acid, magnemsium, and CKD-MBD biomarkers .
- eGFR was calculated using the 4-variable re-expressed MDRD Study equation.
- CAC scores were evaluated using a computed tomography multislice scanner and a total CAC score generated by the Agatston method
- Continuous variables that were not normally distributed (urine ACR, CAC score, PTH) were log transformed prior to analysis.
- Associations between the listed variables and the outcomes was assessed with bivariate analyses. Variables with statistically significant associations were used in the multivariable analyses for the outcomes
- Statistitcal analysis was completed with SPSS

CONCLUSIONS

- In patients with stage 3-5 CKD, independent predictors for mortality differ from those for development of ESKD
- In patients with stage 3-5 CKD, coronary artery calcification is an independent predictor for eGFR decline at 5 yrs, ESKD and mortality at 10 yrs
- In general, increased CAC score was associated with decreased survival and decreased time to ESKD
- Incorporation of a patient's CAC score may be useful in risk stratifying patients in their potential to require dialysis or transplant. This may be useful in identifying patients that would benefit from more aggressive management of their renal disease
- Markers of CKD-MBD (Ca/P product, PTH, OPG, and %ucOc) were independent predictors of ESKD
- Whether strict management of CKD-MBD in early stage CKD prior to development of hyperphosphatemia prevents kidney function decline and improves mortality requires further study.

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Nephrology Dialysis Transplantation

Relationship of coronary artery calcification with renal function decline and mortality in predialysis chronic kidney disease patients

Michelle C. Lamarche[1], Wilma M. Hopman[2,3], Jocelyn S. Garland[1], Christine A. White[1] and Rachel M. Holden[1]

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DR. KAREN YEATES, MD, FRCPC, MPH

- Undergraduate BSc, Anatomy and Cell Biology, McGill University
- Queen's University, Doctor of Medicine
- Internal Medicine training, University of Toronto
- Nephrology Fellowship, Queen's University
- Master of Public Health, Harvard University
- Queen's University Faculty position in Nephrology

RESEARCH INTERESTS:

- Global health/population health and community-based participatory research in Indigenous health
- Implementation Science Research in low and middle-income countries (low resource settings)
- Mobile health interventions to improve provision of health care by non-physician health providers (primarily nurses)
- Non-communicable disease epidemiology, detection and prevention in low-resource settings (primarily East Africa)
- Acute kidney injury prevention, detection and management in low-resource settings (Tanzania)
- Prevention of cardiovascular disease (hypertension control), cervical cancer and detection and management in East Africa

ACTIVE RESEARCH PROJECTS:

- Country PI for The Prospective Urban and Rural Epidemiology Study (PURE) in Tanzania. PURE has 2400 participants that we have followed in a prospective cohort for 8 years as part of a global study of >200,000 participants. PURE is examining the impact of rapid urbanization, country income and health system resources on the development of chronic diseases (heart, stroke, cancer, kidney), mental health, injuries, air pollution etc) (Funding from Wellcome Trust and CIHR)
- PURE Tanzania is starting a COVID-19 sub-study of 1500 participants to examine health and psychosocial impacts of the COVID-19 pandemic in this low-income country (Funding from CIHR)
- Tanzania acute kidney injury study is utilizing a smartphone application and point of care creatinine meter to train and build capacity among frontline non-physician health providers to recognize, diagnose and manage acute kidney injury in adults and children (Funding from Grand Challenges Canada)

ACTIVE RESEARCH PROJECTS (CONTINUED…)

- Smartphone-enhanced visual assessment of the cervix (SEVIA) program for training nurses to provide high quality cervical cancer screening using visual assessment of the cervix and treatment of cervical precancerous lesions-this project is fully integrated into the Tanzanian National Cervical Cancer Prevention Program
- We are part of a National Cancer Institute (U.S) and Gates funded project to develop a deep learning algorithm (AI) software in conjunction with point of care HPV DNA testing for high-risk HPV genotypes followed taking an image of the cervix to provide decision support to frontline screening providers in very low resource settings globally

RESIDENT PROJECT IDEAS:

- Analysis of data collected in Tanzania of a cross-sectional sample of sugar cane workers exposed to extreme heat stress-examining prevalence of chronic kidney disease and related risk factors (data ready to examine)
- Developing and implementing a protocol for tracking of patient lab results (creatinine, blood sugar and electrolytes) and protocolized diabetes and BP management using a simple smartphone application guided by automated communication algorithms and nurse communication with patients among remote living Indigenous patients in Canada

Kidney Medicine

Independent External Validation and Comparison of Death and Kidney Replacement Therapy Prediction Models in Advanced CKD

Susan J. Thanabalasingam, Eduard A. Iliescu, Patrick A. Norman, Andrew G. Day, Ayub Akbari, Gregory L. Hundemer, and Christine A. White

Rationale & Objective: The Kidney Failure Risk Equation (KFRE) is widely used to predict the risk of kidney replacement therapy (KRT) initiation in chronic kidney disease (CKD) stages G3-G5. The new Grams calculator developed for advanced CKD (stage G4+) predicts KRT initiation, cardiovascular events, and death by uniquely incorporating the competing risk of death. We aimed to validate this tool in a stage G4+ cohort for death and KRT.

Study Design: Retrospective cohort study.

Setting & Participants: 442 patients with CKD stage G4+ (mean ± SD age, 73 ± 12 years; mean ± SD estimated glomerular filtration rate, 20 ± 6.2 mL/min/1.73 m^2) who visited the multidisciplinary CKD clinic at Kingston Health Sciences Center in Ontario, Canada.

Outcomes & Analytical Approach: Discrimination and calibration were examined for the outcome of death using the 2- and 4-year Grams scores. The 2- and 5-year KFRE and 2- and 4-year Grams scores were compared in terms of discrimination and calibration for KRT.

Results: There were 91, 161, and 206 death events and 90, 145, and 159 KRT events in our cohort at 2, 4, and 5 years, respectively. The Grams model demonstrated modest discrimination for death at 4 years (area under the curve [AUC] 0.70; 95% CI, 0.65-0.75) and performed worse at 2 years (AUC, 0.63; 95% CI, 0.57-0.70). It only overpredicted death by approximately 10% across most of the predicted range. Both models had similar discrimination for KRT at 2 years (KFRE AUC, 0.83; 95% CI, 0.78-0.88 and Grams AUC, 0.8; 95% CI, 0.76-0.87), 4 years (Grams AUC, 0.82; 95% CI, 0.77-0.86), and 5 years (KFRE AUC, 0.81; 95% CI, 0.76-0.85). There was excellent calibration for KRT using the 2-year KFRE and Grams values for predicted risk thresholds of ≤15% and using the 5-year KFRE and 4-year Grams values for predicted risk thresholds of ≤20%. At higher risk ranges, KFRE overpredicts and Grams underpredicts the KRT risk.

Limitations: This is a single-center study with a primarily White cohort limited by smaller sample sizes at the higher ranges of the predicted risks, particularly for the Grams calculator.

Conclusions: The Grams model provides moderately accurate death predictions, and consideration should be given to its incorporation into patient education and advanced care planning. Both the Grams and KFRE models remain clinically useful for determining KRT risks in advanced CKD.

Visual Abstract included

Complete author and article information provided before references.

Correspondence to C.A. White (cw38@queensu.ca)

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Chronic kidney disease (CKD) is associated with increased risks of cardiovascular events, mortality, and progressive decline in the glomerular filtration rate (GFR) leading to kidney failure.[1,2] However, outcomes among patients with CKD are quite variable. The rate of progression and other outcomes vary between individuals depending on clinical and demographic factors such as the etiology of CKD, degree of reduction of GFR and proteinuria, comorbid conditions, age, access to health care, ethnicity, and many others.[3] Consequently, interest in integrating risk prediction tools into clinical practice has grown so that patients at low risk may be spared from undue anxiety and costly medical testing, whereas patients at high risk can access timely, appropriate interventions such as nephrology referral, enrollment in multidisciplinary clinic, and kidney replacement therapy (KRT) preparation.[4-6]

Although numerous risk prediction tools have been developed in CKD cohorts worldwide, most have not been adequately validated or widely integrated into clinical practice.[7] The Kidney Failure Risk Equation (KFRE) was developed by Tangri et al[8] in a Canadian population (CKD stages 3-5) and are the most validated KRT prediction models.[8-15] The 4-variable iteration uses age, sex, estimated GFR (eGFR), and urine albumin-creatinine ratio (ACR) to predict the risks of CKD stages G3-G5 progressing to KRT initiation using 2-year and 5-year KFRE scores (KFRE-2 and KFRE-5, respectively).[8] Validation involving 31 multinational cohorts with a mean baseline eGFR of 46 mL/min/1.73 m^2 showed the KFRE to have high discriminatory ability and adequate calibration.[16]

In 2018, Grams et al[9] developed a tool (www.ckdpcrisk.org/lowgfrevents/) specifically for the CKD stage G4+ (eGFR < 30 mL/min/1.73 m^2) population to predict both the probabilities and order of KRT, cardiovascular disease (CVD) events, and death at 2 and 4 years. This tool incorporates 9 clinical and demographic characteristics previously shown to be important outcome predictors in CKD stage G4+.[17] This novel tool, which uniquely considered the competing endpoint of death in its development, has not been extensively externally validated. A recent study of 2 cohorts—the Swedish Renal Registry and the European Quality Study—examined its

How does the Grams model compare with the KFRE model in predicting death and KRT initiation in patients with advanced CKD?

Kidney Medicine

Methods

- Ontario, Canada
- Retrospective study
- n = 442
- CKD stage G4+ mean eGFR 20 ± 6.2 ml/min/1.73m^2
- mean age 73 ± 12 yrs

KFRE - Kidney failure risk equations

Results

	Death	Kidney Replacement Therapy
# of events at 2 years	91	90
4 years	161	145
5 years	206	159
Model Discrimination		
2 year KFRE AUC	-	0.83 (95% CI 0.78 - 0.88)
5 year KFRE AUC		0.81 (95% CI 0.76 - 0.85)
2 year Grams AUC	0.63 (95% CI 0.57 - 0.70)	0.81 (95% CI 0.76 - 0.87)
4 year Grams AUC	0.70 (95% CI 0.65 - 0.75)	0.82 (95% CI 0.77 - 0.86)

Model Calibration for KRT

- Excellent for KFRE-2 & Grams-2 for predicted risk ≤ 15%
- Excellent for KFRE-5 & Grams-4 for predicted risk ≤ 20%
- Poor performance of all risk models at higher risk ranges

Conclusion: The Grams model provides moderately accurate death prediction and consideration should be given to its incorporation into patient education and advanced care planning. Both Grams and KFRE are clinically useful for determining KRT risk in advanced CKD.

Reference: Thanabalasingam SJ, Iliescu EA, Norman PA et al. Independent external validation and comparison of death and kidney replacement therapy prediction models in advanced CKD. *Kidney Medicine, 2022.*

Visual Abstract by Krithika Mohan, MD, DNB @krithicism

American Society of Nephrology

View Submission

CONTROL ID: 3763487

SUBMISSION TYPE: Clinical Case Report

TITLE: Early Pregnancy-Associated Atypical Hemolytic Uremic Syndrome (aHUS)

AUTHORS: Michael Che[1], Sarah M. Moran[2], Richard J. Smith[3], Miriam Galbusera[4], Sara Gastoldi[4], Jocelyn S. Garland[1]

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2. Department of Nephrology, Cork University, Cork, Ireland.
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GROUP/TEAM:

ABSTRACT BODY:

Introduction: aHUS in pregnancy is typically reported to occur in the third trimester. Here we report a case of aHUS presenting in the first trimester of pregnancy.

Case Description: A 30 year old G2P0A1 diabetic biracial woman presented at 9 weeks gestation with new hypertension. By 18 weeks, she developed acute kidney injury and macular edema. Investigations revealed hemoglobin 68 g/L, platelets 120 x 10^9/L, LDH 588 U/L, undetectable haptoglobin and schistocytes. Creatinine increased from 50 to 88 umol/L, and microscopic hematuria and proteinuria >1 g/day were detected. ASA 162 mg, low molecular weight heparin, and anti-hypertensives were prescribed.

