Annual Research & Awards Day
Division of Respirology 2025

THURSDAY JUNE 12, 2025
9:00 – 16:00

Division of Respirology
Department of Medicine
Faculty of Medicine

UNIVERSITY OF TORONTO

Li Ka Shing Knowledge Institute
St. Michael's Hospital. 209 Victoria St.

respirologyresearch.com

Program – Annual Research & Awards Day 2025

Location: Li Ka Shing Knowledge Institute (2nd floor) – St. Michael's Hospital. 209 Victoria Street.

8:30 Registration and Poster Set-up

8:30 – 9:15 Continental Breakfast

9:15 – 9:30 Welcome Remarks:

Opening of the Respirology Research Day: Drs. D. Rozenberg & G. Montandon

Director of the Division of Respirology – Dr. Chung-Wai Chow

9:30 – 10:00 KEY-NOTE SPEAKER

Dr. Michael K. Stickland

Professor, University of Alberta

UNIVERSITY OF ALBERTA

Innovations in Pulmonary Rehabilitation for Management of Individuals with Obstructive Airway Disease

10:00 – 10:30 Coffee/Stretch Break/Complete Poster Setup

10:30 – 11:15 ORAL SESSION 1 - Basic Science

10:30 Nele-Marie Hagen - Spatial characterization of distinct B cell subsets in chronic lung allograft dysfunction. Abstract # 21

10:40 Allen Duong -In vitro characterization of pro-inflammatory LILRB2+ and pro-fibrotic SPP1+ pulmonary macrophages in chronic lung allograft dysfunction. Abstract #16

10:50 Bohan Zhu - Compensatory Anti-Ferroptosis Responses in Human Lung Cells Exposed to EVLP Perfusate Steen Solution. Abstract # 53

11:00 Sumiha Karunagaran - Evidence for a neuro-immune axis associated with local B cell responses and fibrosis in chronic lung allograft rejection. Abstract # 26

11:15 – 11:45 KEY-NOTE SPEAKER

Dr. Richard Horner

Professor, University of Toronto

Advancements in sleep apnea over the last 25 years

UNIVERSITY OF TORONTO

11:45 – 12:30 Lunch Break. Rooms 240 & 241.

12:30-14:00 Poster Viewing and Judging

14:00 – 15:00 ORAL SESSION 2 - Clinical and Health Science

14:00 Alina Blazer - Risks Factors for COPD among Never Smokers in Ontario, Canada. Abstract # 8

14:10 Brandon Luu - Trends in antifibrotic prescriptions from a universal health care system. Abstract # 29

14:20 Tony Ning - Rapid-cycle design of a clinical decision support system (CDSS) for asthma management in community pharmacies. Abstract # 27

14:30 Sayaki Ishiwata - Effect of peak flow triggered adaptive servo-ventilation (ASVPF) on mortality in heart failure patients with prolonged Cheyne-Stokes respiratory cycle. Abstract # 23

14:40 Daniel Genkin - Predicting the Occurrence of Baseline Lung Allograft Dysfunction at 1-year Post Bilateral Lung Transplant using Machine Learning with 6-month Oscillometry and Quantitative CT. Abstract # 19

14:50 Lielle Ronen - A machine learning algorithm to quantify smoking damage in donor lungs. Abstract # 41

15:00 - 15:30 Snack and refreshments

15:30 - 16:00 Awards and Prizes of the Division of Respirology

Awards Ceremony for Research: G. Montandon

Faculty Research and Trainee Awards: D. Rozenberg

Organizers:

Dr. Dmitry Rozenberg
Dr. Gaspard Montandon
Ms. Rhiannon Davies
Mr. Ali A. Salman Al-Timimi

Abstract Judges:

Dr. Jane Batt
Dr. Sarah Brode
Dr. Chung-Wai Chow
Dr. Lee Fidler
Dr. Roger Goldstein
Dr. Andrew Kouri
Dr. Ted Marras
Dr. Clodagh Ryan
Dr. Ciaran Scallan
Dr. Nicholas Vozoris

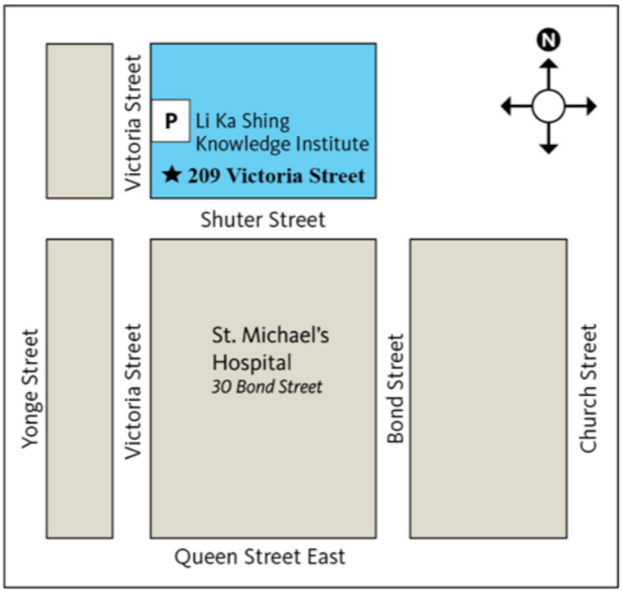
Annual Research & Awards Day 2025
Sponsored by:

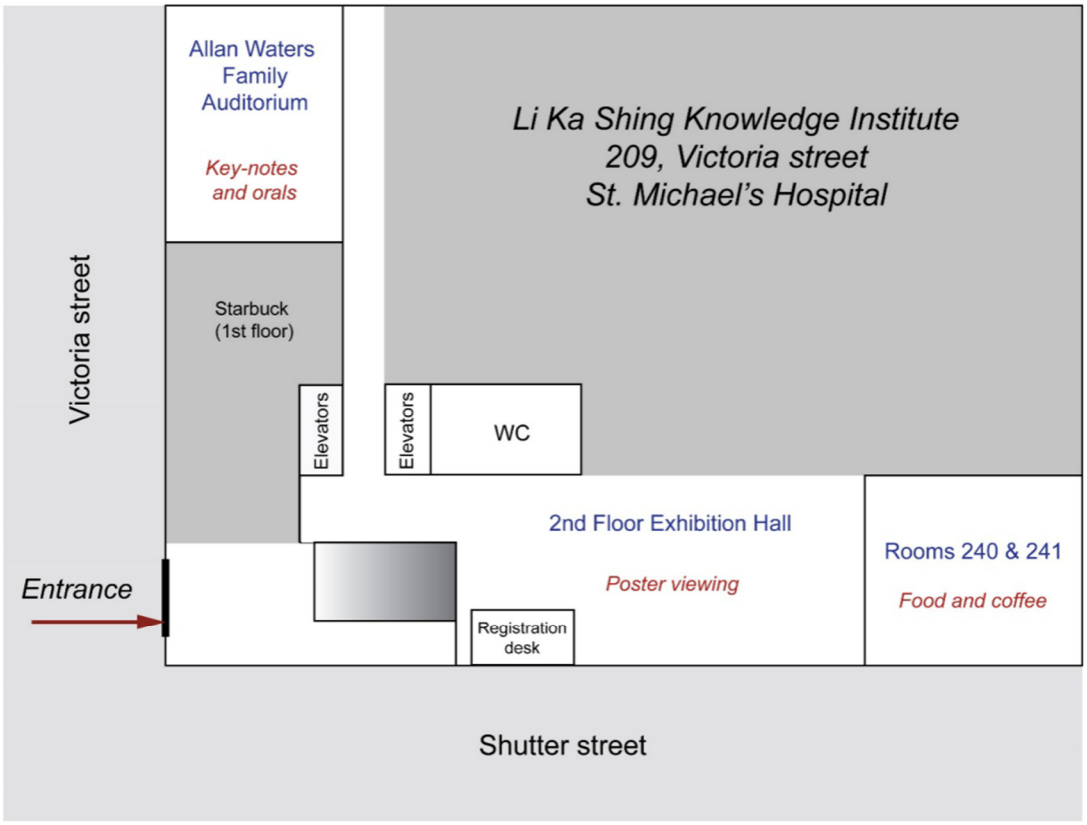
GOLD:

SILVER:

Location and Rooms:

Location: Li Ka Shing Knowledge Institute (2nd floor) – St. Michael's Hospital. 209 Victoria street.





Keynote Speaker

Dr. Michael K. Stickland

Dr. Michael Stickland is a Professor in the Pulmonary Division within the Faculty of Medicine and Dentistry at the University of Alberta, and Director of the G.F. MacDonald Centre for Lung Health. He completed his PhD at the University of Alberta and a postdoctoral fellowship at the University of Wisconsin before joining the Division of Pulmonary Medicine in 2006.

Dr. Stickland is an internationally recognized researcher whose work focuses on understanding exercise intolerance in individuals with pulmonary and cardiovascular disease, as well as developing clinical innovations to enhance the delivery and effectiveness of pulmonary rehabilitation. He has led the development of new testing and rehabilitation protocols for patients with chronic lung conditions,

He serves on the editorial boards of *CHEST* and the *Journal of Applied Physiology*.

Dr. Stickland is also the Scientific Director of the Respiratory Health Strategic Clinical Network for Alberta Health Services and plays key leadership roles in several national organizations, including the Canadian Thoracic Society and the Lung Association of Alberta and Northwest Territories. He is a dedicated educator and mentor, actively involved in training the next generation of medical and research professionals, and was named one of Edmonton's "Top 40 Under 40" by *Avenue* magazine in recognition of his clinical and scientific contributions.

Keynote Speaker

Dr. Richard Horner

Dr. Richard Horner is a Full Professor in the Departments of Physiology and Medicine at the University of Toronto. He served as the Tier 1 Canada Research Chair in Sleep and Respiratory Neurobiology from 2007 to 2021 and recently completed his term as Vice-Chair, Research, in the Department of Physiology (2021–2024). A globally recognized expert in sleep science, Dr. Horner has authored articles and contributed chapters to leading medical textbooks, including *Principles and Practice of Sleep Medicine* and *Murray & Nadel's Textbook of Respiratory Medicine*.

Dr. Horner's research focuses on the neurobiology of sleep and breathing. In recognition of his contributions, he was elected a Fellow of the Canadian Academy of Health Sciences (FCAHS) in 2017 and received the prestigious CIHR-ICRH/Canadian Sleep Society Distinguished Lecturer Award in Sleep Sciences in 2023.

An exceptional educator, Dr. Horner has received multiple teaching awards, including for sustained excellence in graduate mentorship and for integrating research into undergraduate education.

Beyond academia, Dr. Horner actively engages the public in sleep health education through media appearances, public talks, and creative collaborations. He co-created *Somniloquy*, a theatrical exploration of brain function during sleep, and authored *The Universal Pastime: Sleep and Rest Explained*, a book that brings sleep science to a broader audience.

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Abstract 1

The healthcare burden of pediatric cough – Findings from The CHILD Cohort Study

Tabina Ahmed, BSc (1,2), Myrtha E. Reyna, MSc (2), Marija Pajdakovska, MSc (2), Mohammad Kaviul Anam Khan, PhD (2), Elinor Simons, MD, PhD, FAAAAI, FAAP (3), Theo Moraes, MD, PhD, FRCPC (4,5), Padmaja Subbarao, MD, M.Sc, FRCPC (1,2,6)

1. Department of Physiology, Temerty Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada. 2. Translational Medicine Program, The Hospital for Sick Children, Toronto, Ontario, Canada. 3. Section of Allergy and Immunology, Department of Pediatrics & Child Health, University of Manitoba, Winnipeg, Manitoba, Canada. 4. Institute of Medical Sciences, Temerty Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada. 5. Department of Laboratory Medicine & Pathobiology, Temerty Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada. 6. Division of Respiratory Medicine, The Hospital for Sick Children, Toronto, Ontario, Canada

Introduction: Asthma is the most common chronic airway disease among preschoolers, contributing to greater healthcare burden and lower health-related quality of life. Although cough is a clinically relevant symptom, prediction tools prioritize wheeze, and the healthcare burden of cough remains unclear. We aimed to: 1) evaluate associations between cough without cold separately from wheeze, and healthcare utilization in the Canadian pediatric population, and 2) determine longitudinal trajectories of cough from infancy to preschool, and their associations with healthcare utilization.

Methods: Data was leveraged from the CHILD Study, a prospective, longitudinal, Canadian birth cohort. Information on the presence, duration, severity, and frequency of cough without cold (excluding wheeze), wheeze (with/without cough), unscheduled doctor visits (UDV) and hospital visits (HV) during the first 5-years of life were collected via parent-reported questionnaires. Associations between cough features and healthcare utilization outcomes were evaluated using generalized estimating equations. Cough trajectories (excluding wheeze) were identified using group-based trajectory modelling (GBTM) and evaluated for associations with healthcare outcomes.

Results: Among 3,042 participants in infancy (first 12-months of life), 324 (10.6%) had cough without cold, and 737 (24.2%) had wheeze. During preschool visits (2-5 years) (n=2,822), 288 (10.2%) exhibited a cough without cold, and 703 (24.9%) had wheeze. In infancy, cough without cold was associated with UDVs and HVs, while in preschool, cough without cold was associated with UDVs only. Stronger associations were observed for wheeze across both age groups. GBTM identified three cough trajectories among 1917 participants who had a cough without cold (excluding wheeze) throughout early childhood – late-onset [82 (4.3%)], early-onset [245 (12.8%)], and infrequent cough [1590 (82.9%)] – based on AIC/BIC values, posterior probabilities, and clinical interpretability. The late-onset cough trajectory was associated with UDVs.

Conclusion: Cough without cold, without wheeze, carries a high healthcare burden from infancy through preschool, warranting re-evaluation of cough management strategies.

Canadian Institutes of Health Research (CIHR); Allergy, Genes and Environment (AllerGen) Network of Centres of Excellence; Don & Debbie Morrison; The Sick Children's Hospital Foundation

Abstract 2

Evaluation of the content, readability and reliability of education materials on lung transplantation for patients and caregivers.

Mohamed Alobeidli(1), John Wu(1), Ahmad Ibrahim(1), Brandon Luu(1), Josh Shore(1), Megha Ibrahim Masthan(1), Kirsten Wentlandt(1), Dmitry Rozenberg(1,2)

1 Toronto General Hospital Research Institute, University Health Network, Toronto, ON, Canada. 2 Division of Respirology, Temerty Faculty of Medicine, University Health Network, University of Toronto, Toronto, ON, Canada

Introduction & Objectives: Lung transplantation (LTx) is a life-saving procedure for patients with end-stage lung disease requiring comprehensive patient and caregiver education. Understanding the complexities of the procedure is crucial for ensuring adherence to medical recommendations and long-term success. This study evaluates online resources on physical fitness, nutrition and mental health in the pre-transplant period to identify potential gaps and improve the quality of patient and caregiver education resources.

Methods: A total of 174 English websites were sourced from Google using search term “Education materials on lung transplantation for patients and caregivers”. Website content was assessed using scientific consensus criteria (Table 1) and quality evaluated using Modified DISCERN, Global Quality Scale (GQS), Patient Education Materials Assessment Tool (PEMAT), and readability using Flesch-Kincaid Grade Level (FKGL).

Results: The mean content score was 8.5 out of 17 (range: 3–16) for the 46 websites included, with physical activity and nutrition being the most covered topics (91%), while advance care directives and sleep health were not commonly addressed (7%). The mean modified DISCERN score was 3.5 ± 0.8 with the mean GQS of 3.6 ± 0.8, suggesting moderate quality. The mean PEMAT-P understandability score was 68%, while actionability was 61% (threshold of ≥ 70%). The Flesch-Kincaid grade level was 11.

Conclusion: Online educational resources for LTx candidates and caregivers vary in content, with most websites highlighting importance of physical fitness and nutrition, whereas sleep health and advance directives were not commonly discussed. Quality assessments highlight the need for improved, patient-centered materials that are understandable with specific actionable items for patients and caregivers.

MA and DR are supported by Temerty Faculty of Medicine, University of Toronto. DR receives research support from Sandra Faire and Ivan Fecan Professorship in Rehabilitation Medicine.

Figure for abstract 2.