Pre-eclampsia (PET) was ruled out as her symptoms began within the first trimester, and normal uterine artery doppler results were obtained. Placental growth factor levels at 24 and 28 weeks were >100 pg/mL. HELLP syndrome was excluded given the timing in pregnancy (<20 weeks) and normal liver transaminases. TTP was excluded by normal ADAMTS13. Complement Factor H autoantibody was negative.

Complement studies revealed elevated plasma C5b-9 level of 1.05 (normal <0.3 mg/L). aHUS was diagnosed and eculizumab (ECU) was prescribed. Ex-vivo serum C5b-9 deposition on human microvascular endothelial cells (Noris, *Blood*, 2014) was abnormal pre-treatment with ECU (activated 223%, normal <150%), and normalized with ECU therapy (activated 123%, normal <150%). Genetic testing revealed a Complement Factor I mutation, NM_000204.3:c.550G/A, p. Val184Met reported as pathogenic, confirming primary aHUS.

Due to worsening renal function, she delivered a healthy baby at 30 weeks gestation by Caesarean section. A renal biopsy performed 3 weeks postpartum demonstrated features of TMA, mainly chronic (i.e. treated) and advanced diabetic nephropathy. Six months postpartum, she required dialysis. aHUS is in clincial remission on ECU, and she awaits kidney transplantation.

Discussion: aHUS is classically described to occur late in pregnancy or postpartum. Here, this patient presented uniquely during the first trimester with complement function testing aiding the diagnosis. Thus, TMA in pregnancy is not always PET or HELLP and aHUS should be considered as the diagnosis particularly for presentations occurring prior to 20 weeks gestation. Episodes of severe PET/ HELLP should trigger TMA

American Society of Nephrology

View Submission

CONTROL ID: 3766450

SUBMISSION TYPE: Clinical Case Report

TITLE: Severe Postpartum HELLP Syndrome - Is this aHUS?

AUTHORS: Michael Che[1], Sarah M. Moran[2], Richard J. Smith[3], Sara Gastoldi[4], Jocelyn S. Garland[1]

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4. Istituto di Ricerche Farmacologiche Mario Negri-IRCCS; Clinical Research Center for Rare Diseases Aldo e Cele Daccò Ranica, Bergamo, Italy.

GROUP/TEAM:

ABSTRACT BODY:

Introduction: Complement dysregulation is implicated in the pathogenesis of atypical hemolytic uremic syndrome (aHUS) and there is growing evidence to support its role in HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome. Here we present a case of post-partum thrombotic microangiopathy (TMA) in the setting of HELLP syndrome.

Case Description: A 22 year old G1P0 Caucasian woman presents at 37 weeks gestation with abdominal pain and severe hypertension. Labs demonstrated hemoglobin 95, platelets 30, LDH 2597, schistocytes, severe transaminitis (AST 1845, ALT 830), and proteinuric acute kidney injury. She was diagnosed with HELLP syndrome and treated with anti-hypertensives and emergency Caesarean section. Unfortunately, the infant did not survive; there was no placental abruption.

Platelets recovered by day 5 postpartum, LDH by day 7. However, renal function worsened and by day 6 postpartum, she required hemodialysis when creatinine peaked at 812. A renal biopsy revealed acute and chronic TMA. She did not have cortical necrosis. Further workup revealed normal C3, C4 and ADAMTS13 levels. Dialysis was stopped after two weeks. By 6 months, her renal function and proteinuria returned to normal.

Complement function testing revealed negative complement factor H autoantibody, but elevated plasma C5b-9 level (0.42 mg/L, normal <0.3). Ex-vivo serum C5b-9 deposition on human microvascular endothelial cells was assessed both on resting (182%, normal <150%) and on ADP-activated endothelial cells (273%, normal <150%). This test was repeated 6 months postpartum when renal function had normalized, and results were persistently abnormal both on resting (215%, normal <150%) and on ADP-activated endothelial cells (282%, normal <150%). aHUS genetic testing was negative.

Discussion: The severity of HELLP syndrome associated organ dysfunction prompted the assessment for aHUS. Identifiable aHUS genetic mutations only occur in 50% of aHUS patients; however, the persistence of increased C5b-9 deposition mimics the findings of patients who have aHUS (Noris, Blood, 2014). Complement function testing is not routinely assessed for postpartum HELLP, and these unique results suggest the patient may be at risk for recurrent TMA/aHUS, particularly if another pregnancy is being considered. Future research should explore which pregnancy associated TMA patients may benefit from anti-complement therapy.

Palliative Medicine

Dr. Danielle Kain
Division Co-Chair

Dr. Jean Mathew
Research Lead

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

Summary

- *Automative surveillance of unmet palliative care needs of patients*
- *Development of tool for standardize care plan in transition from hospital to home*
- *Identification tools of palliative needs for primary care and specialized care*
- *Phone app and remote-care accessibility tools for improving at home care*
- *Cannabis and psilocybin therapy for symptom and anxiety management in palliative and cancer patients*
- *Identifying palliative care needs in heart failure patients*
- *Screening for aberrant opioid use behaviour in care clinics*
- *Use of opioids for improved outcomes in pulmonary rehabilitation*
- *Identification of disparities in timely access to palliative care among indigenous, ethnic and immigrants communities*
- *Clinical trials for the use of transcranical magnetic simulation for relieving psychological distress in advance illness*
- *Screening tool for identifying palliative care needs in India*
- *Educational evaluation of teaching point-of-care ultrasound to improve health worker skillset*
- *Implementation of Compassionate Community Innovation in Kingston study*

Principal Investigator	Project Title	Status (Planning/Implementation/Evaluation)
Dr. J. Bagg	• Use of an automated prospective clinical surveillance tool (mHOMR) to drive screening for unmet palliative needs among patients in the final year of life. KHSC Palliative Care QIP (with Dr. Herx and Dr. Kain)	
	Looking for resident involvement: No **Role:** **Funding:**	
	• Development of a standardized palliative care plan tool for patients with palliative care needs at transition from hospital to home. FLA OHT Palliative Care QIP (with Dr. Herx and Dr. Polle)	
	Looking for resident involvement: No **Role:** **Funding:**	
	• Implementation of a standardized tool for early identification of patients with palliative care needs in primary care and integration of specialist palliative care consultation - pilot involving two family practice settings. FLA OHT Palliative Care QIP (with Dr. Herx and Dr. Selbie)	
	Looking for resident involvement: No **Role:** **Funding:**	
	• "Text a Palliative Specialist" Pilot project—Sub-project within the embedded clinic project as part of the FLA-OHT Palliative Care QIP (with Dr. Goldie and Dr. Selbie)	
Dr. C. Goldie	• CAFCARS - Cannabis for symptom management (RCT)	Recruiting Patients
	Looking for resident involvement: No **Role:** Site PI	

	Funding: BC Cancer Agency Grant – Held by Dr. Hawley	
	• Psilocybin for death anxiety phase 1/2 pilot trial	Pending Health Canada NOL
	Looking for resident involvement: No **Role:** Site PI **Funding:** Bruyere / U Ottawa Grants – Held by Dr. Downar	
	• Systematic review: scoping review for clinical psilocybin-assisted therapy	Manuscript editing, pending submission to journal
	Looking for resident involvement: No **Role:** Co-Supervisor of PhD student (Ron Shore) first author **Funding:** N/A	
	• Systematic review: scoping review on early palliative care – definitions and implementation	Manuscript editing, pending submission to journal
	Looking for resident involvement: No **Role:** PhD Committee for student (Colleen Kircher) first author **Funding:** N/A	
Dr. M. Iqbal	• Impact of a Remote Care Monitoring (RCM) on symptom burden and healthcare resource utilization for patients supported in an outpatient oncology palliative care clinic & community consult team. Ontario Health East funded Pilot Study	
	Looking for resident involvement: No **Role:** Co-Lead **Funding:** MOH	
	• Identifying Palliative care needs in Heart failure patients (retrospective chart review)	
	Looking for resident involvement: No **Role:** Lead **Funding:** n/a	

	• Dexmedetomidine in agitated delirium at the end of life (RCT)	
	Looking for resident involvement: No **Role:** Co-Lead **Funding:** CIHR	
Dr. D. Kain	• Implementing systematic screening for risk for aberrant opioid use behaviors in the Palliative Care Clinic - a quality improvement initiative	TRAQ and REB approval completed. ORT screening tool approved by forms committee of CCSEO. Implementation planning ongoing.
	Looking for resident involvement: Possibly **Role:** Co-Investigator **Funding:** QUICC Grant	
	• CAFCARS: a Randomized, Double-Blind, Placebo-Controlled, Multiple Crossover N-of-1 Study Design on the Use of Medicinal Cannabis Oil-Based Extracts for Symptom Management in Cancer Patients	Recruiting patients in all study arms
	Looking for resident involvement: No **Role:** Co-Investigator **Funding:** BC Cancer Foundation	
	• Opioids for improved outcomes in pulmonary rehabilitation - A phase III, multi-site, randomized, placebo-controlled, and double-blinded, parallel-arm study of slow-release morphine.	Awaiting funding decision
	Looking for resident involvement: Possibly **Role:** Collaborator **Funding:** CIHR – funding decision pending	
	• Investigating disparities in access to timely palliative care among ethnic and immigrant minorities with advanced cancer: A population-based cohort study utilizing patient-centered outcome measures	
	Looking for resident involvement: Yes, once funding comes through **Role:** Co-Investigator **Funding:** ICES Project for TIME members (Data Science Day 2023 Funding Opportunity)	

	• High dose psilocybin-assisted therapy (PAT) for demoralization syndrome (DS) in people living with advanced cancer (PAC): A multi-site, randomized, controlled, double-blind, mixed-methods trial	Finalizing grant application
	Looking for resident involvement: No **Role:** Co-Investigator **Funding:** CIHR	
	• Transcranial magnetic simulation for psychological distress in patients with advanced illness: A phase 3 Vanguard double-blind sham-controlled parallel-arm clinical trial	Funding application due Aug 31
	Looking for resident involvement: No **Role: Site** PI **Funding:** Canadian Cancer Society (CCS) Challenge Grant 2024 + Accelerating Clinical Trials (ACT) – Evaluate Canadian Biotechnologies with RCTs)	
Dr. J. Mathews	• Queens Global Oncology: Implementing a screening tool for palliative care needs assessment in Kerala, India	Screening tool developed, project proposal drafted, awaiting REB approval from Pallium India for pilot implementation.
	Looking for resident involvement: No **Role:** **Funding:** No	
	• Training the trainer: evaluation of a workshop to improve confidence, knowledge, and skill among palliative medicine staff physicians with performing and teaching point-of-care ultrasound (POCUS).	Workshop and surveys completed. Data extraction completed. Manuscript being developed. Erin McCarthy's scholarly project
	Looking for resident involvement: No **Role:** **Funding:** SEAMO education fund	
	• Implementing systematic screening for risk for aberrant opioid use behaviors in the Palliative Care Clinic - a quality improvement initiative	TRAQ and REB approval completed. ORT screening tool approved by forms committee of CCSEO. Implementation planning ongoing.
	Looking for resident involvement: No **Role:** **Funding:** QUICC grant	

Dr. J. Mathews **(Updated March 2023)**	• 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 (CCSEO)- a quality improvement initiative	6-month implementation completed; manuscript being developed.
	Looking for resident involvement: No **Role:** **Funding:** No	
	• Use of the Palliative Prognostic Index (PPI) to improve clinical prediction of survival (CPS) for patients with cancer admitted to a Palliative Care Unit- a quality improvement initiative	CPSO QI project; Implementation started.
	Looking for resident involvement: No **Role:** **Funding:** No	
	• Implementation of a Compassionate Community innovation in Kingston: The Kingston Cares (KINCARES) Study	REB completed. Planned to start in August 2023
	Looking for resident involvement: No **Role:** **Funding:** Innovation Fund grant	
Dr. E. Polle	• Development of a standardized palliative care plan tool for patients with palliative care needs at transition from hospital to home. FLA OHT Palliative Care QIP (with Dr. Bagg)	
	Looking for resident involvement: No **Role:** **Funding:**	
Dr. A. Selbie	• Psychedelics Research Collaborative; there have been discussions about running a trial at Queens to look at the effect of Psychedelics on the well-being of patients who have cancer, particular in areas of anxiety and existential distress	
	Looking for resident involvement: **Role:**	