Table 1: Criteria for content scoring of Patient Education Materials prior to lung transplantation

Category	Criteria	Other Examples
Physical function/exercise (/7)	Aerobic training	Walking, Treadmill, Cycling, Pulmonary rehabilitation
	Strength training	Free weights, Household items
	Physical activity	Participation in activities of daily living
	Supplemental oxygen	Oxygen saturation with activity
	Flexibility exercises	Discussion of injury prevention
	Safety	Fall prevention
	Sleep health	Sleep cycle maintenance
Nutrition(/4)	Body composition	Monitoring of body weight or BMI
	Nutritional support	Appropriate caloric supplementation, Dietitian support
	Swallowing	Evaluation and management of dysphagia
	Recommended daily requirements	Balanced diet based on food guide
Mental health support and social support (/6)	Social support	Support groups, Social worker
	Goals of care discussion	Advance care directives
	Methods of seeking assistance	Family support programs, Patient advocacy groups
	Emotional well being	Emotional counselling services
	Caregiver roles	Home health aide, Personal care attendant
	In-hospital support	Inpatient wellness and support programs
Overall (/17)		

Abstract 3

Diaphragmatic Function and Association With Patient-Reported Outcome Measures and Physical Function Post-Transplant

Rogih Andrawes[1], Catherine A. Bellissimo[2], Ali Salman Al-Timimi[3], John Wu[3], Ahmed Ibrahim[3], Megha Ibrahim Masthan[3], Vanessa Silano[3], Ewan C. Goligher[4], Shiphra Ginsburg[5], Lisa Wickerson[6], Shaf Keshavjee[7], Chung-Wai Chow[8], Darlene Reid[9], Dmitry Rozenberg[10]

[1] Temerty Faculty of Medicine, Toronto General Hospital Research Institute (TGHRI), University Health Network (UHN), [2] Interdepartmental Division of Critical Care Medicine, TGHRI, UHN, [3] TGHRI, UHN ,[4] Interdepartmental Division of Critical Care Medicine, Division of Respirology, Department of Medicine, TGHRI, [5] Temerty Faculty of Medicine, Respirology, UHN, University of Toronto (UofT), [6] Department of Physical Therapy, Toronto Lung Transplant Program, Ajmera Transplant Centre, UHN, UofT, [7] Lung Transplant Program, Department of Surgery, Toronto General Hospital, UofT, [8] Department of Medicine, Division of Respirology, Temerty Faculty of Medicine, [9] Physical Therapy, Interdepartmental Division of Critical Care Medicine, KITE-Toronto Rehab, UHN, UofT, [10] Respirology and Lung Transplantation, Temerty Faculty of Medicine, UHN, UofT, Toronto, ON, Canada

Introduction & Objectives Diaphragm function and its association with respiratory symptoms, health-related quality of life (HRQL), and physical function is not well characterized in the post-lung transplant (LTx) period. This study aims to: 1) Compare diaphragmatic function, respiratory symptoms, HRQL, and physical function between LTx recipients and LTx candidates; 2) Evaluate the relationship between diaphragm function and post-LTx outcomes.

Methods: Prospective, single-center cross-sectional study of adult bilateral LTx recipients (≥ 3 months post-LTx) with pre-LTx diagnosis of chronic obstructive pulmonary disease (COPD) or interstitial lung disease (ILD), and pre-LTx participants matched for age, sex, and lung disease. Ultrasound of the diaphragm, Medical Research Council (MRC) dyspnea score, six-minute walk distance (6MWD), St. George's Respiratory Questionnaire (SGRQ) and HRQL (Short-Form 36 [SF-36]) were evaluated. Diaphragm thickening fraction (TF) was measured during resting tidal breathing (TFdi-tidal) and maximal inspiration (TFdi-max) with diaphragm reserve (1-[TFdi-tidal/TFdi-max]) calculated.

Results: 38 LTx recipients (64±8 years, 68% ILD, 66% male; median 6.3 months post-LTx) and 18 pre-LTx candidates (61±8 years, 61% ILD, 56% male) were evaluated. Post-LTx participants had a lower resting diaphragm TF, greater maximal diaphragm TF, and a higher diaphragm reserve (72±19% vs. 45±24%, p=0.0002) than pre-LTx participants. HRQL, respiratory symptoms, and 6MWD were better in LTx recipients than candidates ($p < 0.01$ for all comparisons). Multivariable regression showed diaphragm reserve was associated with higher maximal inspiratory pressure (7.9 cmH2O [95% CI: 2.8 to 13.1], p=0.003) and better SGRQ symptoms (-6 points [95% CI: -9 to -3], $p<0.0001$) for every 0.1 increase in diaphragm reserve. No significant associations were observed with MRC, SF-36, or 6MWD.

Conclusion: Diaphragm function, HRQL and physical function were greater in LTx recipients than candidates with diaphragm reserve associated with SGRQ symptoms and inspiratory muscle strength post-LTx. Diaphragm assessment may help guide rehabilitation strategies like inspiratory muscle training to enhance outcomes post-LTx.

Sandra Faire and Ivan Fecan Professorship, Ajmera Transplant Seed Grant, Canadian Institute of Health Research (PJM 185763), Ontario Graduate Scholarship

Abstract 4

Antimicrobial Treatment of Mild Mycobacterium avium Complex–Pulmonary Disease Predicted to Increase Survival and Quality Adjusted Life Years: A Microsimulation Decision Analysis Model

Omri A Arbiv (1, 2, 3), Gemma Postill (2), Yunjoo Im (4), Byung Woo Jhun (4), Petros Pechlivanoglou (2, 5, 6), Sarah K Brode (1, 7), Ahmed M Bayoumi (2, 8, 9, 10), Theodore K Marras (1, 7)

1.Division of Respirology, University of Toronto, Toronto, ON, Canada 2. Institute of Health Policy, Management, and Evaluation, University of Toronto, Toronto, ON, Canada 3.Clinical-Investigator Program, University of British Columbia, Vancouver, BC, Canada 4.Division of Pulmonary and Critical Care Medicine, Department of Medicine, Samsung Medical Center, Seoul, South Korea 5.Child Health Evaluative Sciences, The Hospital for Sick Children, Toronto, ON, Canada. 6.Toronto Health Economic and Technology Assessment Collaborative, Toronto, ON, Canada 7.Division of Respirology, University Health Network, Toronto, ON, Canada 8.Division of General Internal Medicine, St. Michael's Hospital, Toronto, ON, Canada 9. Division of General Internal Medicine, Department of Medicine, University of Toronto, Toronto, ON, Canada 10.MAP Centre for Urban Health Solutions, St. Michael's Hospital, Toronto, ON, Canada

Introduction & Objectives:
Mycobacterium avium complex–pulmonary disease (MAC-PD) requires prolonged antimicrobial treatment with potential toxicities. For patients with mild MAC-PD, it is challenging to decide on antimicrobial treatment or observation. We conducted a patient-centered microsimulation to compare the quality adjusted life years (QALY) and life expectancy associated with treatment or observation.

Methods:
We simulated 10,000 individuals using monthly cycles in a lifetime model, with the base case of a 65-year-old individual with macrolide-susceptible nodular-bronchiectatic MAC-PD and preserved lung function. Individuals started in either observation or treatment, where treatment followed the ATS/IDSA/ERS/ESCMID guidelines and continued for 13-24 months. Toxicity was simulated as a transient decrease in utility. Model outcomes were QALY and life-expectancy. Probabilities and utilities were obtained from the literature. Deterministic sensitivity analyses were performed on each variable by varying across likely ranges, with five two-way sensitivity analyses based on clinical relevance. In a probabilistic sensitivity analysis, 1000 parameter values were simulated from each parent distribution to obtain mean and 95% credible interval (CrI).

Results:
In the base case, utility and life expectancy were greater with treatment. Utility was 16.1 QALYs in treatment and 14.4 with observation. Life-expectancy was 22.4 years in treatment and 19.7 with observation. Treatment was superior to observation in all deterministic sensitivity analyses when measuring utility. Life-expectancy was greater with treatment than observation in all scenarios except for when the hazard ratio of early culture conversion was 1, in which case it was a toss-up. In the probabilistic sensitivity analysis, treatment led to an increase in 1.99 QALYs (95% CrI 0.53-3.89) and 2.65 life-years (95% CrI 1.20-4.19).

Conclusions:
In microsimulation, MAC-PD treatment leads to prolonged survival with greater utility. Findings were robust across multiple sensitivity analyses. We hope that this aids patients and physicians in guiding disease management.

Abstract 5

Management of vasculitis-associated alveolar hemorrhage: A Bayesian reanalysis of PEXIVAS

Omri A Arbiv (1-5), Lee Fidler (2-4), Andrea S Gershon (1-4), Kuan Liu (1)

1. Institute of Health Policy, Management, and Evaluation, University of Toronto, Toronto, ON. 2. Division of Respirology, University of Toronto, Toronto, ON. 3. Division of Respirology, Sunnybrook Health Sciences Centre, Toronto, ON. 4. ICES, Toronto, ON. 5. Clinician Investigator Program, University of British Columbia, Vancouver, BC

Introduction & Objectives:
Diffuse alveolar hemorrhage (DAH) is a life-threatening manifestation of antineutrophil-cytoplasmic antibody-associated vasculitis (AAV). PEXIVAS was a randomized-controlled trial that showed that plasma exchange (PLEX) did not improve outcomes in patients with AAV, and that a reduced-dose glucocorticoid taper was non-inferior to standard-dose taper. However, few patients in PEXIVAS had DAH, limiting generalizability. We used a Bayesian approach to reanalyze PEXIVAS to evaluate these interventions on patients with DAH.

Methods:
PEXIVAS enrolled adults with granulomatosis and polyangiitis or microscopic polyangiitis with either DAH or kidney injury. Individuals were randomized in 2x2 design to PLEX or no PLEX and glucocorticoid taper (standard or reduced). Our outcome was hazard ratio (HR) of 1 year survival. Published results were used modelled as a log-normal distribution using a non-informative prior, implying no prior belief. We obtained the posterior mean HR, 95% credible interval (CrI), and probability that PLEX reduced mortality (HR <1) by calculating area under the curve of each posterior distribution.

Results:
704 individuals were recruited, of which 191 had DAH. Mean HR with PLEX was 0.45 (95% CrI 0.14-1.42) for those with DAH and 0.86 (95% CrI 0.43-1.71) without DAH. We found that PLEX led to a 67% probability of increased survival in those without DAH, but a 93% probability of increased survival in those with DAH. With a reduced-dose glucocorticoid taper, individuals without DAH had a mean HR 0.46 (95% CrI 0.22-0.95), whereas those with DAH had a mean HR 1.33 (95% CrI 0.57-3.11). Reduced-dose glucocorticoids led to 98% probability of reduced mortality overall, but 74% probability of increased mortality in the subset with DAH.

Conclusion:
Individuals with AAV with DAH may benefit from PLEX and derive greater harm from a reduced-dose glucocorticoid taper. This suggests the need for review of treatment strategies in this subpopulation.

Abstract 6

Midbrain somatostatin cells stimulate breathing and motor activity in rodents in vivo

Kayla S. Baker (1, 2), Carolina Scarpellini (2), Gaspard Montandon (1, 2, 3)

1. Institute of Medical Science, University of Toronto, Toronto, Ontario, Canada. 2. Keenan Research Center for Biomedical Science, St. Michael's Hospital, Unity Health Toronto. 3. Departments of Medicine and Pharmacology & Toxicology, University of Toronto.

Introduction: Breathing is an essential function that is automatically generated by neural circuits in the medulla. Although breathing is mostly an automatic process, it is highly flexible and can change during behaviors requiring activation of respiratory muscles, such as sniffing or vocalization. Respiratory neural circuits receive projections from many brain regions so respiratory muscles can be modulated to accommodate motor behaviors. The periaqueductal grey matter (PAG) located in the midbrain sends projections to the medulla. While the PAG is not involved in the automatic production of breathing, it is involved in coordinating autonomic functions such as breathing with behaviours. However, the types of PAG neurons involved in breathing and their functions remain unclear. Somatostatin (SST), an inhibitory neuropeptide found in the medulla but also in the ventrolateral PAG (vlPAG) may be involved in modulating breathing. In addition, SST PAG cells are involved in neuropathic pain. Here, we aim to determine the role of SST vlPAG neurons in modulating respiratory rhythm and their role in motor behaviours such as motor response to pain.

Methods: We used optogenetics to selectively activate SST vlPAG cells while measuring respiratory activity with whole-body plethysmography and motor behaviors with video recording in freely-behaving mice.

Results: We observed that photostimulation of SST vlPAG cells stimulates breathing while simultaneously increasing locomotor activity. To determine whether changes in respiratory activity were due to increased motor activity, we performed the same experiments in anesthetized mice and found that photostimulation of SST vlPAG neurons increased respiratory activity.

Conclusion: Our results suggest that stimulation of SST vlPAG neurons independently modulated respiratory and motor activity and may be involved in the modulation of respiratory muscle activity to produce non-respiratory behaviors.

Abstract 7

A CD8+ CD27+ TIM-3+ T cell cluster uniquely present in human lungs with chronic lung allograft dysfunction (CLAD)

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Latner Thoracic Research Laboratories

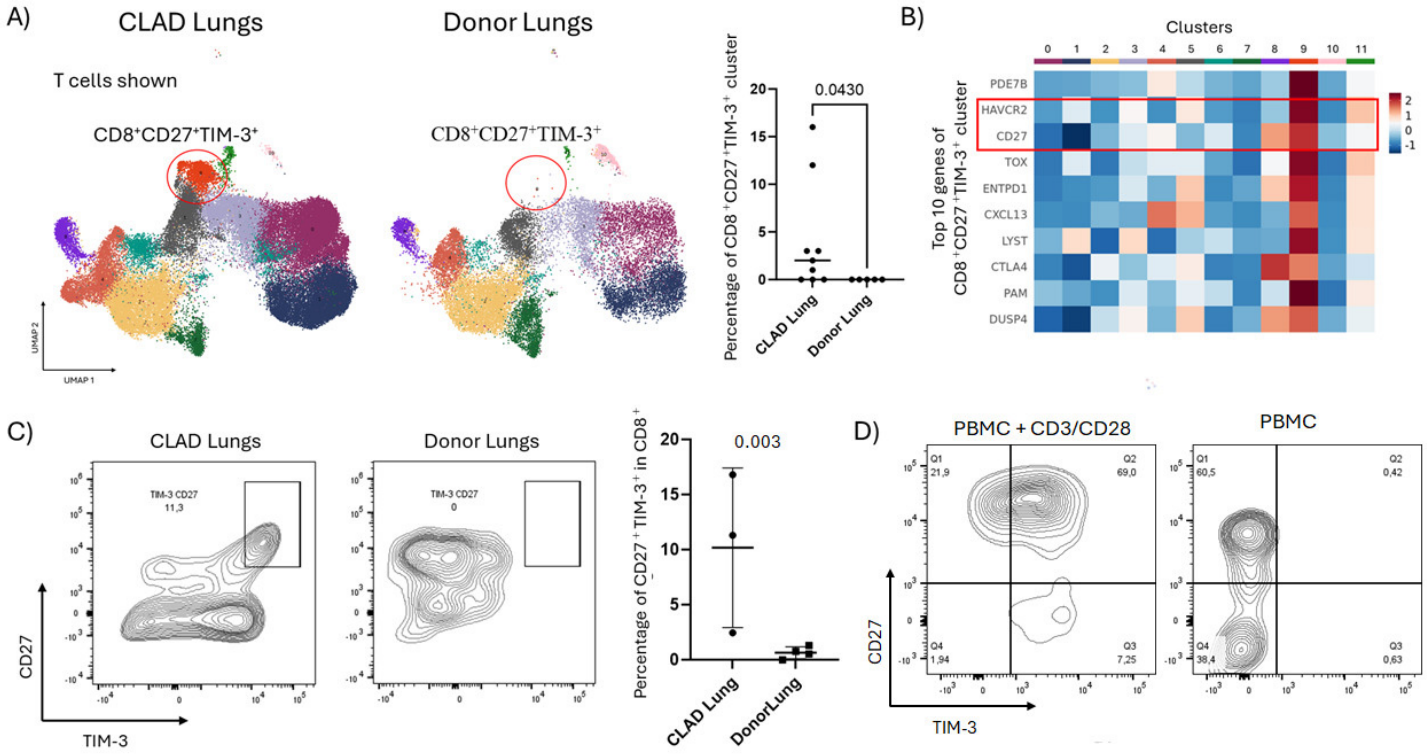
Long-term survival in lung transplantation is limited by the eventual development of chronic lung allograft dysfunction (CLAD), resulting in the loss of the transplanted lung. We hypothesized that analysis of the pulmonary T cell transcriptome would reveal novel T cell populations that drive CLAD pathogenesis.

Human lung tissue samples (9 CLAD, 5 donor as healthy control) were obtained and processed into single cell suspensions. T cells were enriched through magnetic selection of CD45+ leukocytes followed by fluorescence-activated cell sorting. Sorted cells then underwent 5' single cell RNA sequencing (scRNAseq) using 10x Genomics. scRNAseq data was analyzed using Seurat. T cell clusters of interest were validated at the protein level using spectral flow cytometry. Healthy peripheral blood mononuclear cells (PBMCs) were exposed to CD3/CD28 beads to determine factors driving expression of TIM3 and CD27.

Comparison between lung samples revealed a cluster that was only present in CLAD samples (6/9 CLAD lungs vs. 0/5 donor lungs, Fig A), characterized by RNA expression of CD8, CD27 and HAVCR2 (TIM-3, Fig B). A chemokine, CXCL13, known for B cell recruitment, appears to also be highly expressed in this cluster compared to other T cell clusters. Flow cytometry analysis of T cells from CLAD lungs (n=3) and donor lungs (n=4) similarly showed that CD8+ CD27+TIM-3+ T cells were uniquely present in CLAD lungs (Fig C). Preliminary results showed that stimulation with CD3/CD28 beads resulted in expression of TIM3 and CD27 co-expression in PBMC CD8+ T cells after 7 days (Fig D). We conclude that a CD8+ T cell population expressing CD27 and TIM-3 is enriched in CLAD lung T cells. This phenotype is suggestive of a memory/exhaustion state that arises from chronic antigen stimulation and could play an important role in CLAD.

Acknowledgement: CLAD processing team.

Figure for abstract 7.