	Funding:	
	• Implementation of a standardized tool for early identification of patients with palliative care needs in primary care and integration of specialist palliative care consultation - pilot involving two family practice settings (FLA OHT Palliative Care Partnership) --Embedded clinics beginning April 2023	
	Looking for resident involvement: **Role:** **Funding:**	
	• "Text a Palliative Specialist" Pilot project—Sub-project within the embedded clinic project as part of the FLA OHT Palliative Care Partnership. Measure the number of contacts our team as a whole receives from these two Primary care Practices for several months (shared via reporting link). Then introduce to the Primary Care Practices the option of texting the Community Outreach Team phone. Track number of times contacted through this to see if any increase.	
	Looking for resident involvement: **Role:** **Funding:**	
	• FLA OHT Palliative Care Partnership for improving palliative care for homeless and vulnerably housed persons to improve care experiences, access to care and health outcomes (FLA OHT PCP subgroup project)	
	Looking for resident involvement: **Role:** **Funding:** Awarded a Health care Excellence Grant for collaboration between the Kingston Community Health Centres and Queens Palliative Care to "Improve equitable access to palliative care Communities"	
Dr. A. Sinnarajah (Updated March 2023)	• FLA OHT Palliative Care Partnership to Identify Indigenous focused palliative care strategies for care/care planning to improve awareness of and equitable access to culturally safe,	

	and Indigenous focused Palliative Care services for Indigenous populations in the FLA OHT region.	
	Looking for resident involvement: **Role:** **Funding:**	
Dr. A. Sinnarajah	**Looking for resident involvement:** Possibility of crafting a unique research question that can be answered with assembled databases (looking at Palliative care involvement; health care resource use). See examples here: Palliative home care and emergency department visits in the last 30 and 90 days of life: a retrospective cohort study of patients with cancer | BMJ Supportive & Palliative Care Hospital-based acute care in the last 30 days of life among patients with chronic disease that received early, late or no specialist palliative care: a retrospective cohort study of eight chronic disease groups | BMJ Open Palliative care as a predictor of healthcare resource use at end-of-life in adult Albertan lung cancer decedents between 2008-2015: A secondary data analysis. | Journal of Clinical Oncology (ascopubs.org) **Role:** Work with PI to learn and analyse large database. **Funding:** No	
	• EMR trigger for screening patients living with advanced cancer (AB, ON)	
	Looking for resident involvement: Yes **Role:** Drafting protocol and then leading qualitative interviews of oncology clinicians of how EMR triggers impacted their clinical care **Funding:** Yes (Canadian Cancer Society, Health Canada)	
	• Increasing Access to Palliative Care for Advanced Cancer patients from Racialized Communities of African and Latin American Descent	
	Looking for resident involvement: No **Role:** **Funding:** Yes (Lakeridge Health); No (Queens)	
Dr. A. Voeuk (Updated March 2023)	• Increasing EOL home visits in Ontario	Ongoing
	Looking for resident involvement: Potentially Yes **Role:** Can review formulating specific research question with available data, to look at secondary outcomes (work with Ottawa team who are the PIs) **Funding: No**	
	• National Telehealth Palliative Care (ON, AB, BC, NL)	Assembling data still

	Looking for resident involvement: Yes **Role:** Work with PI to create a research question that can be answered with this large database using quantitative analysis methods **Funding:** No	
	• End of life prescribing in LTC (patient and provider characteristics)	Data assembly still ongoing
	Looking for resident involvement: Yes **Role:** Help with analysis and then lead manuscript write-up. Learn about quantitative analysis methods and practice as well using statistical software **Funding:** No	
	• Indigenous Cancer Patient Multidisciplinary Rounds	Ongoing
	Looking for resident involvement: No **Role:** To reflect and capture the process of coming together as team and learning about these rounds **Funding:** No	
	• Implementing Shared Care Letters to strengthen coordination for patients living with advanced cancer	See Dr Matthews entry for this
	Looking for resident involvement: n/a (See Dr Matthews entry) **Role:** n/a (See Dr Matthews entry) **Funding:** n/a (See Dr Matthews entry)	

Early Identification of Patients who need a Palliative Approach to Care: The Road to Improving Quality of Life

Jessy Donelle[1], Dana MacPhail[1], Lori Van Manen[1], Dr. Leonie Herx[1,2], Dr. Danielle Kain[1,2], Melissa Touw[1], Julie Lapenskie[3], Pete Wegier[4], Dr. James Downar[3,5]

1. Kingston Health Sciences Centre 2. Queen's University - Division of Palliative Medicine 3. Bruyère Research Institute 4. Humber River Hospital 5. University of Ottawa – Division of Palliative Care

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

Background

A palliative approach to care helps people with life-limiting illness and their families manage symptoms, prepare for end-of-life choices, understand the dying process, and cope with grief.

Offering patients a palliative approach to care earlier in their journey – and at critical junctures along the way (i.e., during a hospitalization) – gives the patient and their care network the ability to clarify and update their goals of care (GOC). In turn, clearly established GOC enable care providers to ensure that the care provided in hospital is consistent with patients' wishes, ultimately improving the timeliness and quality of care, and most importantly, the patient experience.

Despite these known benefits, most Canadians only receive palliative care in the final weeks of life, as it is difficult for clinicians to reliably identify patients who may benefit from a palliative approach to care. This difficulty has been confounded by the ongoing COVID-19 pandemic.

AIM STATEMENT:
By March 31, 2022, 80% of patients admitted to an internal medicine unit with an elevated risk of death over the next year will experience improved quality of life as measured by better symptom management and improved patient and caregiver experience.

Baseline Data

The mHOMR algorithm was applied retrospectively to admissions at KHSC between June 2019 – February 2020 to generate risk scores. A chart review of 140 admissions with high-risk scores (i.e., an elevated risk of death within the next year) was conducted to gather baseline data on inpatient palliative care interventions (see Figure 2).

For these patients, 49% had organ failure, 27% had frailty, 19% had a terminal illness, and 5% had an other illness identified as their primary life-limiting illness.

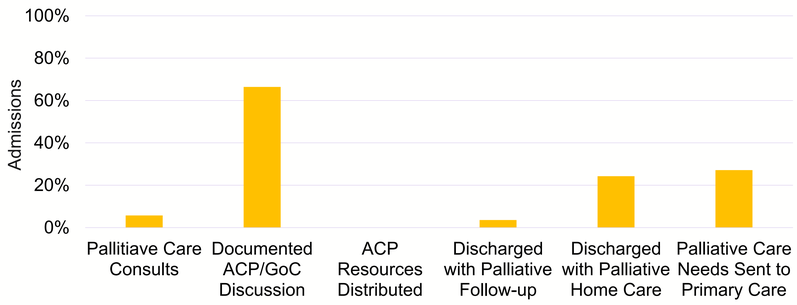


Figure 2: (above) Inpatient palliative care intervention baseline data for the 140 admissions flagged by mHOMR with an elevated risk of death in the next 12 months

Current State

As a result of the COVID-19 pandemic, which mandated restriction of in-person gatherings, there has been a significant delay with critical training on palliative care essentials, including Serious Illness Conversations and LEAP training which both require face-to-face learning. This training needs to be completed to ensure care providers (physicians, nurses, and allied health professionals as required) can confidently carry out the care protocol.

As part of a collaborative research study[1] Kingston Health Sciences Centre (KHSC) implemented the research component of the project in March 2021 which includes an automatic notification of patients who exceed the modified Hospital-patient One-year Mortality Risk[2] (mHOMR) threshold (25%) and the subsequent administration of the ESAS-R and Advanced Care Planning (ACP) Readiness Assessment (see Figure 1).

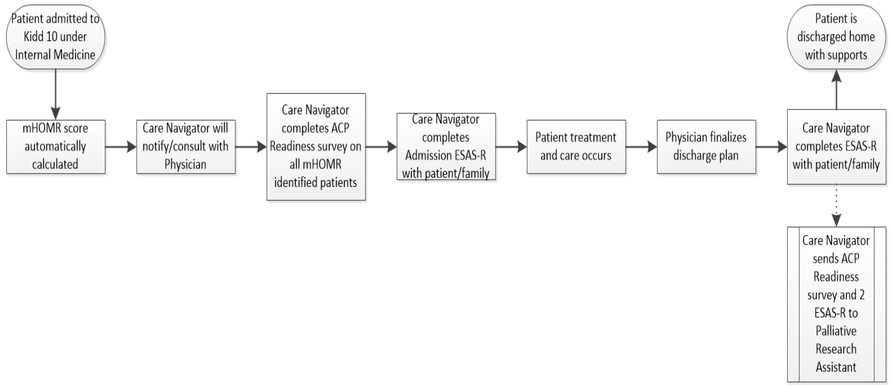
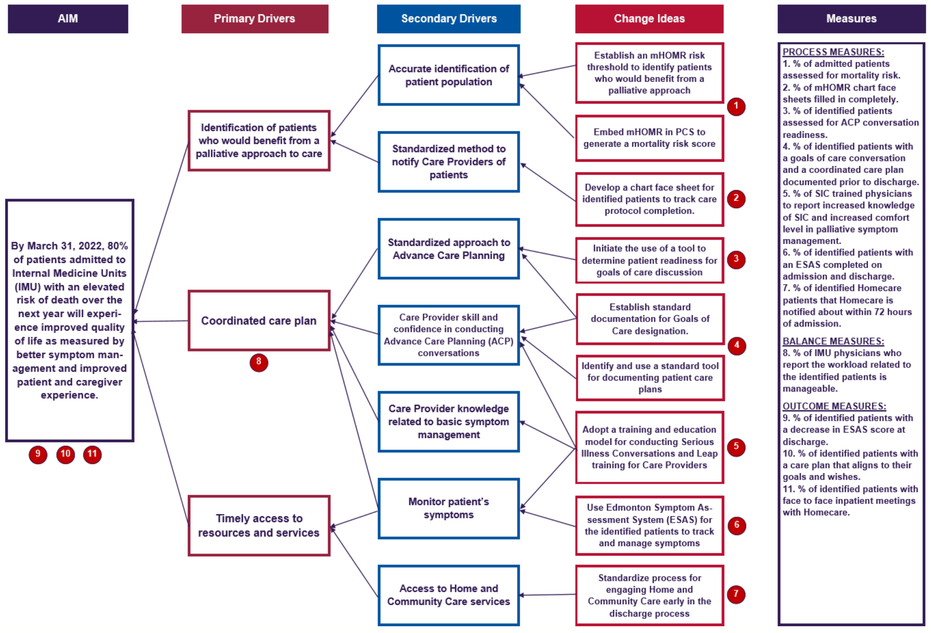


Figure 1: (above) Current workflow for mHOMR identified patients admitted to Kidd 10 at KHSC.

Change Ideas & Measures



Palliative care is person- and family-centred care:

"Palliative care is respectful of, and responsive to, the needs, preferences and values of the person receiving care, their family, and other caregivers. It is facilitated by good communication. Individuals and families have personal preferences and varying levels of comfort in discussing, and planning for the dying process and death itself."

The Framework on Palliative Care Canada

Fiscal 2021-2022 Goal

Internal Medicine clinicians currently have access to automated, real-time information about patients who, at the time of admission, have an elevated risk of dying within the next twelve months, and therefore might benefit from a palliative approach to care.

By March 31, 2022, care providers (such as physicians, nurses, and allied health professionals) will have received training about palliative care essentials, including how to have a conversation about serious illness, and will confidently carry out the care protocol for 80% of admitted patients on select internal medicine units. Standardized documentation will be used to record the conversations and subsequent care plans.

Simultaneously, KHSC and Homecare will communicate about any patients who have a positive mHOMR score (i.e., >=25%) through a patient report developed in the Shared Health Integrated Information Portal (SHIIP). The report will be populated by KHSC to identify those who are proceeding through the Early Identification of Palliative Care protocol and are already receiving homecare services, or require new or enhanced homecare services.

References

1. Use of an Automated Prospective Clinical Surveillance Tool to Drive Screening for Unmet Palliative Needs Among Patients in the Final Year of Life. Canadian Frailty Network Grant, 2019-2021, $224,000. Principle investigators: James Downar I Pete Wegier (co-PIs).