Abstract 8

Risks Factors for COPD among Never Smokers in Ontario, Canada

Alina Blazer (1, 2), Zhiyin Li (2), Jun Guan (2), Teresa To (3), Matthew Stanbrook (1,2), Andrea S. Gershon (1,2,4)

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RATIONALE
While chronic obstructive pulmonary disease (COPD) is traditionally associated with smoking, up to 30% of the global COPD burden occurs in never smokers. Understanding non-traditional risk factors is thus essential for developing new treatments and prevention strategies. This study aimed to identify risk factors for never-smoking-related COPD in Ontario, Canada using a real-world population cohort.

METHODS
We conducted a longitudinal, population-based cohort study using provincial health administrative databases linked to survey data. Adults above age 35 years residing in Ontario between 2000/2001 to 2018/2019 with survey-recorded smoking information were included. Individuals with COPD were identified using a validated case definition. Multivariable logistic regression models assessed associations stratified by smoking status. Analyses were performed using SAS (SAS Institute, Cary, North Carolina, USA).

RESULTS
The total cohort comprised 151,290 individuals, with 48.4% characterized as never smokers. COPD prevalence in never smokers was 9.7%, constituting 25.1% of all identified COPD cases. Never smokers with COPD were diagnosed at an older age (median 72 vs 64) and were predominantly female (67.1%). Asthma history was found to have the highest association with risk of incident never-smoking COPD (aOR 3.95). Other significant associations included high comorbidity (aOR 2.73) and previous respiratory disease (aOR 2.3Environmental tobacco smoke was a notable risk factor, more so for smokers (aOR 1.86) than never smokers (aOR 1.32). Elevated BMI (>30 kg/m²) was associated with COPD only in never smokers (aOR 1.32). Of air pollutants, only PM2.5 was linked to COPD, similarly in both groups. Female sex (aOR 0.86) and higher education levels were protective in never smokers.

CONCLUSIONS

As smoking rates in high-income countries decline, the relative importance of never smoking COPD will increase. This large-scale cohort study identifies key independent risk factors and highlights the significant burden of COPD in never smokers.

Figure for abstract 8.

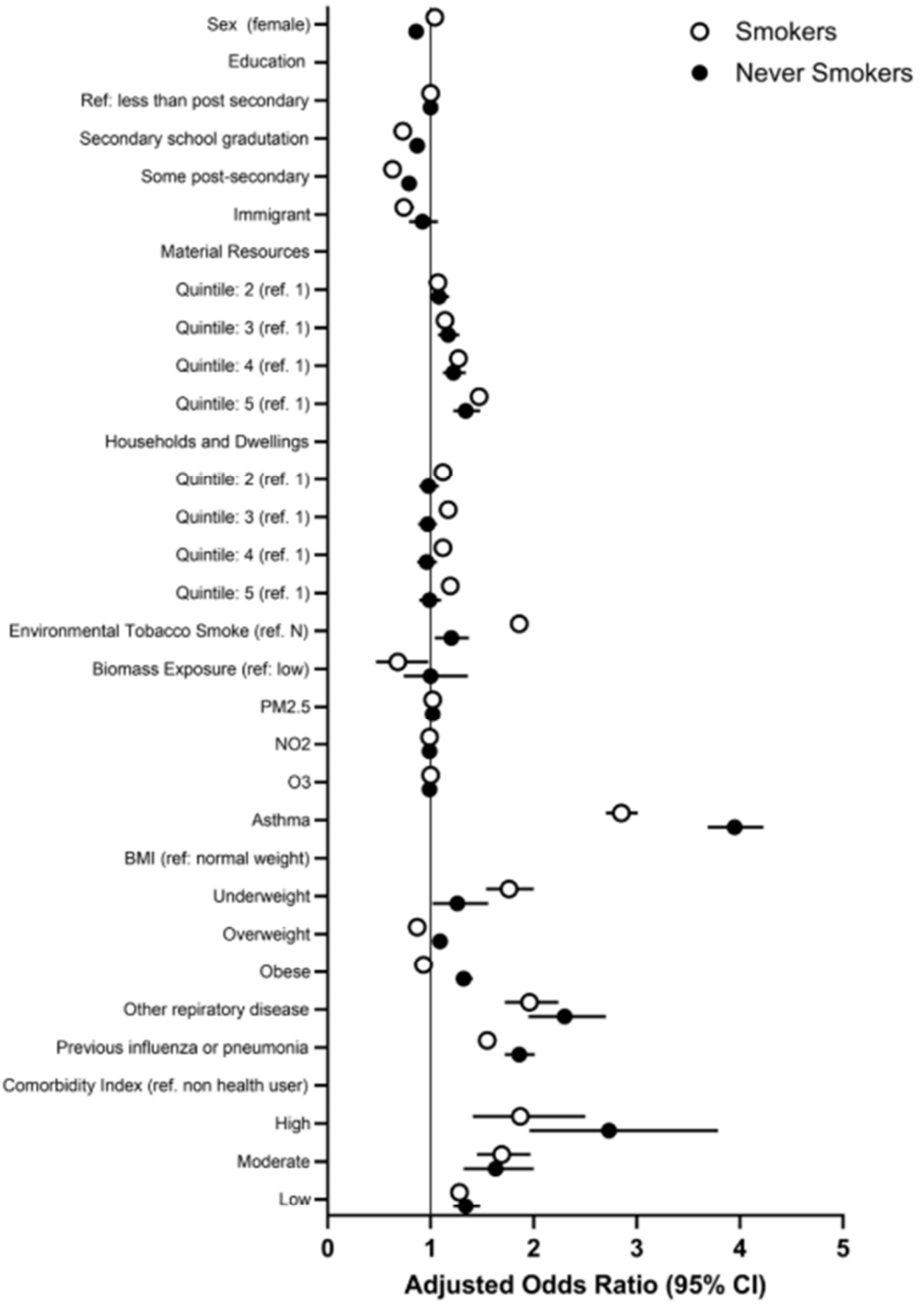

Figure 1. Forest plot depicting adjusted odds ratios (95%CI) for major risk factors for incident COPD in never smokers and smokers

Abstract 9

Connected Care COPD: A Community-Led Pathway for Early Detection and Intervention

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Background
Chronic obstructive pulmonary disease (COPD) is a global health crisis. Up to 5% of adults live undiagnosed, leading to treatment delays and worsened health outcomes. The Connected Care COPD pathway, co-developed by the University Health Network and Toronto Paramedic Services, offers a community-based approach to early detection and care.

Objective
To co-design, implement, and evaluate a care pathway, leveraging paramedic expertise, that improves early diagnosis, optimizes care delivery, and reduces healthcare utilization.

Methods
A multidisciplinary team co-designed and launched the pathway in April 2024, with paramedic-led Wellness Clinics in high-priority settings such as Naturally Occurring Retirement Communities (NORCs) in Toronto, Canada. Clinics provided screening, spirometry, education, and tailored care plans.

Results
The program launched at 3 NORCs with 1521 residents, 62% aged >65 years. Of the 117 residents (7.7%) participating in 4 clinics, 14 (12%) met criteria for further investigation of COPD based on a standardized screening questionnaire (mean age 72; 64% female). Mobile spirometry identified airway obstruction in 2 individuals, suggesting likely COPD. Care coordination led to 2 respirology referrals and 3 primary care referrals. Overall undiagnosed COPD prevalence was 1.7% (2/117) among total participants and 14% (2/14) among those screening positive.

Conclusions
The Connected Care COPD program integrates paramedic-led services to bridge community and hospital care, providing a scalable model for COPD detection and management. Future plans include expanding to more high-risk populations and refining long-term evaluation metrics to improve patient outcomes.

Abstract 10

Chronic Lung Allograft Dysfunction (CLAD) is Characterized by Elevated Basal Cell but Not Club Cell Proliferation

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Introduction & Objectives: CLAD is the major barrier to long-term survival in lung transplant recipients. While depletion of club cells has been implicated in CLAD, underlying mechanisms remain unclear. Our preliminary imaging mass cytometry data showed reduced proliferation of club cells compared to basal cells in CLAD lungs (n=8). We hypothesized that CLAD involves inadequate proliferation of club cells compared to basal cells and compared to homeostatic conditions of control lungs.

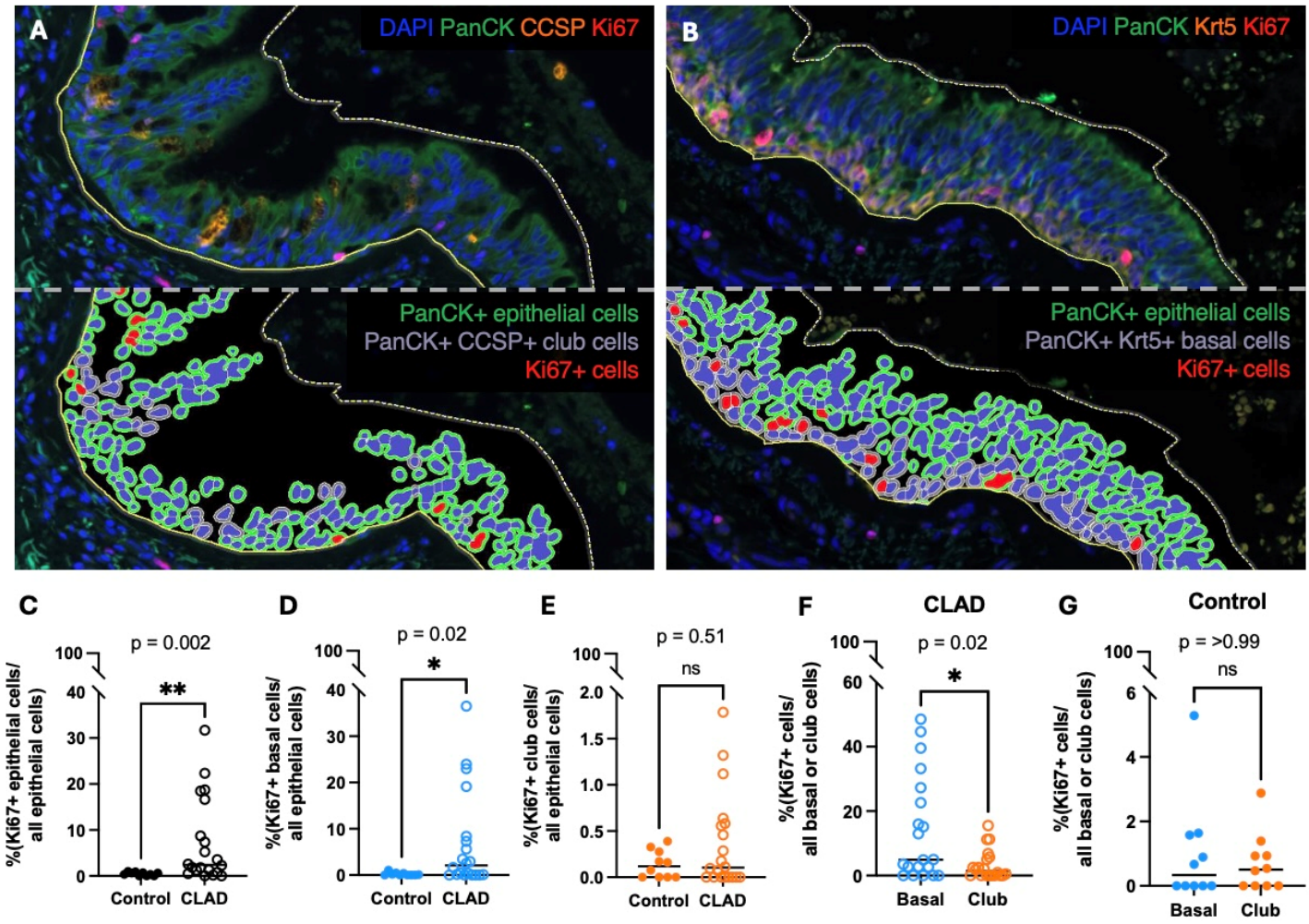
Methods: CLAD lung explants were collected from lung transplant recipients undergoing retransplantation (n=20) 2015-2018. Control lung samples were obtained from discarded excess donor lung tissue (n=10). Club and basal cell proliferation was evaluated using immunofluorescence on formalin-fixed paraffin-embedded tissue sections. Images were analyzed using the HALO software.

Results: Epithelial cells were identified as pan-cytokeratin (panCK) positive, club cells as panCK and club cell secretory protein (CCSP) double-positive, and basal cells as panCK and keratin-5 (Krt5) double-positive, with proliferating cells defined by Ki67 expression (Fig. A-B). Overall epithelial cell Ki67 expression is increased in CLAD compared to control lungs ($p=0.002$). While the proportion of Ki67+ basal cells among all epithelial cells is increased in CLAD ($p=0.02$), the proportion of Ki67+ club cells among all epithelial cells remains similar to that of control lungs (Fig. C-E). The proportion of Ki67-expressing cells is higher among basal cells compared to club cells in CLAD lungs ($p=0.02$), whereas these proportions are similar in control lungs (Fig. F-G).

Conclusions: Our data show that overall small airway epithelial cell proliferation is increased in CLAD, primarily driven by basal cell proliferation. Club cells seem to contribute minimally to epithelial cell renewal in CLAD lungs. Future studies will focus on potential etiologies and mechanisms that may modulate club cell proliferation in CLAD.

We would like to acknowledge the CGS-M, University of Toronto's URF, NSERC USRA, and the Cystic Fibrosis Foundation for the funding. We would also like to thank the TLTP biobank team for help with sample collection, TLTP database team for help with clinic.

Figure for abstract 10.



(A-B) (top) Representative immunofluorescence, (bottom) HALO software cell quantification and analysis.
(C-G) Graphs showing cell quantification. Groups were compared using Mann-Whitney U tests.

Abstract 11

Prognostic Role of Sleep Variables in Mortality of Heart Failure Patients with Cheyne-Stokes Respiration in the ADVENT-HF Trial

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Background: Among patients with heart failure with reduced ejection fraction (HFrEF) enrolled in ADVENT-HF, we showed that longer Cheyne-Stokes respiration (CSR) cycle length (CL) and lung-to-finger-circulation-time (LFCT) are associated with higher mortality. Herein, we aimed to develop a model to predict mortality using polysomnographic (PSG) and demographic variables.

Methods: From baseline PSGs, we analyzed 20 CSR cycles from the beginning of one apnea to the beginning of the next in N2 sleep then average values for all 20 cycles to derive a mean CL. In addition, the following variables were assessed and averaged for the same 20 cycles: apnea length (AL), hyperpnea length (HL), LFCT from the end of an apnea to the time of the minimum arterial oxyhemoglobin saturation (SaO2) measured from a finger oximeter resulting from that apnea and time to peak tidal volume (TPTV) from the end of an apnea until the peak tidal volume reached during the subsequent hyperpnea. We also included routine demographic data collected at the time of the PSG. In 195 patients with HFrEF (of whom 59 died over a maximum 5-year follow-up), we developed various classifiers and feature selection techniques using these PSG variables. The models were tested on 20% of unseen data for evaluation.

Results: The most significant predictors of mortality included the average minimum (SaO2) (0.10), CL (0.09), LFCT (0.08), age (0.08), AHI (0.07), and BMI (0.07) resulting in a prediction accuracy of 75.01%, precision of 66.67%, sensitivity of 66.87%, specificity of 80.40%, and F1 score of 70.48%.

Conclusion: These findings suggest that CSR features related to cardiac output plus demographic data are significant predictors of mortality in HF patients with CSR. Our results underscore the potential significance of detailed polysomnographic analyses and routine demographic data to assist in mortality risk stratification in this population.

Abstract 12

Interstitial Lung Abnormalities in Patients Referred for Workup for Transcatheter Aortic Valve Replacement

Kevin Jia Qi Chen (1), Mariah Obino (2), Anastasia Oikonomou (2), Lee Fidler (3,4,5)

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INTRODUCTION:
Interstitial lung abnormalities (ILA) are incidental pulmonary CT findings that may represent or progress to significant interstitial lung disease (ILD). The presence of ILA in patients referred for transcatheter aortic valve replacement (TAVR) is associated with increased mortality. We aimed to determine the prevalence of ILA in TAVR patients, assess risk factors, and evaluate adherence of practice patterns to the Fleischner Society's schema on ILA management.

METHODS:
We conducted a single-centre, retrospective observational study and reviewed CT scans performed for TAVR workup from January 1, 2020 to January 1, 2024. We extracted data on clinical characteristics, risk factors, and imaging reports. We used descriptive statistics to characterize findings and regression analysis to identify predictors of ILA.

RESULTS:
CT TAVR scans from 1801 patients were reviewed. Patients with pre-established ILD (n=20) and connective tissue disease (n=4) were excluded. The prevalence of ILA was found to be 6.4% (n=118). The most common subtype was subpleural fibrotic (84%, n=99), followed by non-subpleural (12%, n=14), then subpleural non-fibrotic (4%, n=5). The pattern was consistent with UIP in 23% (n=36), probable UIP in 31% (n=27) of patients. The odds of having ILA were higher in males compared to females (OR=4.19, 95% CI [2.45,7.33]), and in smokers compared to non-smokers (OR=1.79, 95% CI [1.09-2.96]). We found that 87% of ILA cases were identified in the original CT report. Among patients with extensive disease on CT, only 34% of the CT reports suggested referral for respirology assessment. In patients with radiological features that indicate risk of progression, 18% of the CT reports suggested repeat imaging.