2. Wegier P, Koo E, Ansari S, et al. mHOMR: a feasibility study of an automated system for identifying inpatients having an elevated risk of 1-year mortality. BMJ Quality & Safety Published Online First: 28 June 2019. doi: 10.1136/bmjqs-2018-009285

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

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

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

Background and Rationale

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

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

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

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

Aims and Objectives

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

Letter

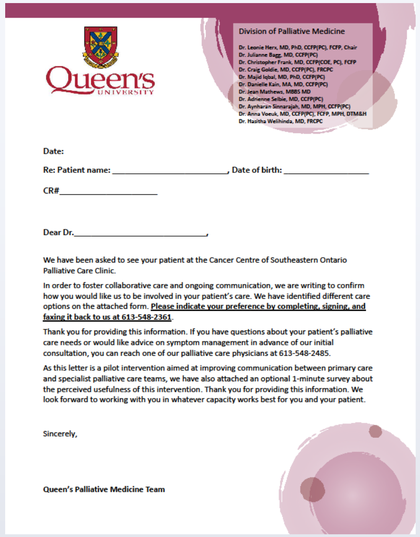
Pages 1-4 comprise the standardized letter sent out to local family physicians.

Page 1 is the introductory page introducing the intervention

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

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

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



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(CCE, PC), FCFP
Dr. Craig Gedye, 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 Sellke, MD, CCFP(PC)
Dr. Aynharan Sinnarajah, MD, MPH, CCFP(PC)
Dr. Anna Vawuk, MD, CCFP(PC), FCFP, MPH, DTM&H
Dr. Hasitha Welliniada, 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**

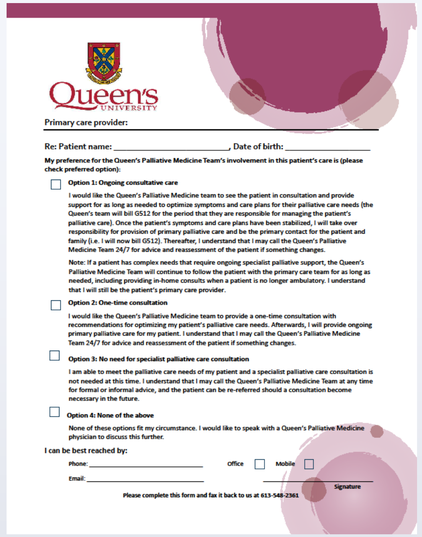
Thank you for providing this information. If you have questions about your patient's palliative care needs or would like advice on symptom management in advance of our initial consultation, you can reach one of our palliative care physicians at 613-548-2485.

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



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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.

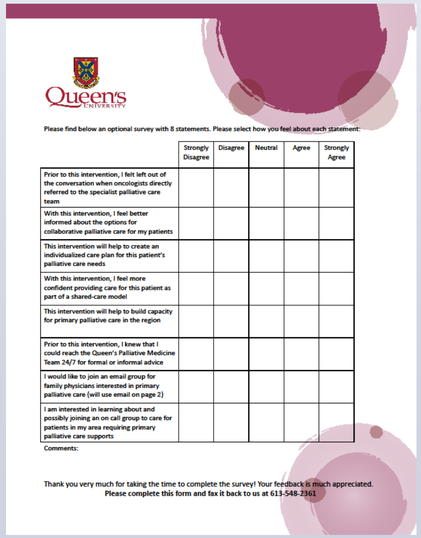
I can be best reached by:

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



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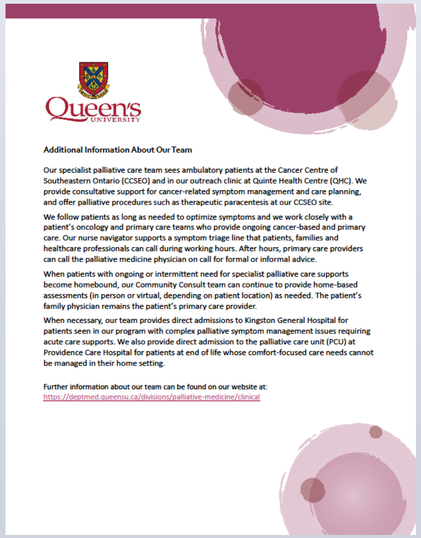
Please find below an optional survey with 8 statements. Please select how you feel about each statement:

	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



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Additional Information About Our Team

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

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

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

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

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

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

Methods

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

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

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

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

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Implementing systematic screening for risk of aberrant opioid use behaviours in the palliative care clinic- a quality improvement initiative

Jean Mathews, Leonie Herx, Aynharan Sinnarajah

OPIOID RISK TOOL

This tool should be administered to patients upon an initial visit prior to beginning opioid therapy for pain management.

Mark each box that applies	Assigned Female At Birth	Assigned Male At Birth
Family history of substance abuse		
Alcohol	1	3
Illegal drugs	2	3
Prescription drugs	4	4
Personal history of substance abuse		
Alcohol	3	3
Illegal drugs	4	4
Prescription drugs	5	5
Age between 16—45 years	1	1
History of preadolescent sexual abuse	3	0
Psychological disease		
ADD, Obsessive Compulsive Disorder (OCD), Bipolar, Schizophrenia	2	2
Depression	1	1
Scoring totals	____	____

Name	Designation	Signature	Date (yyyy/mm/dd)	Time (hhmm)

0 - 3 = low risk 4 - 7 = moderate risk 8 or higher = high risk

Reference:
Lynn R. Webster, Rebecca M. Webster, Predicting Aberrant Behaviors in Opioid-Treated Patients: Preliminary Validation of the Opioid Risk Tool, Pain Medicine, Volume 6, Issue 6, November 2005, Pages 432–442, https://doi.org/10.1111/j.1526-4637.2005.00072.x.

BACKGROUND & RATIONALE

Canada is in the midst of an opioid crisis, with increasing opioid overdoses and opioid-related deaths. Canada has the second-highest rate per capita of opioid prescribing in the world, and rising numbers of medical opioid prescriptions is one of the contributors to the current crisis. National strategies to address the crisis have primarily focused on chronic non-cancer patient populations. There is a pervasive belief that patients with cancer will not be impacted by this crisis, though recent evidence suggests that they are also at risk of aberrant opioid use behaviours (defined as use of prescription opioids in a matter not intended by the prescriber)

One in five cancer patients may be at risk of opioid use disorder, defined as problematic patterns of opioid use (including prolonged use, higher daily doses, and aberrant use) resulting in clinically significant impairment or distress.

AIMS & OBJECTIVES

The primary objective of this pilot study is to implement the Opioid Risk Tool (ORT) for all newly referred patients to the Palliative Oncology Clinic at the Cancer Centre of Southeastern Ontario (CCSEO) and to measure adherence (percentage of patients who completed the ORT screening). Secondary objectives are to report on the findings from a 6-month implementation period including determining the frequency of screen-positive and clinico-demographic factors predicting a risk for aberrant opioid use behaviours. Screen-positive patients will receive a bundle of interventions to improve opioid safety, including lower quantity of opioids prescribed, more frequent follow-up, verbal/written opioid contracts, involvement of addictions medicine, and urine drug screening. This bundle of interventions will be more fully tested in subsequent phases of this study.

METHODS

Phase 1 methodology: In this quality improvement project, all consecutive patients who attend the Palliative Oncology Clinic at the CCSEO as new consults between July 1, 2022 and January 31, 2023 will be included. Patients will be eligible if they are aged ≥18 years, have a current diagnosis of cancer, and have been or are planned to receive treatment with opioids for cancer-related pain. Eligible patients will receive the ORT for self-administration, along with other routinely self-administered screening questionnaires such as the Edmonton Symptom Assessment System. For patients who can't self-administer these questionnaires, the palliative care nurse will administer them to the patient. Clinico-demographic data such as age, sex, cancer diagnosis, cancer treatment intent, and pain intensity, will be collected.

ORT scores will be tallied and a score ≥8 will be considered as screen-positive for high risk for aberrant opioid use behaviours. The palliative care physician will document the screen-positive status in the patient chart and will consider the appropriateness of a previously defined bundle of clinical interventions recommended for screen positive patients.

AREAS FOR FUTURE RESEARCH

Phase 2: Do oncology palliative care clinics in Canada screen for risk of aberrant opioid use behaviors? A national survey.

Phase 3: Predicting the risk for aberrant opioid use behaviors in patients with advanced cancer who are referred to an oncology palliative care clinic- a multi-site validation study of the ORT.

Phase 4: Determining the impact of systematic screening for opioid misuse and an optimized opioid prescription strategy for screen-positive patients with advanced cancer - a randomized controlled feasibility trial.

AFFILIATIONS

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

Respirology & Sleep Mecidine

Dr. Susan Moffatt
Division Chair

Dr. Nicolle Domnik
Research Lead

Summary

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

Introduction Emerging work has explored the impact of sleep quality on physical activity (PA) and exercise capacity (EC) in younger populations; however, the impact of sleep on PA and EC in older adults or those with chronic respiratory disease remains unexplored. This is particularly relevant given the associations between poor sleep quality and diminished spirometry and quality of life in Chronic Obstructive Pulmonary Disease (COPD). We propose exploring the associations between sleep quality, PA and EC in a community-based cohort of older adults with and without COPD. We hypothesize that poor sleep quality will be associated with decreased indices of physical activity and exercise capacity in individuals with COPD. **Methods** We will perform a cross-sectional analysis of data from the Canadian Cohort of Obstructive Lung Disease (CanCOLD), a prospective multicenter longitudinal cohort study, which includes patients with COPD stages GOLD 1-4 and patients without identified obstructive lung disease. Multivariable linear regression analysis will be used to explore the associations between sleep quality, PA and EC while controlling for age, sex, and BMI. **Results** Sleep quality will be quantified by Pittsburg Sleep Quality Index (PSQI), self-reported and functional PA via CHAMPS questionnaire and 6-minute walk distance, respectively, and EC via physiologic endpoints (VO_{2peak} exercise duration, work rate, Borg dyspnea) from incremental cardiopulmonary exercise testing. Primary outcomes will include the association between sleep quality and PA (CHAMPS) and between sleep quality and EC (VO_{2peak}). Secondary analysis will explore the impact of relevant comorbidities (e.g., sleep apnea) on the primary associations. **Conclusions** Reduced PA and EC are associated with worse outcomes. Our investigation of the associations of sleep quality with PA and EC will help set a foundation for further study on the mechanisms underlying these relationships as well as interventions to improve sleep quality in vulnerable populations.

Questions? Contact: 15kem7@queensu.ca or 16acm12@queensu.ca

Associations between Sleep Quality, Exercise Capacity and Physical Activity in the CanCOLD Cohort

Alexandra McCartney[1] Kristin E MacLeod[2], Jennifer D'Cruz[3], J Alberto Neder[2,3], Nicolle J Domnik[2,3] CanCOLD Collaborative Research Group

1. Faculty of Medicine, University of Ottawa 2. Department of Biomedical and Molecular Sciences, Queen's University; 3. Department of Medicine, Queen's University;

Background

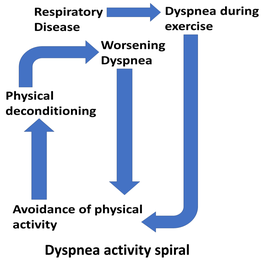
Physical activity (PA) improves health, but barriers to regular PA exist. Low PA can also negatively impact exercise capacity (EC).

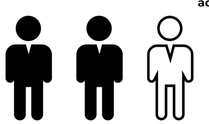
Studies suggest that poor sleep (duration, quality) may impair PA and EC in healthy young adults (1,2) but the impact of sleep on PA and EC in older adults or those with chronic disease is unexplored.

This is a major knowledge gap for two reasons:

1. Physical activity is important in the context of healthy ageing
2. Physical activity may be of especial importance in conditions like Chronic Obstructive Pulmonary disease (COPD), where maintained exercise tolerance has been shown to prevent decompensation (3).

Recent studies show associations between poor sleep quality and worse physiologic (e.g., spirometry, exacerbations) and subjective (e.g., quality of life) outcomes in COPD (4); however, whether poor sleep itself is associated with decreased physical activity or exercise capacity in COPD or older adults is unknown.





2/3 COPD patients remain undiagnosed

Objectives and Hypothesis

- To determine the association between sleep quality and:
  - self reported Physical Activity (**PA**)
  - physiologic Exercise Capacity (**EC**; as measured by cardiopulmonary exercise test (CPET))

  in a sample of the general Canadian population.

- **Hypothesis:** Sleep quality (Pittsburg Sleep Quality Index) will be inversely correlated with self reported physical activity (Community Healthy Activity Model Program for Seniors; CHAMPS) and inversely correlated with perceived exertion and physiologic exercise capacity as measured by selected CPET outcome variables

Methods and Outcomes

The Canadian Cohort of Obstructive Lung Disease (**CanCOLD**) is a longitudinal cohort study which aims to more accurately represent the COPD landscape in Canada by recruiting from the general population as opposed to targeted clinical samples.

Population

The cohort is divided into two **groups** and four ***subgroups***:

- **COPD patients** : ***mild*** disease (*GOLD 1, FEV1/FVC<0.7, FEV1 ≥ 80%*) OR ***moderate to severe*** disease (*GOLD ≥ 2, FEV1/FVC<0.7, FEV1< 80%*) previously recruited from COLD prevalence study
- **Age and sex matched Control participants** : No evidence of COPD on spirometry and have never smoked (***healthy***) OR No evidence of COPD on spirometry and have smoked (***at-risk***)

Group	n	Sex (%male)	Age	PSQI (Global index)
Healthy (never smokers)	280	48.6	66.7±9.5	5.4±3.3
At-risk (ever smokers)	396	58.8	65.5±9.5	5.5±3.5
Mild COPD (GOLD 1)	318	70.4	68.6±9.9	5.3±3.4
Moderate-Severe COPD (GOLD 2+)	250	54	66.6±10.2	5.2±3.3

Preliminary demographics table with data from CanCOLD Visit 1

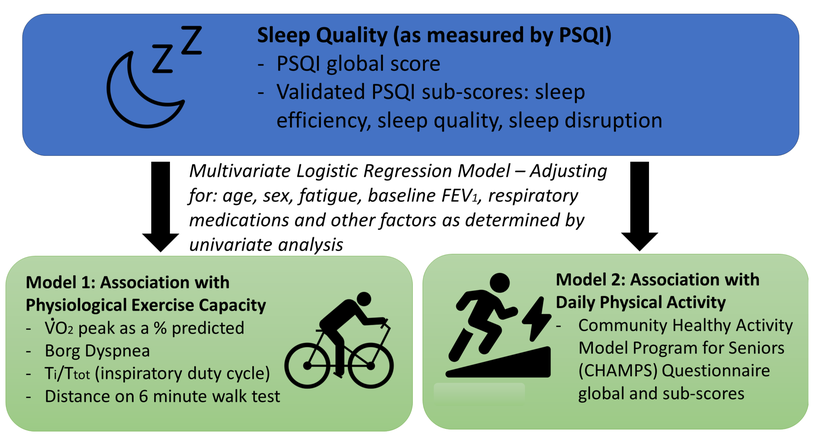
Study Visits Analyzed

- **Visit 1 (2009-2015) -** 1561 participants were recruited at 9 Canadian sites - data collected included: demographics, pulmonary function testing (PFT); cardiopulmonary exercise test (CPET), CT, and blood
- **Visit 2 (2011-2015) –** 6 minute walk distance (6MWD). Additional follow-up visits (2011-present) not used in analysis.

Analysis:

- Associations between sleep quality, CPET, 6MWD and demographic data will be measured using Pearson's correlation and Student's t test or nonparametric Spearman's correlation and Mann-Whitney U test
- Initial associations will determine final variables and covariates in multivariable logistic regression model to determine adjusted associations of sleep quality with exercise capacity and physical activity

Analysis Model and Defined Variables

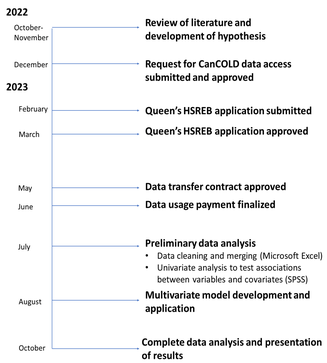


Strengths and Impact

Large, Representative Population
CanCOLD is a uniquely large Canadian COPD cohort which uses data sampled from the general population and therefore includes underrepresented populations missing from other data sources (e.g., those undiagnosed with COPD).

Physiologic Data
CanCOLD combines CPET data and demographics for approximately 1200 COPD patients and controls. This allows for large-scale analysis into mechanisms of disease characteristics and symptoms.

Progress



- **Current phase**: preliminary data cleaning and analysis
- **Next steps**: Building of multivariate model, determination of appropriate covariates

Key References

1. Mougin et al., *Eur J Appl Physiol Occup Physiol* (1991) 2. Rayward et al., *Med Sci Sports Exerc* (2018) 3. Spruit et al., *Breathe* (2016) 4. Shorofsky et al., *Chest* (2019)

Support and Acknowledgements

Supported by a DBMS Research Initiation Grant, Queen's University.

With thanks to: CanCOLD The CanCOLD Collaborative Research Group

Queen's University · Kingston Health Sciences Centre · Centre des sciences de la santé de Kingston · KGH · Integrative Cardiopulmonary Physiology Lab

Epidemiology and healthcare impact of IPF in Ontario from 2013 - 2017

S. Tang[1], O. Moran-Mendoza[1,2], S. Khan[3,4], A. Johnson[4]

[1]Department of Medicine, Queen's University (Kingston, Canada); [2]Division of Respiratory and Sleep Medicine, Queen's University; [3]Health Services and Policy Research Institute, Queen's University; [4]Institute for Clinical Evaluative Sciences, Queen's University

Queen's University

Kingston Health Sciences Centre

Centre des sciences de la santé de Kingston

Background:

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive disease associated with a high burden of illness[1,2]. There is a paucity of information about the incidence, comorbidities and healthcare costs associated with patients with IPF[2].

Aims:

To describe in Ontario, Canada:

1) The incidence and epidemiology of IPF.

2) The most common comorbidities associated with IPF.

3) The healthcare expenditure of patients with IPF.

Methods:

- Data were accessed from the Institute for Clinical Evaluative Sciences (ICES) in Ontario.
- We identified residents aged > 18 years with an IPF diagnosis between January 2013 to December 2017 based on the ICD-10-CA code J84.1 (idiopathic pulmonary fibrosis).
- Incident cases were identified as those with IPF without a prior IPF code 2 years before.
- Common comorbidities were identified using ICD-10-CA codes recorded for in and outpatients during the study period.
- Costs are reported in CAD from the healthcare perspective, adjusted to 2018.

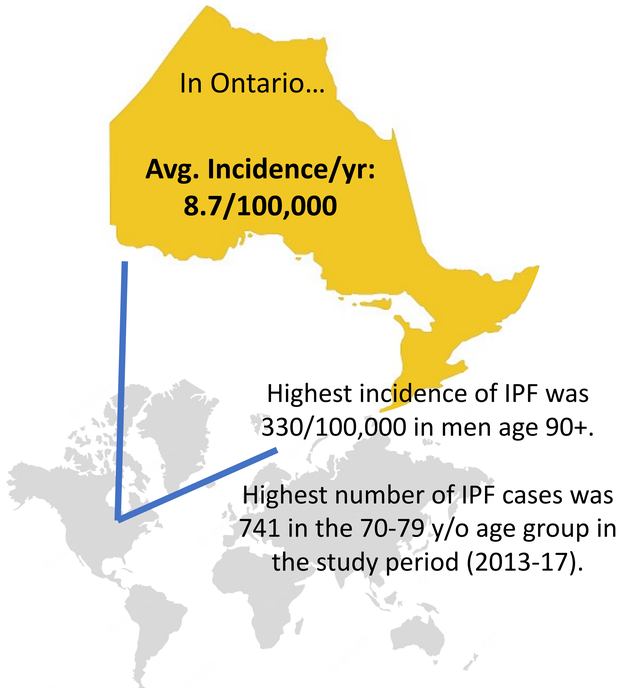


Figure 1. Most common comorbidities associated with IPF.

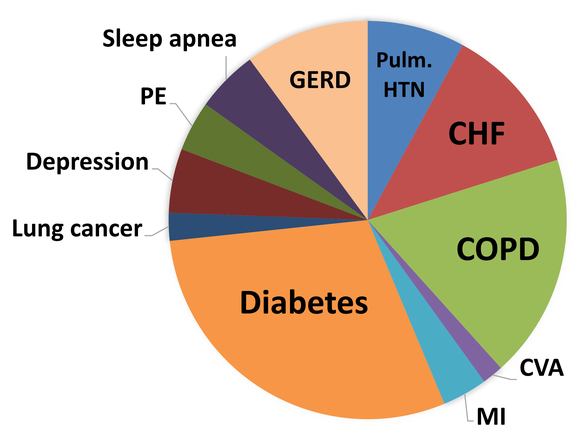


Figure 2. Mean hospital resource utilization 1 year before vs. after IPF diagnosis.

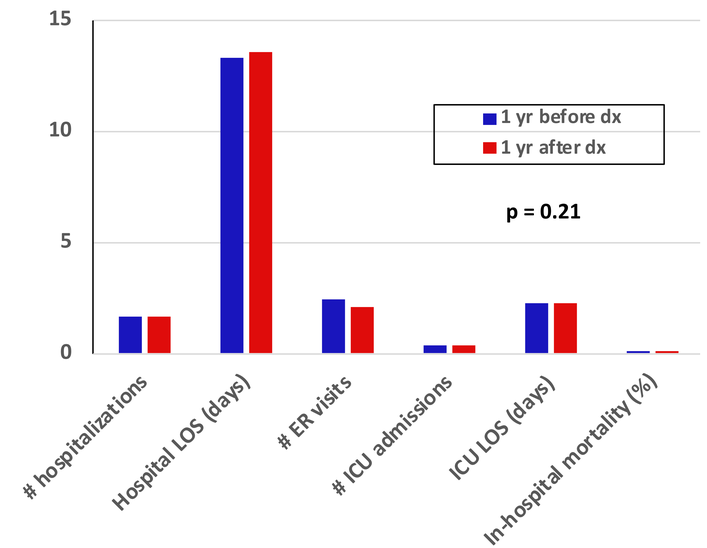
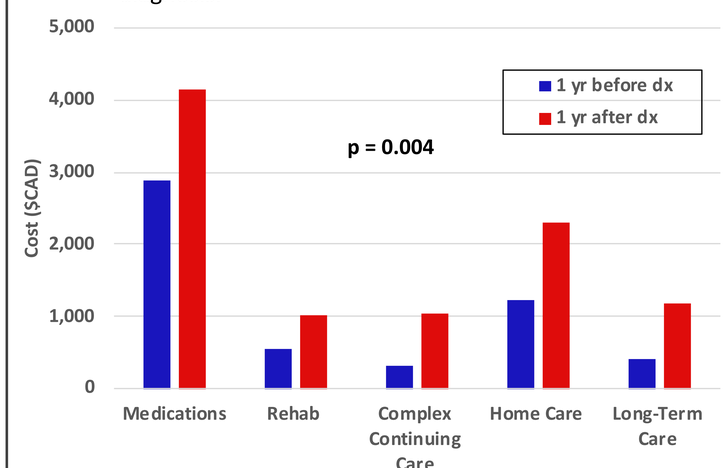


Figure 3. Mean healthcare expenditures 1 year before vs. after IPF diagnosis.



Analysis:

- We report means and SD of data.
- We compared data pre vs post diagnosis using 2-tailed t-tests.

Results:

- The number of incident IPF cases in Ontario varied from 848-952 per year and yearly incidence rates from 8.4 to 9.1 per 100,000 between 2013 and 2017.
- The most prevalent comorbidities were diabetes (20.8%), COPD (12.8%) and CHF (8.6%).
- There were no significant difference 1 year before and after IPF diagnosis in hospitalizations, ER visits, ICU admissions and associated lengths of stay.
- The mean and median healthcare costs per patient almost doubled 1 year after diagnosis compared to 1 year before diagnosis – mostly due to outpatient health care costs.

Conclusion:

IPF significantly increased outpatient healthcare burden and expenditures one year after diagnosis.