CONCLUSION:
ILAs are often found in patients referred for TAVR. Male sex and smoking history are risk factors for having ILA. There is room for improvement in local radiology reports regarding their adherence to guidelines on referral and follow-up recommendations.

Abstract 13

Distance Desaturation Product (DSP) in Lung Transplant Candidates

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INTRODUCTION & OBJECTIVES:
Distance Desaturation Product (DSP), the product of six-minute walk distance (6MWD) and lowest SpO2 during the 6-minute walk test (6MWT), has been identified as an important prognostic marker in chronic lung disease but not evaluated in patients on supplemental oxygen or those listed for lung transplantation (LTx). We aimed to 1) Characterize DSP in LTx candidates with interstitial lung disease (ILD) and Chronic Obstructive Pulmonary Disease (COPD) at time of listing; 2) Assess relationship between DSP and symptoms, lung and physical function, and pre-transplant outcomes.

METHODS:
We conducted a single-centre, retrospective cohort study of listed LTx candidates from July 1, 2022-June 30, 2023. We calculated DSP and adjusted for supplemental oxygen use (FiO2 on room air/FiO2 during 6MWT). We extracted data on demographics, pulmonary function tests, 6MWT, Edmonton Symptom Assessment System (ESAS), Short Physical Performance Battery (SPPB), and pre-transplant outcomes. Descriptive statistics and Spearman correlations were used to assess relationships between DSP and clinical measures.

RESULTS:
171 patients with ILD (67%) and COPD (33%) were evaluated (63±9 years, 65% males). Median time awaiting LTx was 55 [25-141] days. During the 6MWT, mean 6MWD was 326±85m, lowest SpO2 was 86±7%, and median FiO2 was 0.39 [0.33-0.51]. DSP was lower in patients with ILD (148±88m%) than COPD (176±61m%), p=0.017. DSP was lower in patients who presented to the emergency department pre-transplant (264±86m%) than those who did not (290±69m%), p=0.049. DSP was positively correlated with FEV1 (rho=0.201,p=0.009), SPPB (rho=0.429,p<0.001), and inversely correlated with MRC dyspnea (rho=-0.311,p<0.001) and ESAS dyspnea (rho=-0.241,p=0.031).

CONCLUSIONS:
DSP had low-to-moderate correlations with symptoms, lung function, physical function in LTx candidates. Patients with emergency department visits pre-transplant had lower DSP than those who did not. Further study is needed to determine if DSP may be an informative marker of exercise capacity assessments in advanced lung disease.

Funding: KC and DR receive research support from Temerty Faculty of Medicine. DR is supported by the Sandra Faire and Ivan Fecan Professorship in rehabilitation medicine.

Abstract 14

Anti-donor T cell dynamics and CLAD risk in the Assessment of Lung Allograft Rejection – Measurement of T cell immune synapses (ALARM-T) Study

Nicole Chrysler (1,2), Sajad Moshkelgosha (1), Daniel Vosoughi (1,2), Rashi Ramchandani (1), Tsukasa Ishiwata (1), Tereza Martinu (1,2), Stephen Juvet (1,2)

1. Toronto Lung Transplant Program, Ajmera Transplant Centre, Toronto General Hospital 2. Institute of Medical Science, University of Toronto

Purpose: Assessing T cell alloreactivity in lung transplant (LT) recipients may allow risk stratification and immunosuppression optimization. We have developed an imaging flow cytometry (IFC) based immune synapse detection method for quantifying and phenotyping alloreactive T cells. We hypothesized that an increase in peripheral blood alloreactive T cells in LT recipients post-LT would be associated with the development of chronic lung allograft dysfunction (CLAD).

Methods: We prospectively and longitudinally collected peripheral blood lymphocytes and monocytes from 60 LT recipients and their donors (Fig A). Donor and recipient monocytes were differentiated into monocyte-derived dendritic cells (MoDCs) while recipient T cells were isolated pre-LT and every 3 months post-LT for one year. Cells were cryopreserved, recovered for 4h MoDC-T cell coculture, fixed, stained for IFC, and immune synapses were enumerated as a percentage of T-MoDC contacts in a membrane contact gate. Alloreactive T cell frequencies were normalized to the lymphocyte count at each time point (Fig A). CLAD was defined by ISHLT criteria, and results from the first 23 patients are presented here.

Results: Anti-donor T cell counts increased from pre-LT to 6 months post-LT in patients developing CLAD within 5-years ($p=0.0002$, Fig B). In contrast, patients who did not develop CLAD within 5-years post-LT showed a significant decrease in alloreactive T cell count from pre-LT to 6 months post-LT ($p=0.0004$, Fig C). Pre-LT memory CD4+ T cells dominate the alloreactive compartment in patients with later CLAD by 5 years (Fig D).

Conclusions: Our data suggest that T cell alloreactivity changes within the first 6 months post-LT, as identified by our immune synapse detection assay, may impact graft outcome, with pre-LT anti-donor memory T cells linked to CLAD. Ongoing full cohort analysis will clarify the link between alloreactive T cells, CLAD, and other outcomes, considering clinical variables.

Research supported by the Toronto Lung Transplant Program

Figure for abstract 14.

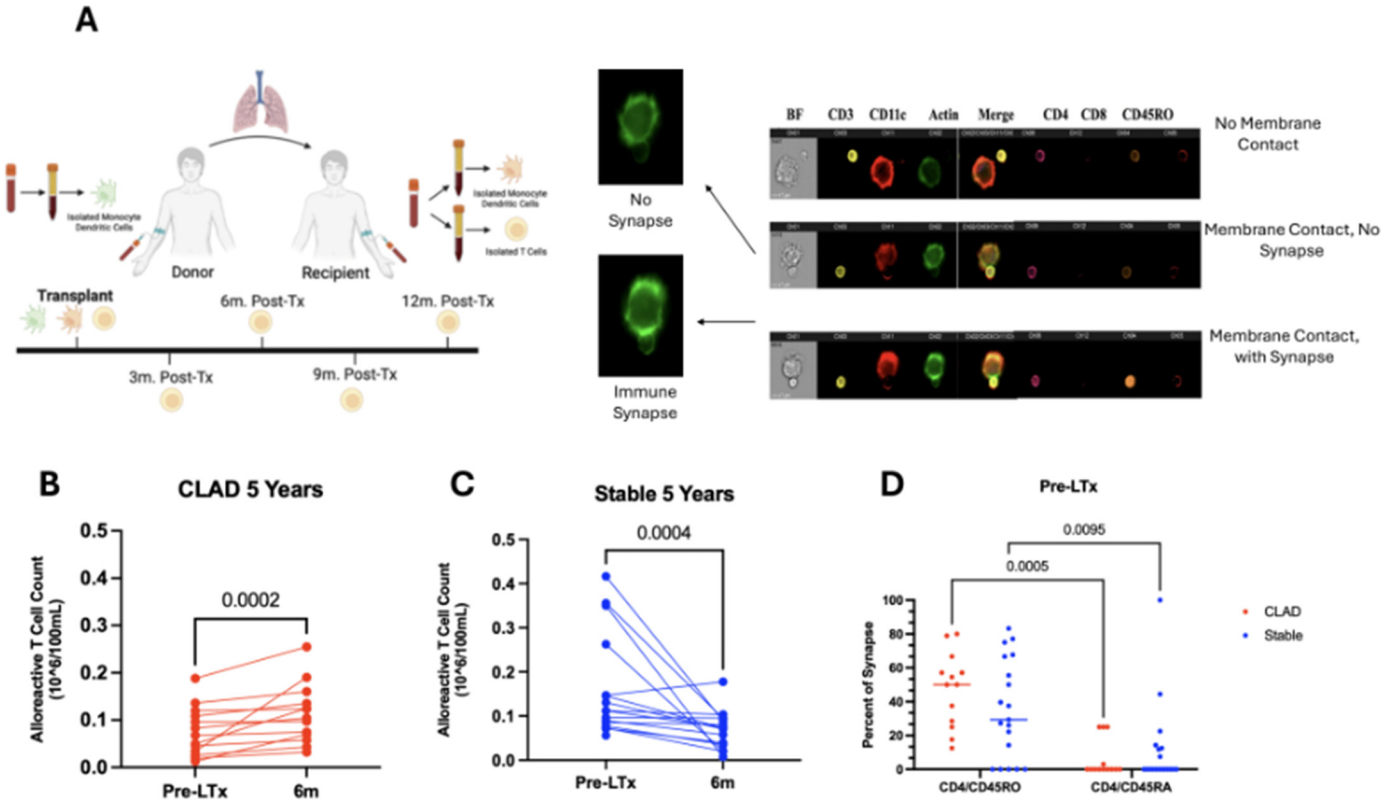

Fig. 1 Immune synapse detection as a tool of T cell alloreactivity. A) Left panel, timeline of sample collection. Right panel shows examples of T-MoDC doublets with and without membrane contact. **B)** Pre-LT alloreactive T cell count compared to 6 months post-LT of patients with CLAD 5 years post-LT (n= 17). **C)** Pre-LT alloreactive T cell count compared to 6 months post-LT of patients that remained stable 5 years post-LT (n=24). **D)** Pre-LT alloreactive CD4+ T cell subsets categorized by CLAD status, displaying the frequencies of CD4+/CD45RO+ memory and CD4+/CD45RA+ naïve cells in CLAD and stable patients (n=42).

Abstract 15

Establishing Excellence in Care: The Respirology Program for Ehlers-Danlos Syndromes (EDS) and Generalized Hypermobility Spectrum Disorder (G-HSD)

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Introduction & Objectives: EDS/G-HSD are genetic connective tissue disorders with multi-system manifestations, including respiratory sequelae. This population has a high prevalence of dyspnea, cough, and exercise intolerance, resulting from a complex interplay of structural, functional, and inflammatory contributors. The EDS Respirology Program, part of the GoodHope EDS Program at Toronto General Hospital, is the only clinic in Canada offering multidisciplinary, tailored respiratory care for individuals with EDS/G-HSD. We aim to describe the management pathway implemented within this program.

Methods: We conducted a qualitative description of the EDS/G-HSD Respirology Program, which launched in July 2017. Common reasons for referral, diagnostic tools, and management strategies are presented.

Results: 4367 new patients (March 2017-September 2024) were assessed at the GoodHope EDS clinic. The most common specialties consulted were rehabilitation (n=1311), pain management (n=735), psychology (n=715), dietitian (n=485), gastroenterology (n=338), cardiology (n=262), immunology (n=175), and respirology (n=46). The most common reasons for respirology referral were exertional dyspnea and respiratory sequelae including asthma, atopic symptoms, exertional intolerance, diaphragmatic dysfunction, and sleep disordered breathing. Individuals with EDS/G-HSD undergo routine pulmonary function tests and thoracic imaging, with additional muscle strength testing, diaphragm ultrasounds, laryngoscopy, sleep studies, and exercise assessments, including cardiac autonomic function. Exercise training focuses on aerobic, resistance, stretching, and proprioception exercises at the GoodHope Exercise and Rehabilitation program to help manage symptoms. Further, education for self-management and community resource engagement support is discussed for a holistic care delivery model. Additional management strategies for respiratory manifestations include pharmacotherapy, inspiratory muscle training, compression vests, and dysautonomia management.

Conclusion: The GoodHope EDS/G-HSD Respirology Clinic provides a comprehensive, multidisciplinary model for addressing respiratory concerns in EDS/G-HSD. Ongoing initiatives aim to refine diagnostic strategies, optimize care, and improve overall quality of life in this complex patient population.

Funding: University Health Network; Sandra Faire and Ivan Fecan Professorship in Rehabilitation Medicine.

Abstract 16

In vitro characterization of pro-inflammatory LILRB2+ and pro-fibrotic SPP1+ pulmonary macrophages in chronic lung allograft dysfunction

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Introduction & Objectives: Chronic lung allograft dysfunction (CLAD) is the leading cause of death in lung transplant recipients. Our preliminary single cell RNA sequencing data has identified two macrophage (MΦ) subsets enriched in CLAD: a pro-inflammatory subset with high expression of interferon-γ induced genes and transcripts associated with phagocytosis (LILRB2+ MΦ) and a pro-fibrotic subset with high inferred interactions with fibroblasts (SPP1+ MΦ). We hypothesize that LILRB2+ and SPP1+ MΦ drive inflammation and fibrosis in CLAD, respectively.

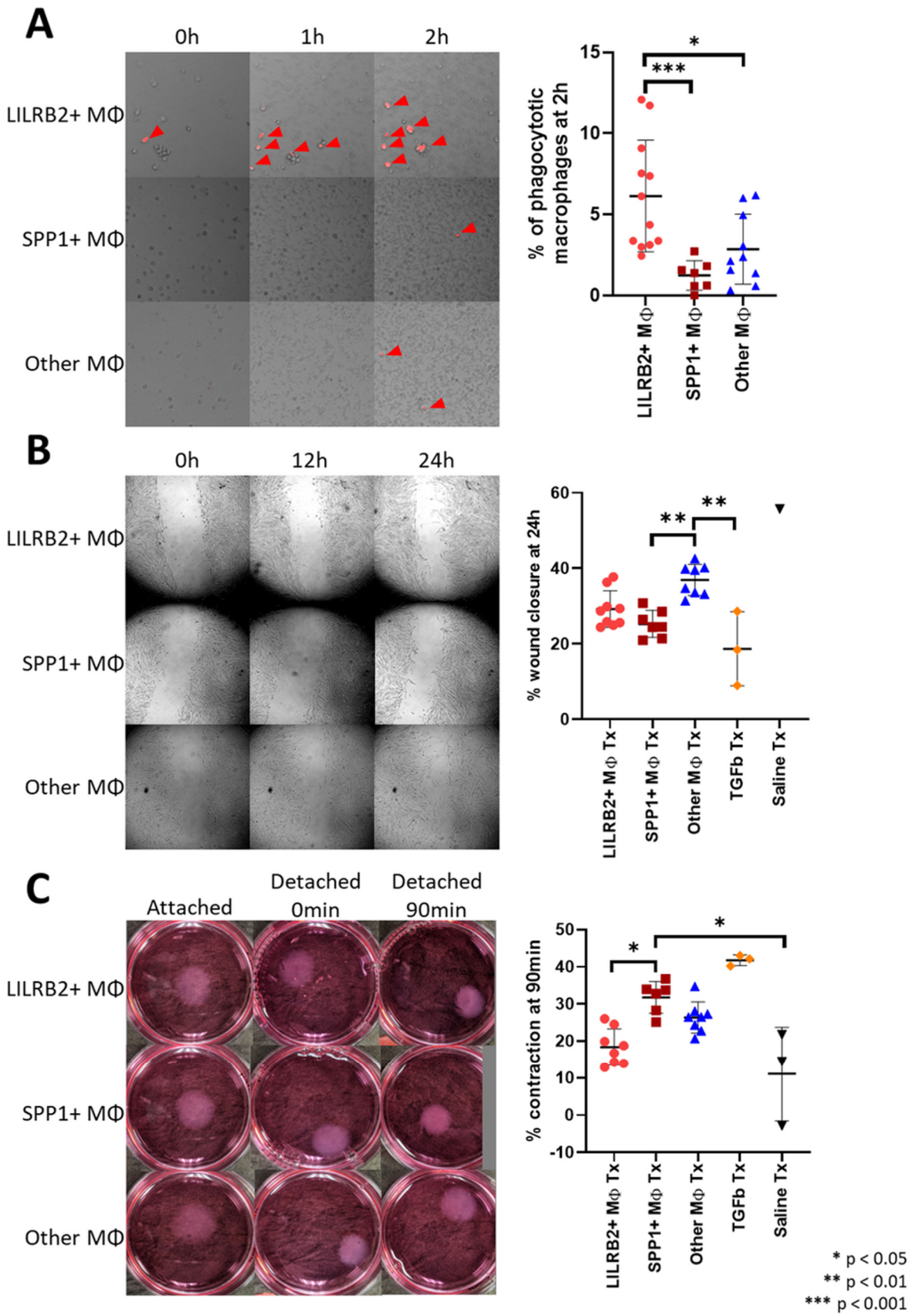
Methods: Thawed single cell suspensions of CLAD (n = 9) and non-CLAD (n = 3) lungs underwent spectral-enhanced fluorescence-activated cell sorting to isolate LILRB2+, SPP1+, and LILRB2- SPP1- (Other) MΦ. Sorted MΦ were cultured for 24 hours. Following culture, supernatants were harvested, and a phagocytosis assay was performed and imaged every 30min for 2h. MRC-5 lung fibroblast cells were grown in media supplemented with SPP1+ MΦ, LILRB2+ MΦ, Other MΦ supernatant, transforming growth factor beta (TGFβ, 2ng/ml), or saline until reaching confluency. A wound healing assay was performed, with the closure of in vitro scratch wounds imaged every hour for 24h to assess fibroblast migration. After imaging, the treated MRC-5 fibroblasts were embedded within collagen gels. Reduction in gel diameter following detachment was measured as an indicator of fibroblast contraction.