References:

1. Diamantopoulos A, Wright E, Vlahopoulou K, Cornic L, Schoof N, Maher T. The Burden of Illness of Idiopathic Pulmonary Fibrosis: A Comprehensive Evidence Review. PharmacoEconomics. 2018;36(7):779-807.
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Correspondence: stang@qmed.ca

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S. Tang[1], O. Moran-Mendoza[1,2], S. Khan[3,4], A. Johnson[4]

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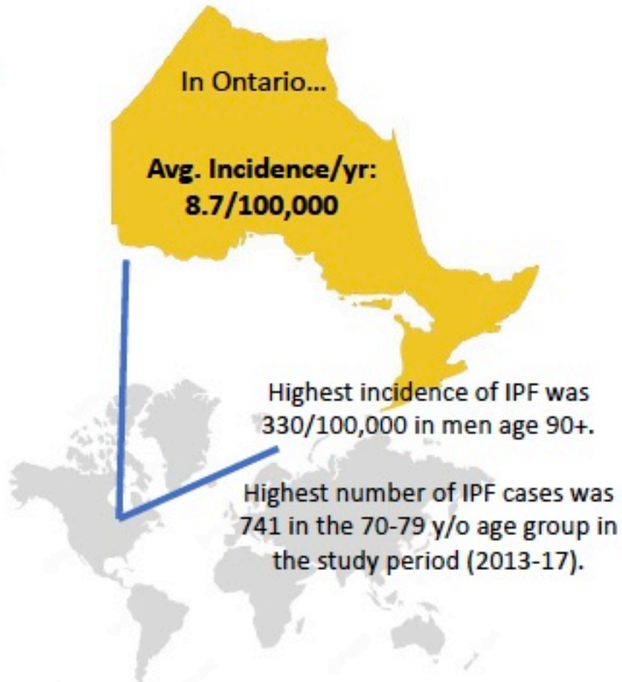

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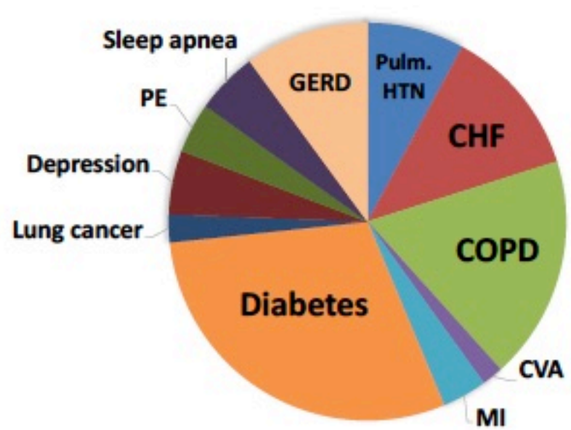

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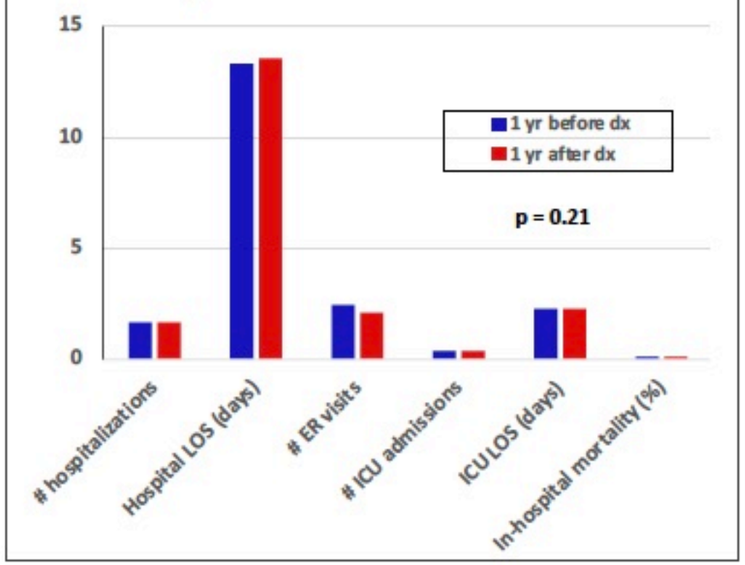

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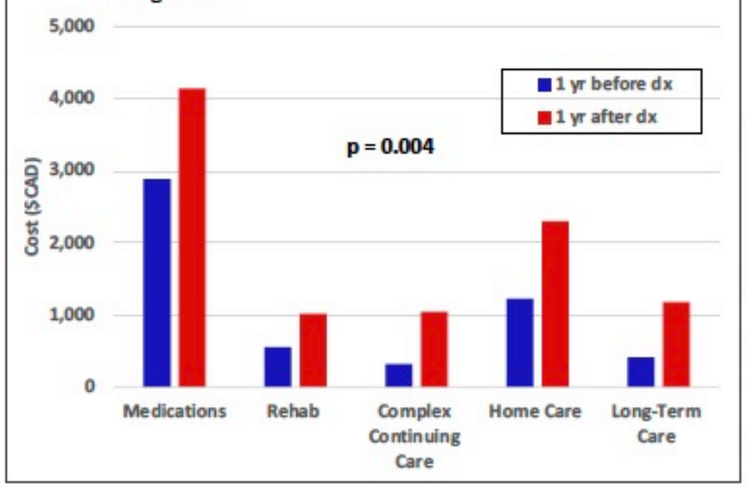

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Characterizing Regional Variability in Health Resource Utilization During the Diagnostic Phase of Lung Cancer – A Population-Based Analysis

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Geneviève C. Digby
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Acknowledgements: J Shellenberger for data analysis.

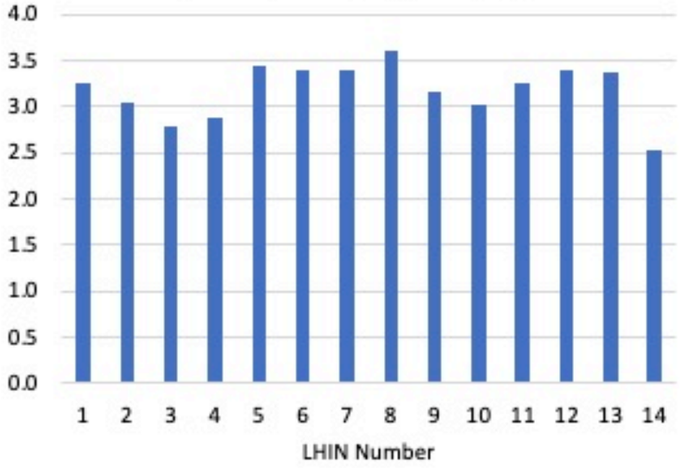
BACKGROUND:

- Significant differences in lung cancer (LC) relative survival exist within Ontario (ON), Canada
- We aimed to characterize regional variability in LC care through assessment of health resource utilization (HRU) across ON health regions (Local Health Integration Networks [LHIN])

METHODS

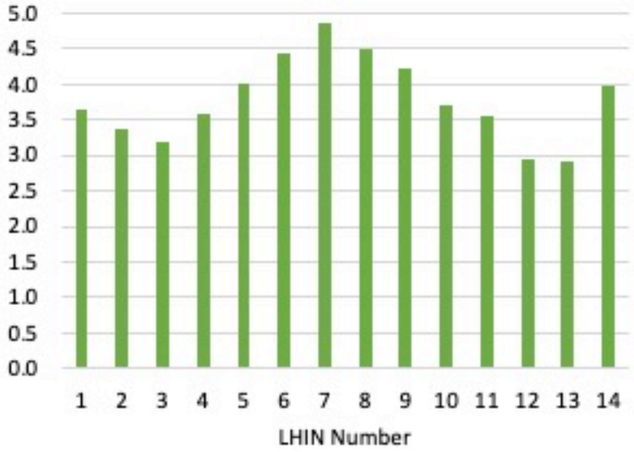
- Retrospective, population-based cohort study
- All patients diagnosed with LC in ON from Jan 2007-Dec 2017
- Data collected from 90 days prior to LC diagnosis until first treatment, or up to 120 days after diagnosis if no treatment

Average number of staging tests in the diagnostic phase per patient, by LHIN



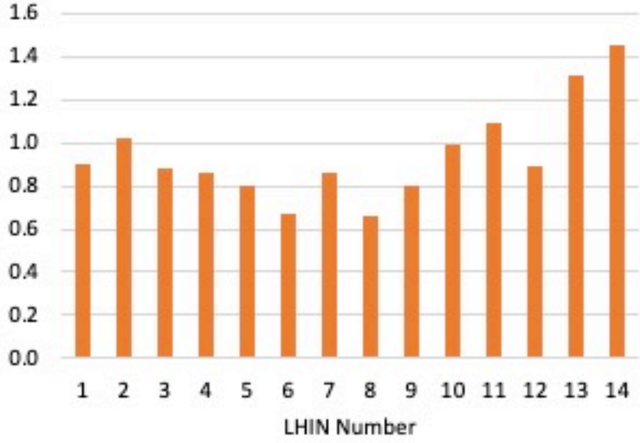
Average number of staging tests varied with each stage from Stage I at 2.97 to highest in Stage III at 3.43

Average Number of Specialist Visits in the diagnostic phase per patient, by LHIN



Average number of specialist visits also varied by stage from lowest in Stage I at 3.37 to highest in stage III disease at 4.23

Average Number of ED visits in the diagnostic phase per patient, by LHIN



Average number of ED visits increased across LC stages from 0.92 visits for Stage I disease to 1.68 visits for Stage IV disease

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Acknowledgements: J Shellenberger for data analysis. *This study was supported by ICES, which is funded by an annual grant from the Ontario Ministry of Health (MOH) and the Ministry of Long-Term Care (MLTC). This study also received funding from William M. Spear Endowment Fund in Pulmonary Research and the Richard K. Start Memorial Fund . Parts of this material are based on data and information compiled and provided by CIHI, NARCS, LHIN, OCR and RPBO. The analyses, conclusions, opinions and statements expressed herein are solely those of the authors and do not reflect those of the funding or data sources; no endorsement is intended or should be inferred.*

Health resource utilization in the diagnostic phase of lung cancer varies by stage of disease and health region across Ontario. This project aims to identify disparities in care that may contribute to the variability in LC outcomes

Development of an Assessment Tool for Advanced Care Planning Communication Skills

Mirna Attalla, Heather Braund, Suzanne Bridge, David Taylor, Andrew Hall, Christopher Parker
Departments of Medicine, Emergency Medicine and Critical Care Medicine, Queen's University, Kingston, ON

Introduction

Learners have identified the challenges of establishing goals of care (GOC) and advanced care planning (ACP), including a lack of educational interventions, and desire feedback that serves to address these gaps. GOC discussions have a significant impact on patient quality of life and use of resources. **Surveyed resident physicians do not feel prepared to lead advanced care planning discussions at the start or residency, despite being expected to independently do so. 84% had never been observed conducting a GOC discussion or given feedback. (1)**

Although assessment tools have been developed for evaluating other essential communication skills, assessment of communication around goals of care has been limited by the lack of validated tools. (2) Our study aims to develop an effective evaluation tool for ACP communication skills.

Methodology

We conducted a multi-centre focus group discussion with experts on ACP skills to guide development of an initial assessment tool. The discussion identified themes and items that were important for assessment of competency in ACP and shared decision-making. Using a modified Delphi approach, a feedback rubric was constructed with defined milestones for levels of competency. The tool was evaluated by multiple assessors using videotaped simulated patient interactions to establish inter-user reliability.

Multi-center focus group with advanced directive experts

↓

Identify themes for competency in ACP discussion

↓

Modified Delphi process to prioritize competencies

↓

Create a rubric for each competency

↓

Create assessment tool

↓

Assess inter-user reliability with two assessors observing simulated discussions

Conclusion

The communication skills required to effectively lead advanced care planning discussions with patients is complex and requires thoughtful verbal and non-verbal communication. The use of a validated assessment tool is important for ensuring these skills are developing adequately during medical training, and for assessing the effectiveness of related education interactions.