Results: A significantly higher proportion of LILRB2+ MΦ demonstrated phagocytosis at 2h when compared with SPP1+ and Other MΦ (Figure 1A). MRC-5 fibroblasts treated with SPP1 MΦ supernatant showed significantly reduced migration at 24h post-scratch compared to fibroblasts treated with Other MΦ supernatant comparable to TGFβ treated fibroblasts (Figure 1B). Fibroblast-populated collagen gels treated with SPP1+ MΦ showed greater contraction than those treated with LILRB2+ and Other MΦ (Figure 1C).

Conclusions: LILRB2+ MΦ exhibit greater phagocytic capacity compared to other pulmonary MΦ, which is likely associated with interferon-γ activation and inflammation. SPP1+ MΦ likely influence fibroblasts through soluble factors, reducing fibroblast migration and promoting greater contraction, which is associated with increased fibrosis. Altogether, LILRB2+ and SPP1+ MΦ, which are enriched in CLAD lungs, may contribute to inflammation and fibrosis. Additional in vitro assays will further characterize these MΦ subsets and their roles in inflammation and fibrosis.

Supported by: Canadian Society of Transplantation Research Training Award, Sanofi Award

Figure for abstract 16.



Abstract 17

Hospitalization Trends and Risk Factors in Rheumatoid Arthritis Related Interstitial Lung Disease: An Observational Study from Ontario, Canada

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Introduction & Objectives: Rheumatoid arthritis (RA) related interstitial lung disease (RA-ILD) represents an important disease manifestation of RA. There is a scarcity of population level information on hospitalization rates in RA-ILD. We aimed to describe the current rates and trends in all-cause and RA-ILD related hospitalizations in patients with RA-ILD.

Methods: We performed a retrospective observational study using health services data from Ontario, Canada between 2003 and 2022. We identified people with RA-ILD using the Ontario Rheumatoid Arthritis Database and required repeated physician claims for ILD prior to cohort entry. We estimated age- and sex-standardized annual all-cause and RA-ILD related hospitalization rates during the study period. We performed multivariable logistic regression to ascertain factors associated with a RA-ILD diagnosis during a hospitalization and generated a Fine-Gray subdistribution hazards regression model with competing risks to assess the time to RA-ILD related hospitalization.

Results: We identified 7,075 people with RA-ILD during the cohort period. Standardized all-cause hospitalization rates increased from 6.4 to 12.9 admissions per 100,000 population between 2003 and 2022 (101% increase, $p<0.001$). RA-ILD related hospitalizations increased from 2.6 to 3.5 admissions per 100,000 (37% increase, $p=0.045$). In-hospital mortality from RA-ILD related admissions was 19.5 deaths per 100 admissions in 2022, having remained stable over time ($p=0.62$). Patients in the lowest income quintile [OR 1.35 (1.06-1.72), $p=0.02$] and residing in rural areas [OR 1.37 (1.11-1.70), $p=0.004$] were more likely to be diagnosed with RA-ILD during a hospitalization. Patients diagnosed with RA-ILD during a hospitalization had an increased hazard for future RA-ILD related admissions [HR 1.44 (1.24-1.68), $p<0.001$].

Conclusions: All-cause and RA-ILD related hospitalizations are increasing. In hospital mortality has not changed over time but remains substantial. Socioeconomic factors are associated with receiving an RA-ILD diagnosis in hospital, which appears to be an important risk factor for future RA-ILD related admissions.

Abstract 18

Combined Spirometry and Oscillometry Score at 3 months Post-Transplant is Associated with Chronic Lung Allograft Dysfunction

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Background: Long-term survival after lung transplant is limited by chronic lung allograft dysfunction (CLAD), defined as a >3-month sustained drop in the FEV1 (forced expiratory volume in 1 second) to ≤ 80% of the highest value achieved post-transplant. Oscillometry is a highly sensitive pulmonary function test (PFT). We hypothesize that oscillometry at 3 months post-transplant is associated with CLAD.

Methods: Double lung transplant recipients were enrolled for oscillometry at the first post-transplant PFT lab visit. The cohort comprised of patients enrolled from December 2017- March 2020 with ≥ 3 years follow-up. We included patients who died within 3 years if a CLAD diagnosis was ascertained. We excluded re-transplantation and patients missing 3-month oscillometry-spirometry data. Statistical analysis used the Mann-Whitney U and Pearson's chi-square tests for group comparisons and logistic regression to assess the associations between PFTs and CLAD, and receiver operator characteristic curves to identify the optimal discriminatory threshold value for CLAD for each parameter.

Findings: In the cohort, 75 patients developed CLAD while 129 remained CLAD-free at 3 years post-transplant. The pre-and peri-operative characteristics of CLAD and CLAD-free patients were similar. At 3 months post-transplant, CLAD patients had lower %FEV1 and FEV1/FVC (forced vital capacity), and worse lung mechanics with high R5 (resistance at 5 Hz), low X5 (reactance at 5 Hz) and high AX (area of reactance). %FEV1, FEV1/FVC, AX, R5 z-score, and R5-19 (difference in resistance from 5 to 19 Hz) were independently associated with CLAD. AX exhibited the highest area under the curve (AUC: 0.86) while %FEV1 had the highest AUC (0.78) among the spirometry metrics. A 5-parameter ordinal score composed of %FEV1, FEV1/FVC, AX, and %R5 provided the strongest association with CLAD.

Conclusions: A combined spirometry-oscillometry score at three months post-transplant provides risk stratification of future CLAD. Earlier interventions could minimize the risk of CLAD.

The study was funded by the CIHR-NSERC Collaborative Health Research Projects and the Peterborough K.M. Hunter Charitable Foundation Graduate Award (AF). Dr. Hantos is supported by Hungarian Scientific Research Fund Grant K128701. We thank all the Toronto

Abstract 19

Predicting the Occurrence of Baseline Lung Allograft Dysfunction at 1-year Post Bilateral Lung Transplant using Machine Learning with 6-month Oscillometry and Quantitative CT

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Introduction: Failure to achieve normal lung function after lung transplant (LTx), known as baseline lung allograft dysfunction (BLAD), increases the risk for impaired survival.1 Pre-/peri-operative clinical features have been shown to be associated with future BLAD.1,2 However, it is unknown if measurements reflecting lung structure/function, such as post-LTx oscillometry or quantitative computed tomography (qCT), can predict BLAD.

Objectives: To evaluate machine learning (ML) model performance for predicting BLAD at 1-year post-LTx using combinations of pre-/peri-operative clinical, and 6-month post-LTx oscillometry and qCT features.

Methods: Patients from Toronto General Hospital who underwent bilateral-LTx and had sufficient spirometry to adjudicate baseline lung function were analyzed. BLAD was defined as failure to achieve an average forced expiratory volume-in-1-second (FEV1) or forced vital capacity (FVC) ≥80% using 2 maximum values measured at-least 3 weeks apart.1,3 Pre-/peri-operative clinical (N=15) and 6-month post-LTx oscillometry (N=8) and qCT (N=6) features were included in various combinations. A random forest classifier was trained using 2-fold cross validation with hyperparameter tuning using a 50:50 training/testing split. Model performance was evaluated on the test data using the area under the receiver operating characteristic curve (AUC) and DeLong's test, while feature importance was determined through a SHapley Additive exPlanations (SHAP) analysis.

Results: The cohort of 106 patients (age=61.6±8.3; N=39 females) included 53 BLAD and 53 normal spirometry patients. The qCT-only model (AUC=0.78) outperformed the clinical-only model (AUC=0.62; $p<0.05$), but not the oscillometry-only model (AUC=0.74; $p>0.05$). Stepwise addition of oscillometry features (AUC=0.78; $p<0.05$) and qCT features (AUC=0.80; $p<0.05$) to the clinical features achieved the best performance. SHAP analysis identified the 5 most important features as inspiratory reactance, total lung volume, recipient age, lung density histogram skew, and days spent in the intensive care unit.

Conclusion: The addition of 6-month post-LTx oscillometry and qCT features to ML models incorporating pre-/peri-operative clinical features improved predictive performance for BLAD at 1-year.

References: 1Liu, et al. JHLT, 2018; 2Hanafi, et al. ERJ, 2022; 3Crapo, et al. Am Rev Resp Dis, 1981.

We acknowledge the TLTP database and the team for the data included herein.

Abstract 20

Investigating the Diagnostic Utility of a Fifth Nap in the Multiple Sleep Latency Test

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Principal Investigator: Dr. Clodagh Ryan

Background: Excessive daytime sleepiness is highly prevalent and reported in up to 25% of the general population. The determination of the underlying etiology can often be difficult. The Multiple Sleep Latency Test (MSLT) is a diagnostic tool used to elucidate whether causation is due to a central disorder of hypersomnolence. In December 2021, the American Academy of Sleep Medicine (AASM) updated the protocol for the MSLT, from a 4-nap to a 5-nap protocol. This is associated with extra cost and burden both on healthcare resources and the patient.

Objective: To investigate the diagnostic utility of adding a fifth nap to the MSLT protocol in a population of patients being worked up for central disorders of hypersomnolence.

Methods: This is a single centre retrospective review of all adult patients (age ≥ 18 years) who underwent a 5-nap MSLT at University Health Network between December 2021 and December 2023. All patients had a polysomnogram during the night before the MSLT. The mean sleep onset latency (SOL) and sleep onset rapid eye movement periods (SOREMP) after 4 and 5 naps were calculated from the same 5-nap MSLT for each patient. The primary endpoint was the number of patients whose diagnosis changed after the fifth nap opportunity.

Results: A total of 47 patients were included in the study. The mean age was 34.5 years (±14.3 years) with 27.6% of patients being male. The mean BMI was 26.7 (±6.25) and the mean Epworth Sleepiness Score was 10.5 (±4.6). Under a 4-nap protocol, 31.9% of patients reached a diagnosis and the mean SOL was 11.1 minutes. Under a 5-nap protocol, 27.7% of patients reached a diagnosis and the mean SOL was 11.9 minutes. There was no statistically significant difference in the mean SOL between the two protocols, p=0.49. The removal of the fifth nap resulted in a loss of 5 SOREMPs across the entire study population. We identified 3 patients (6.4%) who had a change in their diagnosis after the inclusion of the fifth nap opportunities. Among these 3 patients, 2 patients were no longer deemed to have central hypersomnolence, and 1 patient's diagnosis changed from idiopathic hypersomnolence to narcolepsy.

Conclusions: Among patients undergoing an MSLT at our site during the work-up of excessive daytime sleepiness, the inclusion of the fifth nap changed the diagnosis in a minority of cases.

Abstract 21

Spatial characterization of distinct B cell subsets in chronic lung allograft dysfunction

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Background: Chronic lung allograft dysfunction (CLAD), driven by chronic immune rejection, is the main factor limiting long-term survival after lung transplantation. B cells have been implicated in CLAD pathogenesis, but their recruitment, activation, and spatial distribution in lung tissue remain poorly defined. We hypothesized that CLAD is associated with altered B cell phenotypes and increased proliferation. To test this, we utilized imaging mass cytometry (IMC) to analyze B cell subsets and determine their spatial distribution in CLAD lungs.

Methods: Explanted lung tissue from 8 CLAD patients and 4 controls was formalin-fixed, paraffin-embedded, and stained with 35 metal-tagged antibodies targeting structural and immune markers. Three 1 mm^2 airway-centered regions per sample were analyzed using IMC. Data were quantified using HALO software with a focus on B cell phenotypes.

Results: As previously demonstrated, we confirmed through the HALO unbiased quantification approach, that CLAD lungs have significantly higher cellularity and B cell (CD45+CD20+) frequencies compared to controls (Renaud-Picard et al. JHLT 2025). B cells were predominantly localized within lymphoid aggregates throughout the lung tissue. B cell subsets were further characterized based on expression of additional markers that were available in the panel: Ki67 (proliferation marker), CD11c (autoimmunity-associated), and CCR6 (reported to be expressed in GC memory B cell precursors). While Ki67+ B cells were increased as a proportion of total CD45+ leukocytes, their frequency among B cells was similar in CLAD compared to controls (Fig.1A). Additionally, CLAD and control lungs have similar proportions of CD11c+ B cells (Fig.1B) and CCR6+ B cells (Fig.1C).

Conclusions: IMC enabled detailed spatial and phenotypic profiling of B cells in CLAD lungs. B cell enrichment and lymphoid aggregate formation were confirmed, suggesting a role in CLAD pathogenesis. However, the lack of increased proliferative activity supports the hypothesis that B cell accumulation results from infiltration rather than local expansion.

Figure for abstract 21.

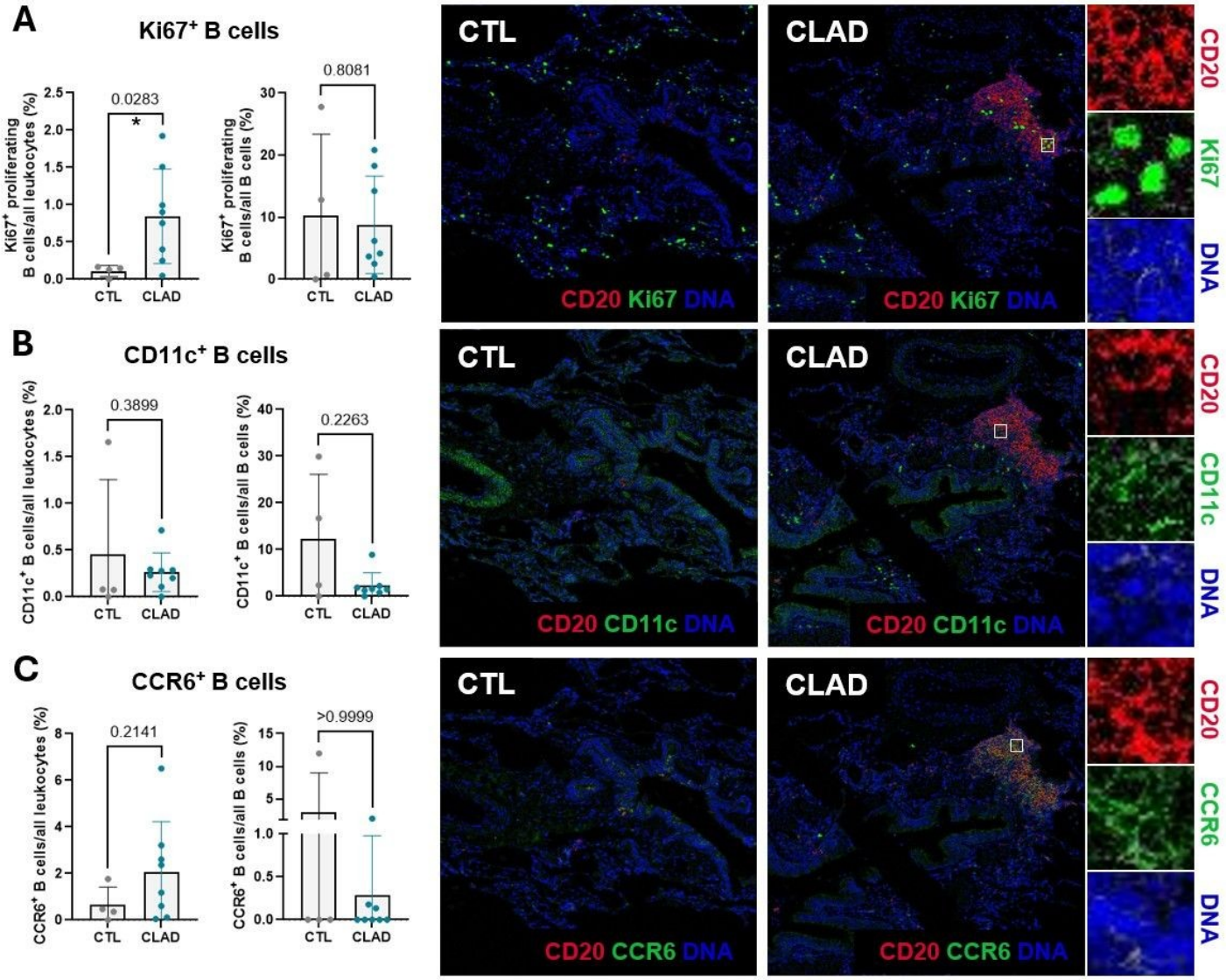

Fig 1. Quantification of **A.** CD45+CD20+Ki67+, **B.** CD45+CD20+CD11c+, and **C.** CD45+CD20+CCR6+ B cells among all CD45+ leukocytes (left) and all CD45+CD20+ B cells (right) in CLAD and controls. Cells were quantified using HALO software and groups were compared using Mann-Whitney U tests; representative imaging mass cytometry images on CLAD and control lung tissue; areas shown in white boxes have been zoomed out to show images for individual markers.

Abstract 22

Conferring tacrolimus-resistance to regulatory T cells to promote lung transplant tolerance

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Background: Lung transplantation is a lifesaving therapy for end-stage pulmonary diseases. Despite the use of immunosuppressive drugs, the median survival following transplant is only 6 years. To lessen the reliance on immunosuppressive drugs, we aim to deliver regulatory T cells (Tregs) to the donor lung prior to transplant through ex vivo lung perfusion, to promote an immunoregulatory environment around the organ. However, tacrolimus (an immunosuppressive drug given to patient's post-transplant) can have detrimental effects on Treg phenotype. Tacrolimus complexes with the FKBP12 protein, preventing NFAT de-phosphorylation and translocation into the nucleus, thereby shutting down key Treg pathways.

Objective: We aim to investigate the mechanisms by which tacrolimus-mediated NFAT inhibition influences Tregs phenotype and function and assess whether FKBP1A KO is sufficient to render Tregs resistant to tacrolimus.

Results: Preliminary experiments revealed that tacrolimus-treated Tregs differ phenotypically from un-treated Tregs. Tregs were plated in the presence and absence of tacrolimus and collected for flow cytometry. Following treatment with tacrolimus, Tregs had reduced mean fluorescence intensity of FOXP3, CD25, AREG, CD73, and LAP, and an increased CD3 MFI (Figure 1A). There was also a reduction in the percentage of FOXP3+HELIOS+ cells accompanied by an increase in FOXP3-HELIOS- cells compared to untreated groups (Figure 1B-C).

To investigate whether these differences can be rescued by FKBP12 KO, we have optimized a protocol to generate FKBP1A KO Tregs from PBMCs using an mRNA encoded cytosine base editor (Figure 2A). This approach yielded high nucleofection efficiencies, and cells remained viable throughout culture (Figure 2B-C). Conclusions/ future directions: In the future, we plan to assess whether FKBP1A KO provides these cells with a selective advantage over WT cells. We predict that these FKBPIA KO Tregs will be able resist the effects of tacrolimus, which may provide enhanced therapeutic efficacy in the context of lung transplantation.

Figure for abstract 22.

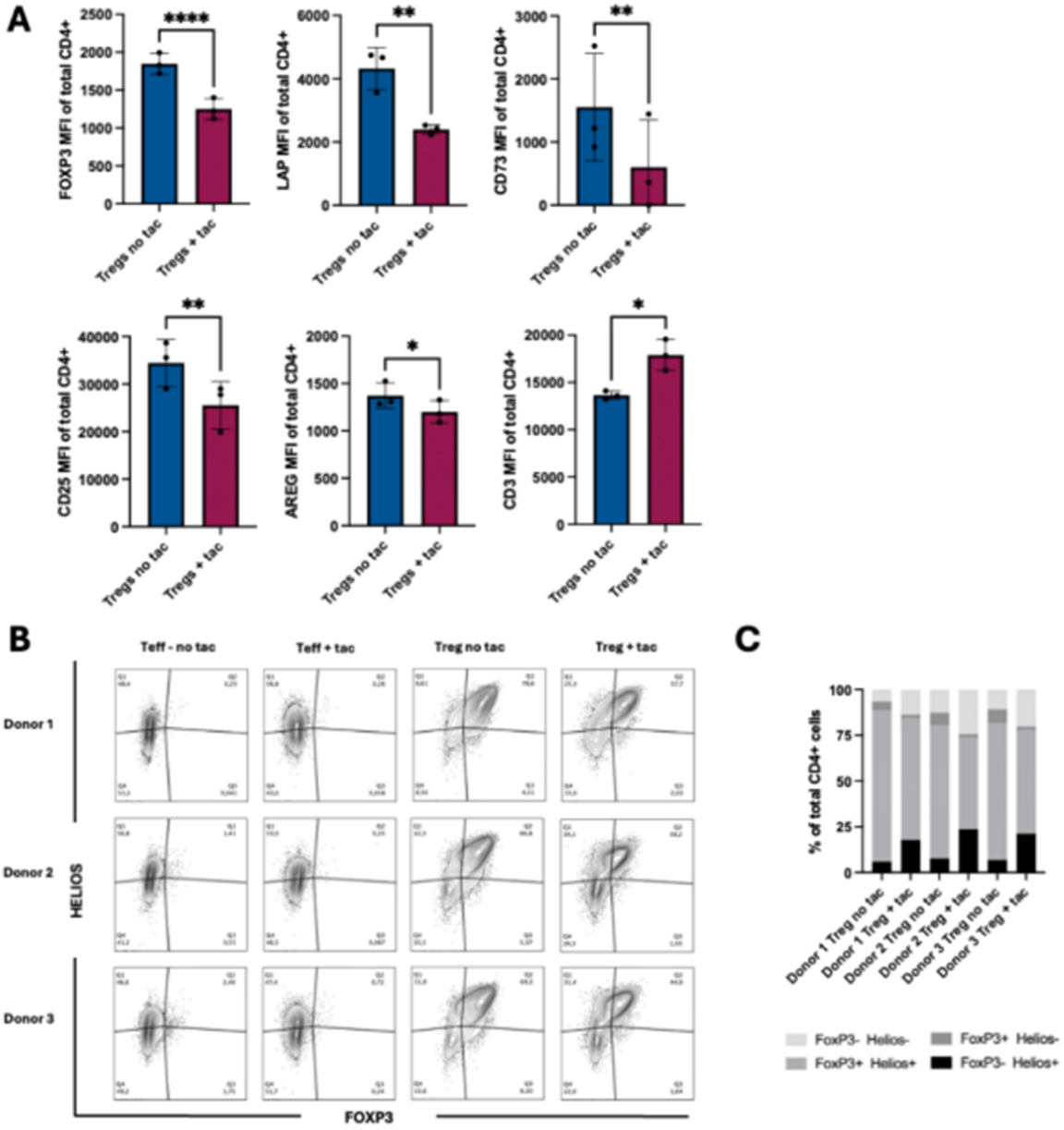

Figure 1: Phenotypic differences in regulatory T cells (Tregs) following treatment with tacrolimus. Tregs were isolated from PBMCs by sorting on CD4+ CD25^{high} CD127^{low} cells. Tregs were then stimulated with CD3/CD28 beads at a 4:1 bead:cell ratio and cultured without tacrolimus or with 40ng/mL of tacrolimus. 4 days post culture, cells were harvested and stained for flow cytometric analysis. **(A)** Flow cytometry analysis of mean fluorescence intensity (MFI) of key Treg markers (FOXP3, LAP, CD73, CD25, AREG, and CD3) in the presence or absence of tacrolimus. Data are presented as mean ± SD from three biological donors. Each data point represents an individual donor. Statistical significance was determined using a paired t-test (*$p < 0.05$, **$p < 0.01$, ****$p < 0.0001$). **(B)** Flow cytometry analysis of the proportion of FOXP3+HELIOS+, FOXP3+HELIOS-, FOXP3-HELIOS+, and FOXP3-HELIOS- cells of total CD4+ cells from 3 donors cultured in the presence and absence of tacrolimus. **(C)** Graphical representation of the flow plots depicted in (B).

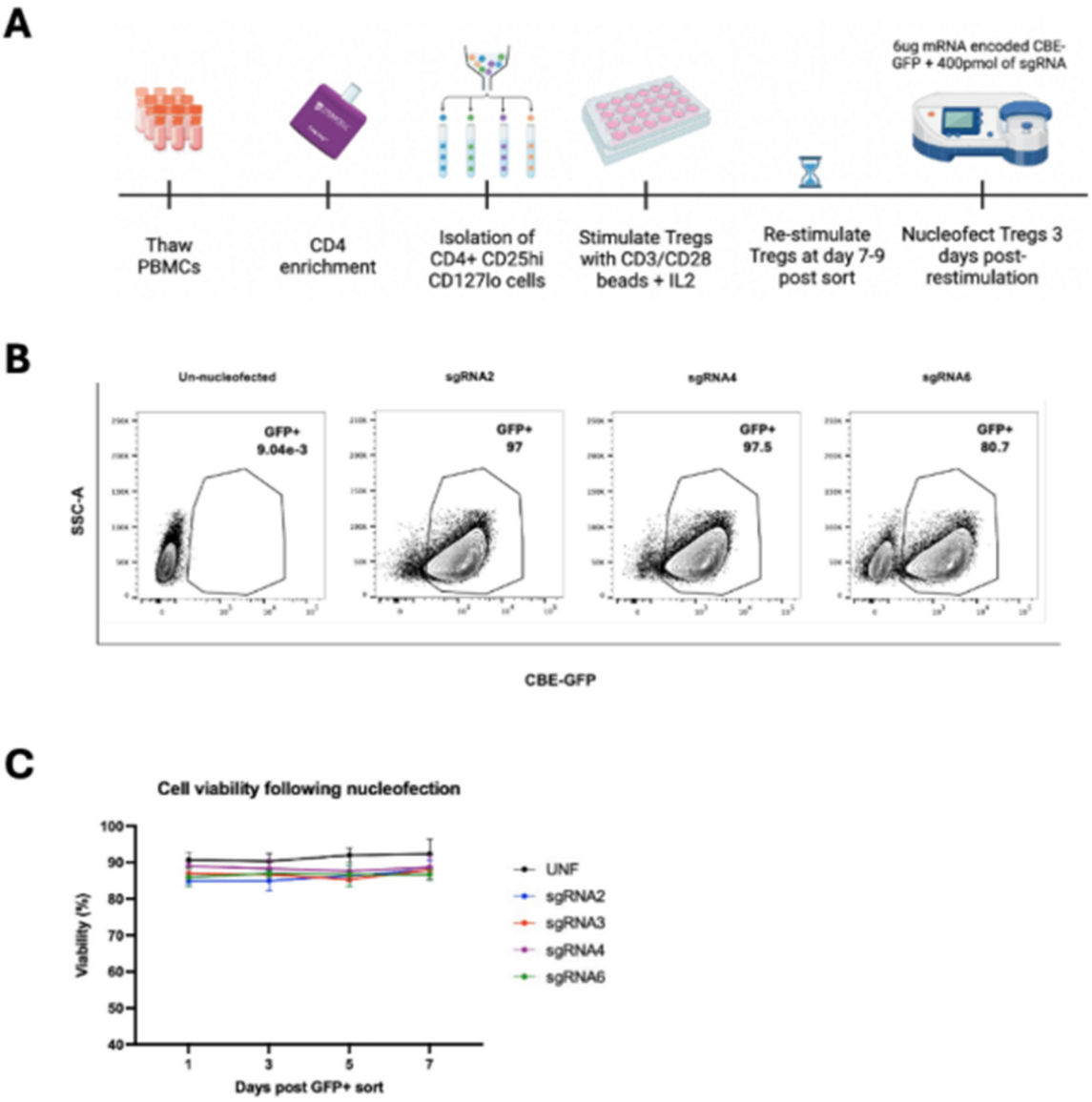

Figure 2: Optimization of a protocol to generate FKBP12 knock-out (KO) Tregs.
(A) Schematic overview of optimized base-editing protocol to achieve FKBP12 KO in CD4+ $CD25^{high}$ $CD127^{low}$ cells. **(B)** Representative flow plots of nucleofection efficiencies achieved with our optimized nucleofection protocol. Nucleofection efficiency is determined by assessing the proportion of GFP+ cells, of total CD4+ cells. **(C)** Cell viability of nucleofected and un-nucleofected (UNF) cells following culture post-nucleofection, measured by trypan blue dye.

Abstract 23

Effect of peak flow triggered adaptive servo-ventilation (ASVPF) on mortality in heart failure patients with prolonged Cheyne-Stokes respiratory cycle.

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Introduction and Objectives: In ADVENT-HF, treating obstructive sleep apnea (OSA) and central sleep apnea with Cheyne-Stokes respiration (CSA-CSR) with ASVPF did not affect overall mortality, but there was a trend towards lower mortality in those with CSA-CSR (HR, 0.74, 95%CI 0.44-1.23, p=0.25). Patients with CSA-CSR had more severe HFrEF, suggesting that ASVPF might be more effective in sicker patients. Because CSA-CSR cycle length (CL) is inversely proportional to cardiac output, we hypothesized that: 1) in patients with CSA-CSR in the control arm, mortality would be greater in those with longer than shorter CL; and 2) ASVPF would reduce mortality in those with longer but not shorter CLs.

Methods: In 305 patients with HFrEF and predominantly CSA-CSR or predominantly OSA with a central apnea-hypopnea index (cAHI) of ≥10 (OSA-CSA) we measured and averaged CL of 20 CSA-CSR cycles from the beginning of one apnea to the beginning of the next. We divided them into short and long CL groups based on median CL of the CSA-CSR group (54.9 sec). We then compared mortality between the 2 control groups and effect of ASVPF on mortality in the short and long CL groups.

Results: Among controls, 62 with longer CL (67.8±10.9 sec) had higher mortality than 102 with shorter CL (43.0±6.7 sec) (50.0% vs 15.7%, p<0.0001). In patients with longer CL, mortality was significantly lower in those randomized to ASVPF than to control (HR, 0.56, 95%CI 0.32-0.99, p=0.0467), but ASVPF had no significant effect in the shorter CL group (HR, 1.08, 95%CI 0.52-2.24, p=0.8401).

Conclusion: In HFrEF, mortality was higher in those with untreated CSA-CSR and OSA-CSA with longer than shorter CL. Most importantly, ASVPF reduced mortality in the longer CL group. This is the first demonstration that treating a particular phenotype of sleep apnea in HFrEF can reduce mortality.

Abstract 24

Disparities in Concurrent Asthma and COPD Prevalence: The Role of Sociodemographic, Area-level Marginalization, and Primary Care Access

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Introduction and Objective: Individuals with both asthma and chronic obstructive pulmonary disease (COPD) face worse outcomes and greater healthcare use. We examined how COPD prevalence among individuals with asthma varies across sociodemographic groups.

Methods: This was a population-based cross-sectional study of adults 35years or older with prevalent asthma in 2022 using Ontario's health administrative data. We estimated COPD prevalence overall, and by age groups, sex, rostered to a primary care physician, rural residence, and area-level income and material resources-related marginalization. Modified Poisson regression estimated adjusted prevalence ratios (PR) with 95% confidence intervals (CI).

Results: Among 1,201,522 adults 35+ years with asthma, COPD prevalence was 8.83% (95% CI: 8.78 – 8.88%). Prevalence increased with age, from 0.3% in those aged 35-44years to 24.8% among those 75+. COPD prevalence was higher in males than females (9.3% vs 8.6%), rural versus urban residents (11.1% vs 8.6%), and those rostered to a primary care physician versus not rostered (8.9% vs 8.6%). Prevalence was higher in individuals residing in the lowest versus highest income quintile areas (10.6% vs 7.8%) and in neighbourhoods with high versus low material resources-related marginalization (12.9% vs 6.2%). After adjustment, COPD prevalence was 78 times higher in adults aged 75+ versus those 35-44years, 1.2 times higher in males versus females, and 1.3 times higher in rural versus urban residents. Adults rostered to a primary care physician had 10% lower prevalence compared to those not rostered (PR=0.9). Prevalence was 1.3 times higher in low- versus high-income neighbourhoods and 1.8 times higher in areas with high versus low material deprivation.

Conclusion: Concurrent asthma and COPD disproportionately affects older adults, males, rural residents, and those living in marginalized areas. Lower prevalence was observed among individuals rostered to primary care physicians. These findings highlight health inequities that can inform health system planning and targeted preventive services.

Supported by Vanier Canada Graduate Scholarship, Connaught Doctoral Award, Novo Nordisk Network for Healthy Populations Graduate Award, Data Sciences Institute Data Access Grant, and The Canadian Institutes of Health Research Project Grant.