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Characterizing Regional Variability in Lung Cancer Outcomes Across Ontario -A Population-Based Analysis

Monica Mullin[1], Marlo Whitehead[2], M. Diane Lougheed[1,3], Michael Brundage[4], Elizabeth Eisenhauer[4], Christopher M. Parker[1,3] and Geneviève C. Digby[1,3]

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Lung cancer survival varies across Ontario health regions

- This survival difference is present and statistically significant even after adjusting for stage of disease, histologic subtype, rurality, age, and comorbidities
- LC incidence and stage of disease at diagnosis vary across health regions
- Understanding these differences can help identify regional barriers to LC care and overcome variability in outcomes

BACKGROUND

- Significant differences in lung cancer (LC) survival exist across health regions in Ontario, Canada
- We sought to identify patient, disease, and system factors that contribute to regional differences in LC outcomes

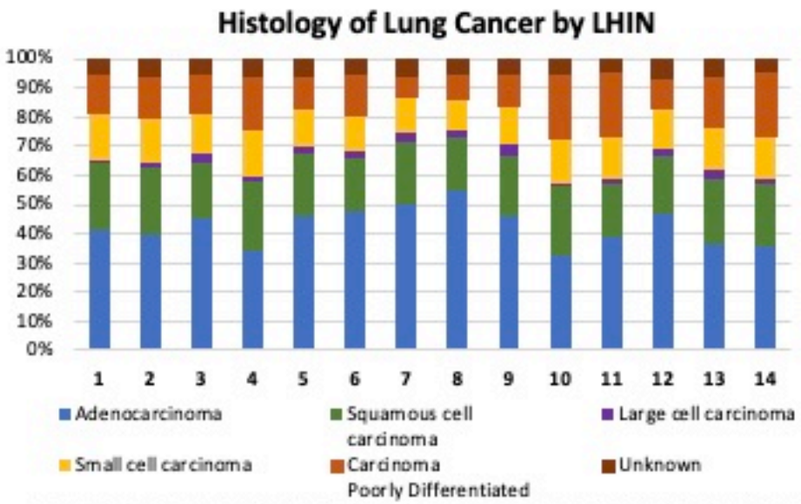
METHODS

- Retrospective, population-based cohort study
- All patients diagnosed with LC in Ontario from Jan 2007-Dec 2017
- Descriptive data collected by health region (Local Health Integration Network [LHIN])
- Logistic regression analysis

RESULTS

- 70,749 patients with LC identified
- Median age at LC diagnosis 70 years; 47.5% female

LHIN	Region	Rate / 10,000	% Stage IV at Diagnosis	5-Year Cancer-Specific Survival (All Patients)	Unadjusted All-Cause Mortality Hazard Ratio (p-value)	Adjusted Cancer-Specific Mortality Hazard Ratio (p-value)
1	Erie St. Clair	8.2185	2,060 (47.73%)	0.235 (0.220 - 0.251)	1.05 (0.0513)	1.01 (0.7492)
2	South West	7.3993	2,726 (48.21%)	0.228 (0.215 - 0.242)	**1.09 (0.0005)**	1.00 (0.9842)
3	Waterloo Wellington	6.1463	1,792 (49.15%)	0.223 (0.206 - 0.240)	**1.07 (0.0163)**	**1.07 (0.0203)**
4	Hamilton Niagara Haldimand Brant	7.4866	4,172 (48.24%)	0.230 (0.219 - 0.241)	**1.07 (0.0012)**	0.98 (0.2747)
5	Central West	3.7700	1,135 (44.18%)	0.283 (0.263 - 0.304)	**0.93 (0.0234)**	**0.82 (<0.0001)**
6	Mississauga Halton	4.3618	1,866 (45.86%)	0.280 (0.263 - 0.296)	**0.93 (0.0066)**	1.01 (0.6242)
7	Toronto Central	4.7349	2,452 (49.03%)	0.256 (0.241 - 0.271)	**Reference**	Reference
8	Central	4.5533	3,284 (49.48%)	0.294 (0.280 - 0.307)	**0.88 (<0.0001)**	**0.88 (<0.0001)**
9	Central East	6.7417	3,933 (45.83%)	0.282 (0.271 - 0.294)	**0.92 (<0.0001)**	**0.92 (0.0003)**
10	South East	9.1285	1,723 (46.35%)	0.222 (0.205 - 0.238)	**1.07 (0.0097)**	**0.89 (<0.0001)**
11	Champlain	7.6452	3,320 (41.52%)	0.270 (0.258 - 0.282)	**0.92 (0.0005)**	**0.90 (<0.0001)**
12	North Simcoe Muskoka	8.6524	1,338 (41.72%)	0.290 (0.270 - 0.309)	**0.93 (0.0104)**	1.00 (0.8786)
13	North East	10.445	2,045 (40.82%)	0.268 (0.253 - 0.284)	**0.95 (0.0401)**	0.98 (0.3918)
14	North West	8.0355	730 (45.91%)	0.231 (0.206 - 0.257)	1.03 (0.3446)	0.98 (0.5662)



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Rheumatology

Dr. Mala Jonaja
Division Chair

Dr. Tanveer Towheed
Research Lead

Summary

- *Case studies may including documenting rare cases and rare presentations of disease*
- *Systematic reviews of therapeutics uses for osteoarthritis and osteoporosis*
- *Educations training on professionalism and postgraduate learning*
- *Use of a derivative of hyaluronic acid and glucuronic acid's pro-inflammatory properties in gout (through MatrixBiology)*
- *Investigation into mental illness's affect on lupus*
- *Identification of barriers for vaccination for patients with rheumatoid arthritis*
- *Therapeutics use associated with increased risk of infection for patients with low bone mineral density*
- *Risk assessment of fractures in rheumatoid arthritis patients*

Current and Upcoming Research Opportunities

The main areas of local expertise include: Osteoarthritis, Osteoporosis, Vasculitis, Inflammatory arthritis (including ultrasound), Education, and Matrix Biolog

(See Arthritis Research Centre Team Description for individual Staff contacts)
Research Ideas by Residents are strongly encouraged

1. Clinical Cases and Review of Literature.
These tend to be unusual cases encountered during clinical exposure to Rheumatology, leading to a review of the literature.

2. Systematic Reviews.
There is expertise in specific areas of Osteoarthrtis, Osteoporosis, and nutraceuticals such as glucosamine.

3. Educational Research.
The foci are in professionalism and post-graduate learning.

4. Canadian Multicenter Osteoporosis Data base.
This very large, 20 year data base can be used to address a variety of research questions, both locally and nationally. Collaborative projects with Dr. Rachel Holden (Nephrology) may be also offered nationally. Collaborative projects with Dr. Rachel Holden Nephrology) may be also offered.

5. Short Clinical Studies.

There are several clinical studies that Staff members are interested in, in where Residents can participate. These Studies generally require attendance at Rheumatology outpatient clinics, either in one long block, several shorter rotations, or in collaboration with another Center. Some of the studies are in areas of interest of Rheumatology Fellows. Many can be done without outside financial support. The Arthritis Society, Physicians Services Inc., or SEAMO, provides support on a competitive basis. However, the Resident would need sufficient lead time to write and submit the Application and obtain approval from the Queen's/Kingston Hospital Research Ethics Board.

Examples include: (i) The relation of skin thickness to osteoporosis (BMD) and collagen markers; (ii) Nailfold video capilaroscopy in inflammatory myopathies.

6. Basic Science Research.

Laboratory work is on matrix biology. The current focus is on hyaluronic acid (HA), a linear polymer of N-acetyl glucosamine and glucuronic acid. HA has essential structural and rheological properties when an intact huge polymer is generally pro-inflammatory when degraded to low molecular weights (LMW HA). We have IP with Queen's on how the pro-inflammatory effects of LMW HA can be abolished by substituting the N-acetyl group with other N-acyl groups, e.g. N-butyryl. There is also an ongoing collaboration with China on a gout animal mode and the use of N-butyryl LMW HA derivative that a Resident could participate in. An interested Resident would need a significant time commitment for the Laboratory work.

The Arthritis Research Centre (ARC) provides various opportunities for research in rheumatic diseases and in connective tissue biology.

ARC Research Fields and Academic Staff contacts:

- ***Osteoarthritis*** *(epidemiology, basic science):*

Dr. Towheed (TT) tt5@queensu.ca , Dr. Anastassiades (TA) anastass@queensu.ca

- ***Osteoporosis*** *(Clinical, CaMos data base):* TT, TA
- ***Vasculitis*** *(clinical):*

  Dr. Clements-Baker (C-B) marie.clements-baker@medportal.ca
- ***Inflammatory Arthritis*** *(Clinical, basic*):*

  MJ, C-B, TT, TK, TA.
- ***Ultrasound of inflamed joints*** *(Clinical):*

  Dr. Kung (TK) tabitha.kung@queensu.ca
- ***Matrix Biology*** *(*hyaluronic acid derivatives, Gout, a collaborative project in China is possible):* TA
- ***Education*** *(professionalism, post grad):*

  Dr. Joneja (MJ) mj6@queensu.ca

Selected Rheumatology Fellows, considering Academic careers, are encouraged to also explore the Clinical Investigation Program at Queen's (CIP),
https://meds.queensu.ca/academics/cip
and/ or the Translational Medicine Graduate Program of the Department of Medicine,
http://deptmed.queensu.ca/translational_medicine_graduate_program

Prevalence and Metric of Depression and Anxiety in Lupus: a Systematic Review and Meta-analysis

E Bangert [1], A Moustafa [2], M Hassanein [3], L Eder [3], S Marzouk [4], J E Wither [3], J Su [3], W Fung [3], P Lambiris [3], Z Touma [3]

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[3] University of Toronto Lupus Clinic, Centre for Prognosis Studies in the Rheumatic Diseases, Toronto Western Hospital, Toronto, Canada; [4] Department of Psychiatry, Neuropsychiatry Division, University of Toronto, Canada

Background

Neurological and psychiatric symptoms, as part of neuropsychiatric manifestations (NPSLE), commonly occur in patients with systemic lupus erythematosus (SLE) (Table 1). Mood and anxiety disorders are one of the most frequent manifestations of NPSLE (Figure 1). These symptoms negatively impact health-related quality of life [1]. Depression and anxiety are associated with increased cardiac risk [2-3], development of personality disorder [4], and withdrawal from social activities [5]. Further, it can impact a patient's perception of treatment efficacy, emotional response to illness, medical costs due to in-hospital costs [6], poor sleep quality [7-8] and medication non-adherence [9,10].

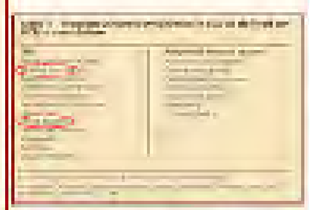
Objectives

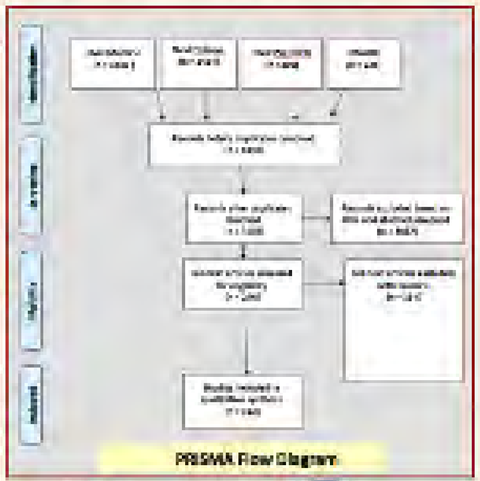
Systematically review the literature on:

- Prevalence of depression and anxiety in SLE patients
- Metrics of depression and anxiety (Diagram 1)
- Psychometric properties of different screening instruments