Abstract 25

Pleural Cavity-resident B Cells And Macrophages Form Immune Scaff olds On The Lung Surface In Response To Bacterial Stimuli

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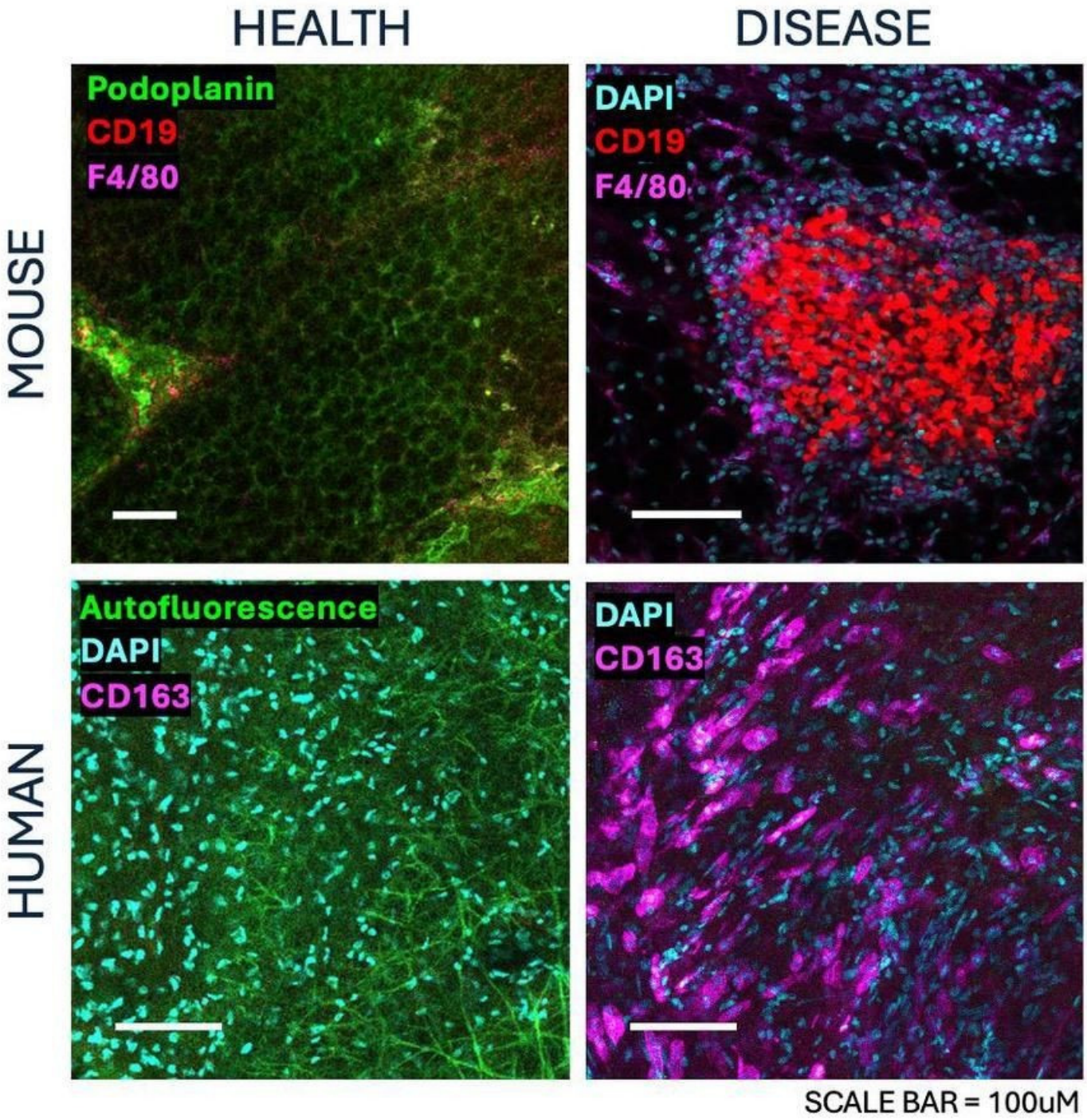
Rationale: Infectious and inflammatory pulmonary diseases can involve the pleural cavity, a unique immune niche that contains various leukocytes in mice and humans. The role of these cells in the response to thoracic infection remains largely unexplored. Herein, we test the hypothesis that patrolling pleural cavity immune cells are recruited to the pleural surface in response to bacteria or their components, contributing to infection resolution and concomitant lung inflammation.

Methods: Using an intercostal approach, we administered vehicle (PBS, n=5), LPS (0.05 μg/μL, n=7), or pHRhodo green+ E.coli bioparticles (n=4) into the pleural cavities of WT B6 mice and LPS into B cell-deficient muMT mice (n=6). We also performed intratracheal administration of LPS (n=2 WT B6mice). Naïve WT B6 (n=10) received no intervention. Pleural cavity lavage and chest walls with intact pleura were collected to quantify free-floating and tissue-adherent leukocytes, respectively. Human pleural tissue from healthy donor lung (n=4) and diseased lung explants (n=3), and pleural fluid from lung transplant recipients (n=9) were also collected for analysis by flow cytometry and whole-mount tissue confocal imaging.

Results: Compared to naïve controls, pleural lavage F4/80hi CD11b+ resident macrophages and CD19+ B cells were significantly reduced and Ly6G+neutrophils were increased in LPS- but not PBS-treated mice. Accordingly, we found numerous resident macrophage-B cell immune scaffolds adherent to the pleura 4 hours post-intrapleural or intratracheal administration of LPS, absent in naïve mice (Fig 1, top left). Reminiscent of bronchus-associated lymphoid tissue found in inflamed lungs, these adherent pleural leukocytes form remarkably circumscribed and organized structures, with B cells located centrally (Fig 1, top right). Strikingly, immune scaffolds were absent in B cell-deficient muMT mice post-intrapleural LPS challenge, indicating a pivotal role for B cells in organizing macrophages and other immune cells on the pleural surface. After administration of pH-sensitive E.coli bioparticles which fluoresce only in the acidic environment of phagolysosomes, immune scaffolds were highly pHRhodo green+, suggesting they function to phagocytose and clear bacteria during infection. We observed adherent resident macrophages and neutrophils on human pleural tissue from diseased explants (Fig 1, bottom right) but not healthy controls (Fig 1, bottom left) and identified CD19+ B cells, CD163+ CD11b+ resident macrophages and CD66+ CD11b+ neutrophils in human pleural fluid.

Conclusions: Our data suggest that B cell-dependent formation of immune scaffolds on the pleural surface functions to clear pulmonary bacterial infection, implicating this phenomenon as an essential component of the host response to infection.

Figure for abstract 25.



Abstract 26

Evidence for a neuro-immune axis associated with local B cell responses and fibrosis in chronic lung allograft rejection

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1. University Health Network, Toronto, Canada

Background: Chronic lung allograft dysfunction (CLAD) limits long-term survival after lung transplantation (LTx). CLAD patients with fibrotic opacities on chest computed tomography (CT) have worse outcomes. We previously showed that B cells were required for tertiary lymphoid organ formation, rejection, and fibrosis after prolonged ischemic storage of the graft in a mouse orthotopic LTx model. Recent publications have implicated sensory neurons and neuropeptides in pulmonary inflammation. In this study, we hypothesize that neuro-immune interactions in the lung influence local B cell responses leading to fibrosis in CLAD.

Methods: LTx after prolonged ischemic storage of the donor lung was performed using minor alloantigen-mismatched C57BL/10SnJ (B10) donors and C57BL/6J (B6) recipients (ALLO LONG). Controls included naïve B6 lungs, B6→B6 syngeneic grafts (SYN LONG), and B10→B6 allografts with minimal ischemic storage (ALLO MIN). Grafts underwent bulk-RNA sequencing 28 days post-LTx. Day 3 and 28 sera were analysed by ELISA. Bulk-RNA sequencing analysis was conducted on human CLAD lung and healthy donor lung tissue (NL). CLAD lung sections were interrogated by immunofluorescence (IF) enabling visualisation of neurons (TUBB3+), B cells (CD19+) and nuclei (DAPI+).

Results: ALLO LONG recipients displayed upregulated intragraft Aicda (reflecting local germinal centre responses, p=0.01) and neuronal transcripts including Calca (encoding neuropeptide CGRP; Fig 1A), as well as serum CGRP (Fig 1B). In humans, CXCL13 (B cell chemoattractant), was highly differentially expressed in CLAD (Fig 2A) and was associated with canonical B cell genes and elevated expression of neuronal-specific β-tubulin gene TUBB3 (Fig 2B). Strikingly, TUBB3 was highly upregulated in CLAD with fibrotic opacities on chest CT (FIB+; Fig 2C). IF revealed B cells near nerve bundles in CLAD (Fig 2D).

Conclusions: Our preliminary investigation suggests an association of B cells with an ischemia-induced intrapulmonary neurological response during chronic lung allograft rejection; ongoing work aims to confirm this relationship.

Figure for abstract 26.

Figure 1. Mouse LTx Model

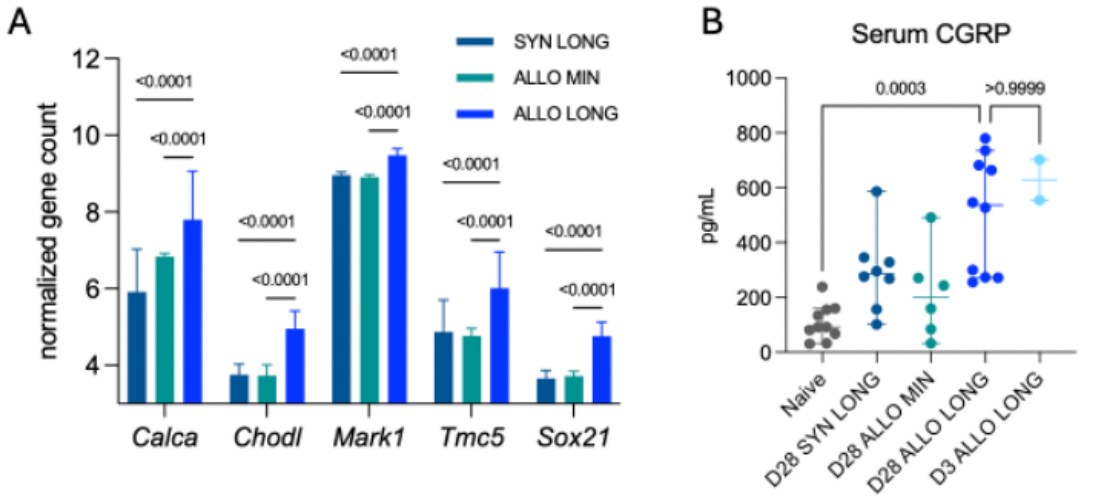
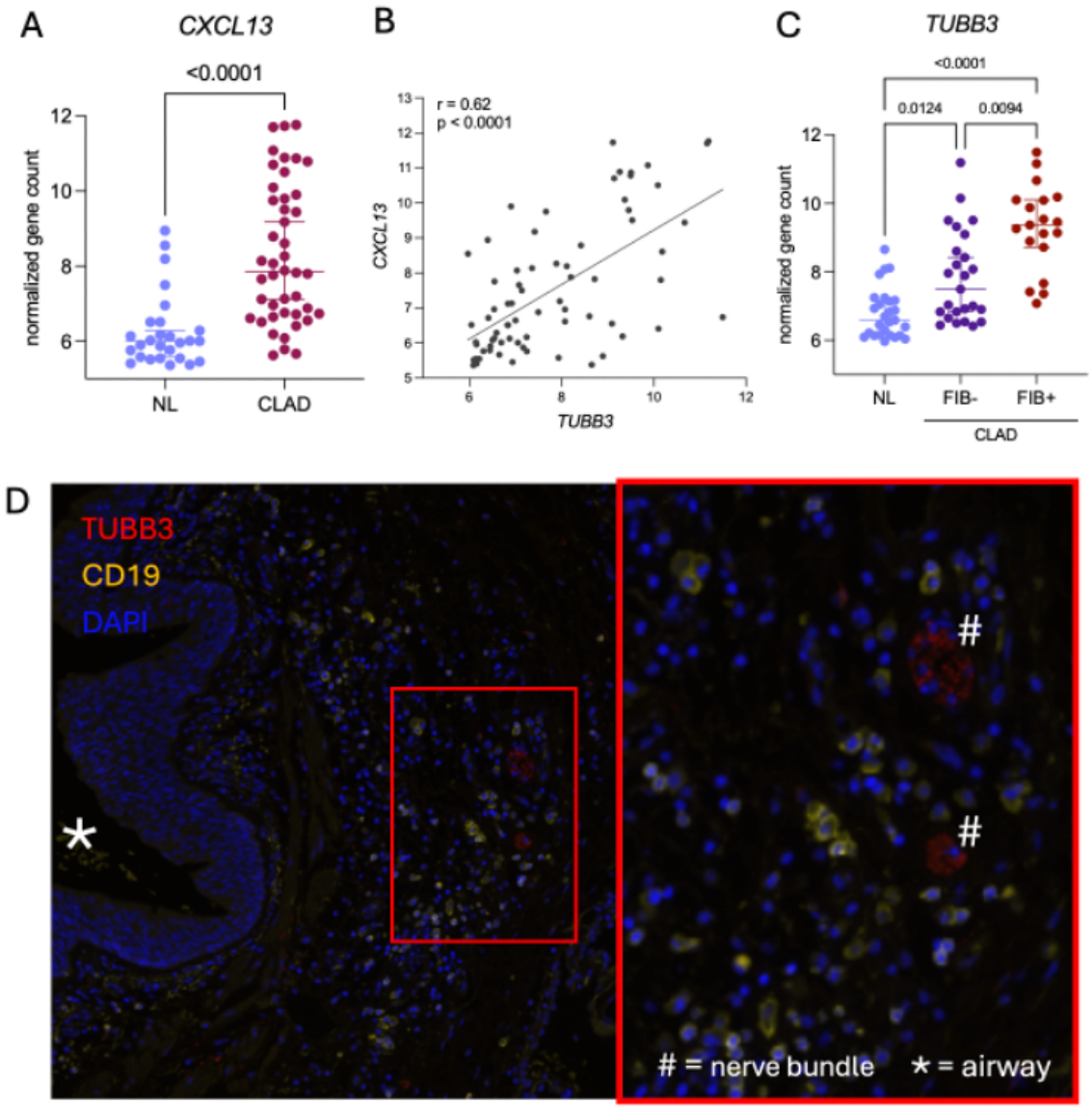


Figure 2. Human CLAD



Abstract 27

Rapid-cycle design of a clinical decision support system (CDSS) for asthma management in community pharmacies

Tony Ning (1), Terry Li (2), Jamie Kellar (3), Samir Gupta (4, 5)

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Introduction & Objectives: Chronic disease CDSSs are being implemented in physician settings, but pharmacy CDSS systems are largely limited to drug dosing/interaction alerts and support for minor ailments. Given the expanding role of pharmacists in chronic disease care, we adapted a primary care CDSS – the Electronic Asthma Management System (eAMS) – for pharmacy settings ("eAMS-Pharm"). Herein, we sought to: (a) collect feedback from community pharmacists and staff to optimize workflows and user interfaces; and (b) identify community pharmacy team members' thematic preferences and priorities for chronic disease CDSSs.

Methods: Starting with the eAMS-Pharm prototype, we employed a rapid-cycle design process comprising of three steps: (1) collecting qualitative and quantitative (e-questionnaire) feedback on the eAMS-Pharm in moderated focus groups with 3-5 pharmacy team members; (2) reviewing focus group transcripts for critical findings requiring design changes; and (3) optimizing the eAMS-Pharm in accordance with critical feedback, before the next focus group. This process was repeated until saturation (no new critical findings identified). Focus group participants were community pharmacists, registered pharmacy technicians, or pharmacy assistants, recruited via snowball sampling through investigators' networks. Qualitative themes were identified through inductive analysis.

Results: Six focus groups (n=28 participants) were conducted until saturation. Likert scale ratings of system content and format/usability remained high across all focus groups. The average System Usability Scale (SUS) score was 82.9 +/- 16.8, corresponding to a "good" or higher rating. From the qualitative analysis, identified themes included: the need to integrate the CDSS within existing pharmacy software and processes; technology as a facilitator/barrier for information flow; and the importance of efficient, timely, and bidirectional communication with prescribers.

Conclusion: We developed an asthma-specific CDSS for use in pharmacies. Pharmacy team members found the system to be both usable and useful. Identified themes can inform the design of other chronic disease CDSSs for pharmacy use.

This project was funded by the Network for Improving Health Systems (NIHS). The views expressed in this abstract are those of the authors and do not necessarily reflect those of the funder.

Abstract 28

Inhaler Education Practices and Perceptions Among Individuals with Chronic Lung Disease and Physicians in Ontario: A Survey Study

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Introduction and Objectives:
Proper inhaler technique is crucial for effective asthma and COPD management; however, errors with technique are prevalent. Despite guideline recommendations for routine technique reassessment, previous studies suggest that both education and supervision of inhaler use are inconsistent. This study evaluates the practices of physicians related to inhaler education, compares them to patient-reported experiences, and explores the role of online resources with inhaler education.

Methods:
A cross-sectional survey was administered to respirologists and family physicians across Ontario. Individuals with asthma and/or COPD at a tertiary care center in Toronto, were also surveyed. Patients were surveyed with respect to their inhaler use, reassessment of technique, and reliance on online resources. Physicians were randomly selected from the College of Physicians and Surgeons of Ontario registry, while patients were recruited through direct invitations from respirology clinics and study advertisements. Physicians were asked about their inhaler education practices, prescribing patterns, and utilization of online resources.

Results:
A total of 49 physicians and 74 patients participated. While most physicians addressed inhaler technique at some point, only 10% reassessed it at every visit. 38% of patients reported never having their technique reassessed after initial instruction, with 12% indicating they never received inhaler education. Despite 84% of physicians having recommended an online resource, only 9% of patients reported receiving physician recommendations for online content. 81% of patients stated they would trust online resources to a greater extent if recommended. Additionally, 60% of physicians felt there was insufficient guidance for prescribing inhalers in those with comorbidities, potentially impacting inhaler use efficacy and technique.

Conclusion:
Significant gaps exist between physician-reported inhaler education practices and patient reported experiences. Supervision remains inconsistent, and online resources are underutilized and not always trusted by patients and physicians. Regular technique reassessment, targeted online resource use, and direct prescribing guidelines may help improve inhaler technique and disease management.

This work was supported by a grant from the PSI Foundation (Grant R23-20) and the Temerty Faculty of Medicine (BL and DR). DR is supported by the Sandra Faire and Ivan Fecan Professorship in Rehabilitation Medicine.

Abstract 29

Trends in antifibrotic prescriptions from a universal health care system

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Introduction & Objectives:
Idiopathic pulmonary fibrosis (IPF) and progressive pulmonary fibrosis (PPF) are debilitating lung diseases. Their courses are modified with antifibrotic medications such as nintedanib and pirfenidone. In Ontario, access requires Ministry of Health (MOH) approval via the Exceptional Access Program (EAP). We aimed to describe antifibrotic prescribing trends, rejection patterns, and medication costs in Ontario.