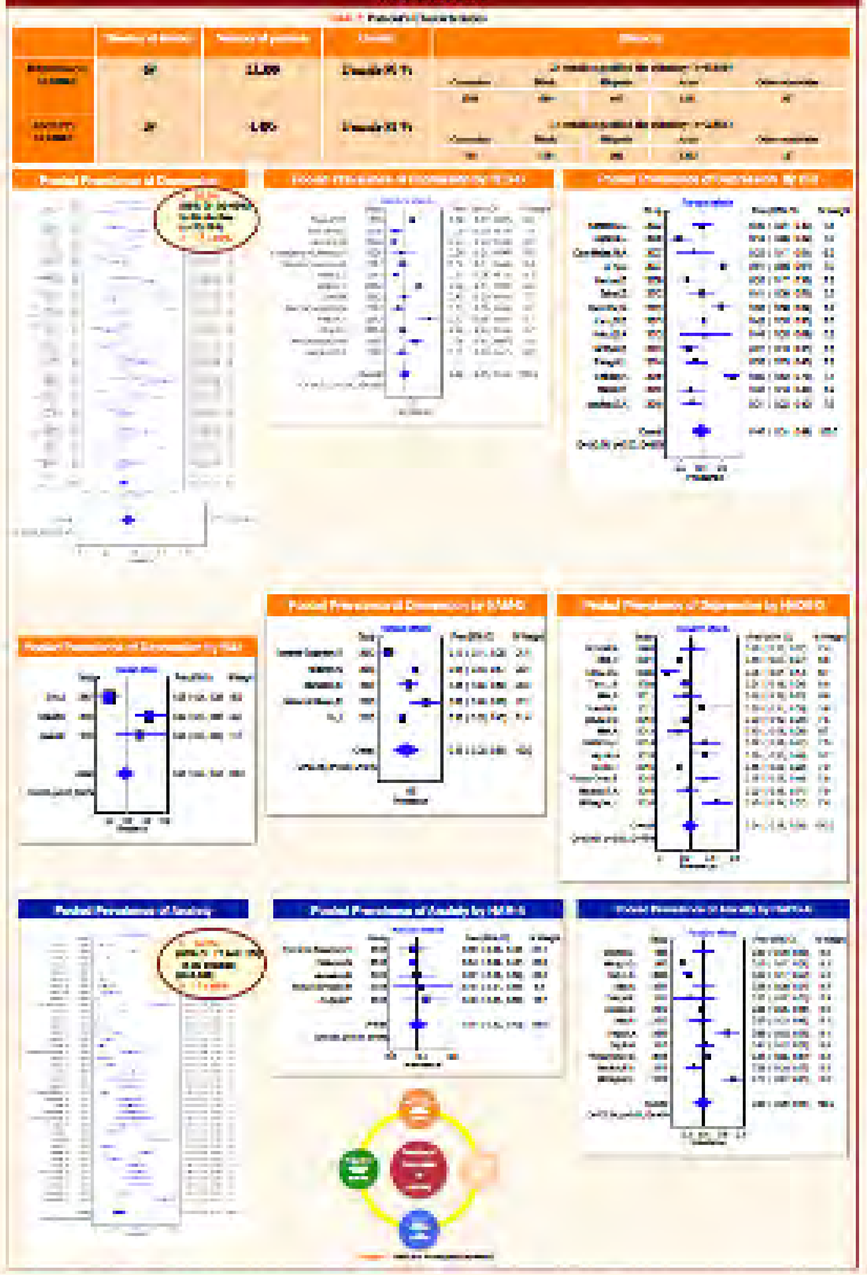
Methods

- PRISMA P guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols) (Figure 2) was used and in-depth searches in four databases (1964-2010; Ovid-based Medline, Embase, PsychINFO and CINAHL) to identify for articles on the prevalence of depression and/or anxiety in adult SLE patients or on the metrics of depression/anxiety.
- Articles were included if they noted using a metric of depression and/or anxiety. Included studies were critically appraised and analyzed.
- Prevalence of depression and anxiety was studied for all instruments, and whenever possible, pooled prevalence (PP) was determined for more commonly used measurement instruments.





Results:



Results

- A total of 4694 references were identified, 278 were selected for detailed review and 127 were included in the final analysis (Figure 2).
- Overall Prevalence: The depression PP, obtained from 70 studies representing 23369 SLE patients, was 35.2% (95% CI: 30.1%-40.5%). The anxiety PP, obtained from 39 studies representing 4495 SLE patients, was 24.2% (95% CI: 17.3%-31.2%).
- Prevalence per instruments/metrics used: The more commonly used instruments included the Centre for Epidemiological Studies - Depression (CES-D), Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Hospital Anxiety and Depression Scales (HADS-A/D), & Hamilton Rating Scales for Depression/Anxiety (HAM-D/A).
- CES-D was utilized in 18 studies including 1898 SLE patients, depression PP was 41.5% (95% CI: 35.1%-48.1%).
- BDI/BDI-II was utilized in 14 studies including 1285 SLE patients and the BAI in 3 studies including 493 patients; depression PP was 39.9% (95% CI: 31.1%-49.1) and anxiety PP was 38.4% (95% CI: 34.2%-42.8).
- HADS-D/A – HAD-D was utilized in 14 studies including 1838 SLE patients & HADS-A in 12 studies including 1039 patients; depression PP was 24.4% (95% CI: 18.1%-30.1%) and anxiety PP was 38.8% (95% CI: 29.1%-47.5%).
- HAM-D/A – HAM-D was utilized in 4 studies including 333 SLE patients and the HAM-A in 5 studies including 359 patients respectively; depression PP was 43% (95% CI: 27.9%-58.1%) & anxiety PP was 37.3% (95% CI: 31.1%-43.2%).
- The statistical heterogeneity between studies was high (I² > 75%).

Conclusions

- There was high variability in the prevalence of depression and anxiety, ranging from 5.7%-70.6% and 1.1%-71.4%, respectively.
  This could be attributed to the:
  1) Lack of standardization in the metrics and definitions of depression and anxiety in SLE
  2) Variability in other demographics such as patients age, education levels and others (factors that were associated/predicted depression and/or anxiety in few studies)
- The prevalence of depression/anxiety is high in patients with SLE, ranging from 6-79% (PP 35%) and 1-71% (PP 24%) respectively.
- The CES-D, BDI, HAM-D yielded a similar prevalence of depression, ranging between 28-49%, whereas the prevalence by HADS-D was lower (24%).
- All metrics (BAI, HADS-A, HAM-A) of anxiety yielded a similar prevalence of anxiety prevalence ranging between 29-48% (PP 24%).

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ORIGINAL ARTICLE

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WILEY

Identifying perceptions and barriers regarding vaccination in patients with rheumatoid arthritis: A Canadian perspective

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Abstract

Aim: Canadian guidelines recommend that patients with rheumatoid arthritis (RA) receive pneumococcal, influenza and shingles vaccinations. The aim of this study was to identify and understand vaccination rates in Canadian patients with RA.

Methods: We conducted an observational study to evaluate uptake of herpes zoster (HZ), influenza and pneumonia vaccination in a cross-section of patients with RA in Kingston, Ontario, Canada. Data were collected using a self-administered questionnaire in patients attending at an academic rheumatology clinic. If vaccination was not received, the reason was established.

Results: Ninety-eight out of a total of 103 patients surveyed met the inclusion criteria and were evaluated: 72.4% had received the influenza vaccination in the past year encompassing a period of 2017-2019. Of the 27.6% who did not, the most common chosen reason was personal preference not to get vaccinated (55.6%). Regarding HZ, 18.4% had received vaccination. Of the 2 available types of vaccines, more participants received Zostavax (66.7%) as compared to Shringrix (33.3%). For those not vaccinated (81.6%), "Other" was the most chosen option (37.5%) with the reasons subsequently specified as cost, concern over interaction with treatment and waiting until age ≥65 years. In terms of pneumococcal vaccination, 36.7% were vaccinated, with the majority being vaccinated with Pneumovax-23 (63.9%) compared to Prevnar-13 (16.7%) or both (19.4%). Of the 63.3% of the participants who did not receive vaccination, the most cited reason was they did not know they should receive pneumococcal vaccination (48.4%).

Conclusions: Vaccination rates among Canadian patients with RA are suboptimal.

KEYWORDS

herpes zoster, influenza, pneumoccocal, rheumatoid arthritis, vaccination rates

1 | INTRODUCTION

Rheumatoid arthritis (RA) is an insidious autoimmune inflammatory condition that typically presents as a polyarticular process. This chronic systemic condition is 2 to 3 times more prevalent in women and can present at any age; however, there is a predilection for the 6th decade of life.[1] It is estimated that 1% of Canadians are currently affected by RA and with an aging population there is evidence of an increasing incidence rate.[2] Given the nature of the disease and the immunosuppressive treatment modalities available including conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and biologics, there is higher propensity for

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REVIEW ARTICLE

International Journal of Rheumatic Diseases
WILEY

Is denosumab associated with an increased risk for infection in patients with low bone mineral density? A systematic review and meta-analysis of randomized controlled trials

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Abstract

Aim: Denosumab increases bone mineral density through inhibition of the receptor activator of nuclear factor κ-B ligand (RANKL). RANKL has known immunomodulatory effect. The largest study to date that reviewed denosumab efficacy in osteoporosis demonstrated an increased incidence of serious adverse events of infection (SAEI). We aimed to further evaluate risk of infection and SAEI in denosumab-treated patients.

Method: PubMed, Embase, Cochrane Central Register of Controlled Trials, and Web of Science were searched for randomized controlled trials. Studies comparing denosumab 60 mg every 6 months with placebo or bisphosphonate for treatment of low bone mineral density were included. Trials were excluded for use of denosumab in cancer patients treated for skeletal-related events, immunosuppressed patient populations, or for comparison to teriparatide. Risk ratios (RR) with a 95% confidence interval (CI) were pooled using a fixed effects model, or a random effects model if heterogeneity occurred.

Results: Twenty-four randomized controlled trials (20 470 patients) were analyzed. An increased incidence of any infection (RR 1.11; 95% CI 1.02-1.20; $P = 0.02$) was observed in denosumab-treated patients compared with bisphosphonates, but not when compared with placebo. In contrast, a higher incidence of SAEI (RR 1.21; 95% CI 1.03-1.43; $P = 0.02$) was seen with denosumab when compared with placebo, but not compared with bisphosphonates.

Conclusion: Denosumab-treated patients with low bone mineral density have slightly increased incidence of SAEI compared with placebo, but not when compared with bisphosphonates. Application of these results requires consideration of the entire body of data available regarding denosumab safety.

KEYWORDS
bone diseases, denosumab, infections, meta-analysis, metabolic, osteoporosis

Is Rheumatoid Arthritis a Risk Factor for Fractures: A Systematic Review of Observational Studies

A Gupta, MD, S Pipe, BSc, T Towheed, MD, Anastassiades T, MD, PhD

Background: Rheumatoid Arthritis (RA) is a risk factor for osteoporosis. There are many factors that contribute to this increased risk, including the use of glucocorticoids, systemic inflammation due to the disease and relative physical inactivity. Only a few studies have assessed the risk of fractures in RA. The objective of this systematic review was to assess the risk of fractures in adults with RA compared with controls from the general population.

Methods: Two authors screened citations from the following electronic databases: MEDLINE, EMBASE, Cochrane Database of Systematic Reviews and CINAHL. Included citations were written in English, included patients greater than or equal to 18 years of age and compared fracture incidence/prevalence between RA patients and a control group. Case control, cohort and cross-sectional studies were included. Abstracts and conference proceedings were not searched. The primary outcome was fracture incidence and/or prevalence. Two authors extracted data using a standardized data extraction form. The quality of the studies was assessed using the Newcastle-Ottawa Scale (NOS).

Results: The searches resulted in 3451 citations, and after applying the inclusion criteria, we selected seventeen observational studies. The risk of fracture was elevated in RA compared to controls in 14 of the 17 studies. Thirteen studies adjusted for glucocorticoid use and there was an increased risk of fracture with glucocorticoid use in 4/13 of these studies. Seven studies analyzed RA severity or functional impairment as a risk factor for fracture and the risk of fracture was elevated in 2/7 of these studies

racture ascertainment was performed by searching medical records in seven studies, analyzing spine radiographs in six studies, self-reported history in two studies and by multiple methods in two studies. Eight studies evaluated fractures at multiple sites, whereas nine studies evaluated fractures only at a single site. Only two studies reported specific data on fragility fractures, whereas in the remaining studies, the fracture mechanisms were not defined. Assessment using the NOS revealed that the studies were of high quality.

Limitations of the studies included: studies enrolled a diverse range of patient and control group populations, and generally included all types of fractures determined by various methods and involving multiple sites. These differences between the studies made it difficult to directly compare them. Due to the marked study heterogeneity, a meta-analysis was not performed.

Conclusion: The risk of fracture in RA is elevated compared to the general population.