Methods:
A retrospective analysis was performed using complete Ministry of Health data for antifibrotic applications from July 1, 2018 to April 1, 2024. New and renewal approvals were analyzed by indication (IPF vs. PPF), drug type, and patient demographics. The MOH rejects antifibrotic renewal in the setting of lung function decline >10% while on treatment. We evaluated for differences in renewal rejection rates between nintedanib and pirfenidone. Drug costs were estimated using public pricing and standard MOH approval durations.

Results:
Among 14,391 antifibrotic approvals (5,559 new; 8,832 renewals), 68.4% of new approvals were for nintedanib and 31.6% for pirfenidone. A total of 4,129 IPF and 816 PPF patients received antifibrotics; 14.9% of IPF patients switched antifibrotics. Between 2019 and 2023, the annual number of new and renewal antifibrotic approvals increased from 1,965 to 3300 ($p=0.0008$). The proportion of antifibrotic prescriptions for nintedanib compared to pirfenidone increased significantly over time ($p<0.0001$). Among IPF patients, the proportion of renewal applications rejected was higher with pirfenidone than nintedanib (5.7% vs. 4.0%, $p=0.0001$). The estimated cost of nintedanib and pirfenidone considering both initial and renewal approvals were $295.3 million and $116.8 million dollars, respectively during the study period.

Conclusion:
Real-world data from Ontario suggests an increase in antifibrotic approvals over time with higher use of nintedanib as compared to pirfenidone. A lower proportion of nintedanib renewal applications were rejected compared to pirfenidone, which may suggest less lung function decline with nintedanib. Antifibrotics represent a significant public expenditure.

Abstract 30

Improved time to antifibrotic approval using an online drug application portal

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Introduction & Objectives:
Idiopathic pulmonary fibrosis (IPF) and progressive pulmonary fibrosis (PPF) are progressive interstitial lung diseases with high morbidity. In Ontario, public coverage for antifibrotics (pirfenidone and nintedanib) requires Ministry of Health approval through the Exceptional Access Program (EAP), which historically relied on fax-based submissions. In recent years, the Special Authorization Digital Information Exchange (SADIE) portal was introduced. We aimed to assess whether electronic applications improved approval times and reduced administrative inefficiencies compared to traditional fax submissions.

Methods:
We conducted a retrospective observational study of all antifibrotic EAP applications approved in Ontario between March 1, 2020 and April 1, 2024. Outcomes included time to approval, frequency of additional communications, and rejection rates, stratified by submission method (fax vs. SADIE). Statistical analysis included Mann-Whitney U tests and chi-square testing. Subgroup analysis was conducted for physicians who submitted applications via both methods.

Results:
Among 11,240 antifibrotic applications (4,173 new; 7,067 renewals), 22.5% were submitted electronically. Median approval time was significantly faster using SADIE for new (1.0 vs. 3.0 days, $p<0.001$) and renewal applications (1.0 vs. 2.0 days, $p<0.001$). Fewer applications using SADIE required ≥30 days for approval (new: 4.3% vs. 9.3%; renewals: 0.9% vs. 5.9%; $p<0.001$) or additional communications (new: 17.9% vs. 42.0%; renewals: 4.7% vs. 12.3%; $p<0.001$). Rejection rates were similar across methods. Although use of SADIE increased over time, it represented only 43.6% of submissions in 2024.

Conclusion:
Electronic antifibrotic applications through an online submission portal significantly reduced approval times and administrative burden compared to fax. These findings support broader adoption of digital submission platforms to improve timely access to treatment and reduce clinician workload.

Abstract 31

Correlation of Plethysmography Measured Airway Resistance to Oscillometry Metrics of Respiratory Resistance.

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Introduction: Airway resistance (RAW) is typically measured in the body plethysmograph with patients panting against a closed shutter, a procedure that is often uncomfortable to patients. While commonly measured, its clinical utility is debatable. Respiratory oscillometry is a novel pulmonary function test (PFT) that measures the mechanical properties of the respiratory system during normal tidal breathing by superimposing multi-frequency oscillations. Resistance at 5 Hertz (R5) measures total resistance while resistance at 19 Hz (R19) reflects the airway resistance in the medium sized airways. The objective of this study is to evaluate the correlation between RAW to spirometry and oscillometry.

Methods: From December 2017 to September 2024, 1145 patients with diverse lung diseases were evaluated with oscillometry and standard PFT on the same day at the Toronto General Pulmonary Function laboratory. The relationships between RAW, PFT metrics of airflow obstruction, and oscillometry metrics of resistance were evaluated using linear models along with a correlation matrix.

Results: RAW has a low correlation with all oscillometry and spirometry measures, the highest being R5 ($R2 = 0.24$), followed by R19 ($R2 = 0.18$). RAW was significantly associated with both R5 and R19 ($p < 0.001$). A 1-unit increase in RAW is associated with a 1.1-unit (95% CI:[0.96,1.18]) increase in R5 and a 0.62-unit (95% CI:[0.55,0.70]) increase in R19, respectively.

Conclusion: RAW is poorly correlated with FEV1/FVC (forced expiratory volume in 1 second/forced vital capacity), the current gold standard metric of airflow obstruction. Raw is also poorly correlated with oscillometry metrics (R5, R19, and R5-19). However, RAW exhibits a near 1 to 1 relationship with R5. These findings underscore that oscillometry and standard PFT measure different aspects of lung physiology. Given the advantages of oscillometry from the patient perspective and its relationship with RAW, oscillometry could be used in place of measurements with body plethysmograph.

Abstract 32

Quality Improvement Initiative for Mount Sinai Hospital Smoking Cessation Clinic

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Background:
Smoking-related lung diseases are a leading cause of morbidity and mortality. Despite guidelines recommending the routine offer of both pharmacotherapy and behavioural smoking cessation support, only a minority of individuals are offered comprehensive, multimodal interventions. The respiratory therapist (RT) led Smoking Cessation Clinic at Mount Sinai Hospital (MSH) is well positioned to address this gap but remains underutilized and lacks pharmacotherapy access. This quality improvement (QI) initiative aims to improve the accessibility and delivery of smoking cessation care at MSH and expand its reach to University Health Network (UHN)-affiliated populations, including pre-lung transplant patients, with a specific objective to increase attendance rates by 20% in 1 year.

Methods:
Utilizing a Plan-Do-Study-Act (PDSA) methodology, referral patterns were first retrospectively reviewed starting from June 2023. Through engagement with stakeholders including RTs and physicians, key barriers and possible interventions were identified, including additional staff training, facilitating methods of referral, improving pharmacotherapy access, and enhancing clinic visibility. Attendance rates were tracked monthly using run charts.

Results:
Baseline review showed 12 referrals between May 2023 and May 2024, all internal to Sinai Health. Following initial PDSA cycles, 16 referrals were received over the subsequent 10 months, with 50% originating from external sources. Key barriers included limited institutional awareness, lack of prescribing capacity, and cost of nicotine replacement therapy (NRT). Interventions included recruiting a prescribing physician, engaging with other smoking cessation programs to address NRT access, and targeted outreach to referring providers. Implementation and evaluation are ongoing.

Conclusions:
This QI initiative demonstrates early progress in identifying systemic barriers and implementing evidence-based strategies to enhance smoking cessation support. Future cycles will focus on service redesign (including pharmacotherapy access), formal referral pathways, and evaluating reach to high-priority populations such as pre-transplant patients. Sustained stakeholder engagement and continuous evaluation will guide further expansion across the MSH/UHN network.

Abstract 33

Inflammatory Gene Expression Profile of Bronchoalveolar Lavage CD8+CD57+ CD69+ T Cells Suggests a Functional Role in the Pathogenesis of Lung Allograft Dysfunction

Sajad Moshkelgosha, Stephen Juvet

Tornto lung transplant ptogram, UHN

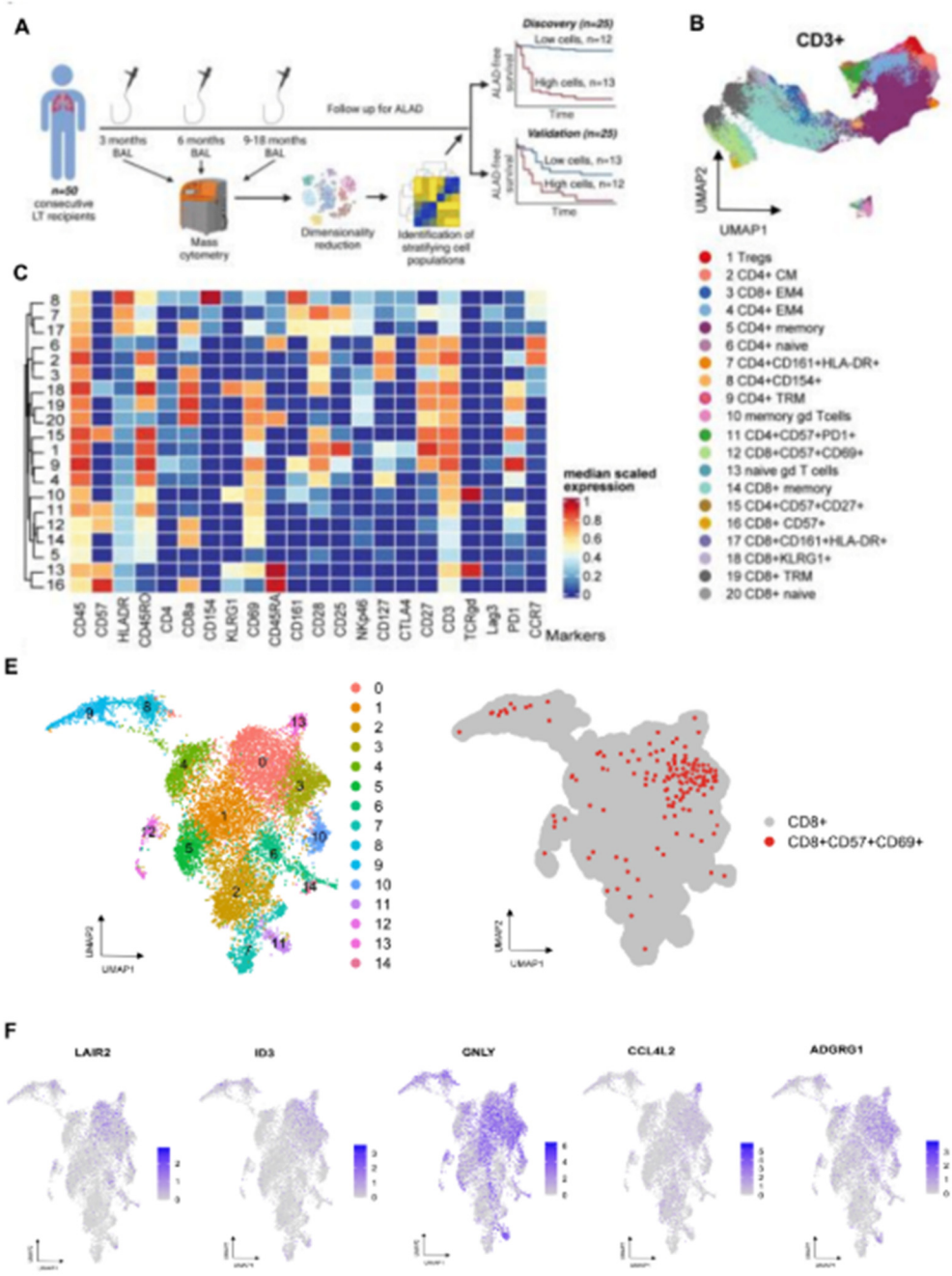
Purpose: Lung transplantation is beset by a high rate of allograft failure driven by intragraft inflammation and alloimmunity which is incompletely understood. We applied mass cytometry to bronchoalveolar lavage (BAL) cells from a longitudinal cohort of lung transplant recipients (LTRs) in an effort to identify novel cellular biomarkers and mediators of acute lung allograft dysfunction (ALAD). We previously reported that CD4+CD57+PD1+ T cells in the BAL are associated with incident ALAD, but also observed an association with CD8+CD57+CD69+ T cells. Here we report the phenotypic and transcriptional features of the latter cell population.

Methods: Mass cytometry was applied to BAL cells from 50 consecutive LTRs at 3-, 6- and 9-months post-transplant (Fig 1A). A semi-supervised algorithm identified significantly differentially represented cell populations associated with ALAD. CITEseq was performed with a panel of 15 oligo-tagged antibodies against surface markers on 4 independent BAL samples from patients with ALAD. Cells then underwent gene and oligo library preparation before sequencing. CD8+CD57+CD69+ T cells were identified based on protein expression. We then examined the differentially expressed genes between this cell subset and other CD8+ T cells.

Results: Our anlasis on mass cytometry data identified 20 subsets of T cells (Fig 1B, C), where a semi-supervised algorithm identified CD8+CD57+CD69+ T cells as a significantly differential cell subset between stable and LAD patients (Fig 1D). CITEseq data revealed BAL CD8+ T cells from patients with ALAD fell into 15 subclusters in multidimensional space (Fig 1E). Based on CD57 and CD69 protein expression, CD8+CD57+CD69+ T cells assembled mainly in Cluster 3 (Fig 1E), expressesing several cytotoxicity-, tissue residency- and exhaustion or senescence-related transcripts (Fig 1F).

Conclusion: These data suggest that BAL CD8+CD57+CD69+ T cells may represent a tissue resident memory cytotoxic population that might drive lung allograft injury. Functional studies on this cell population are underway and may lead to improved prediction of ALAD and CLAD and a better understanding of lung transplant immunobiology.

Figure for abstract 33.



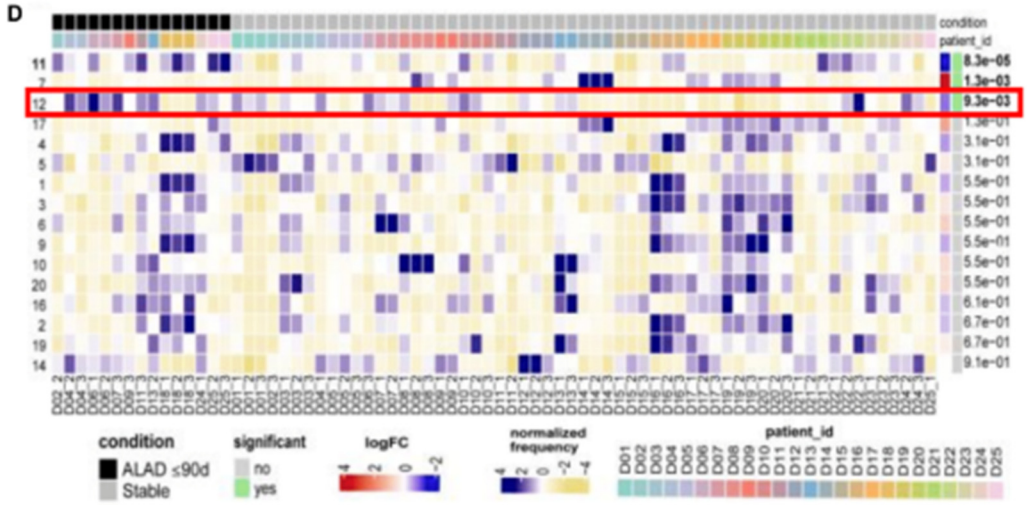


Fig 1. Identification of a BAL CD3+ T cell population associated with lung allograft dysfunction to Investigation of potential function of $CD8^+CD57^+CD69^+$ T cells in the BAL of LTRs using CITEseq. A. Study schematic. Fifty consecutive patients presenting for bronchoscopy at 3 months post-transplant were enrolled. For each enrolled patient, BAL cells at three time points (3, 6, and 9 months or next available) were collected. BAL cells were cryopreserved and subjected to CyTOFa; all samples from each patient were analyzed in the same CyTOF experiment. Patients were randomly divided into discovery (n=25) and validation (n=25) subsets to enable evaluation of differentially represented cell populations. **B.** Uniform manifold approximation and projection (UMAP) plot of BAL CD3+ cells falling into 20 clusters (highlighted in different colours) identified by FlowSOM. Annotation of cell populations is shown below the UMAP. **C.** Heatmap depicting relative expression of 22 T cell-associated proteins across the 20 T cell populations in the discovery cohort. **D.** Differential analysis heatmap of arcsine square root transformed cell frequencies that were subsequently normalized per cluster (rows; numbers along left side correspond to cell populations annotated in B). Statistically significant clusters are highlighted by green boxes at right along with p-values. **E.** After integration of BAL T cells from 4 ALAD cases, BAL CD8+ T cells (CD3+CD8+CD4- were displayed on UMAP plot revealing 15 distinct cell clusters (left UMAP plot). Right panel displays CD57 and CD69 expression (red dots) on a feature plot showing all BAL CD8+ cells. **F.** UMAP plots highlighting gene expression of a selected list of genes that are deferentially express in associated with cluster 3. This gene signature suggested that $CD8^+CD57^+CD69^+$ T cells are cytotoxicity-related and senescent population.

Abstract 34

Clinical Implications of Body Composition, Physical Fitness and Exercise Capacity in Patients with Chronic Thromboembolic Pulmonary Hypertension: A Systematic Review

Nawazish Naqvi (1) , John Wu (2) , An Ha (2) , Rozhan Momen (2) , Noor Al Kaabi (2) , Daniel Santa Mina (2), Indranil Balki (2) , Karan Chohan (2) , Sahar Nourouzpour (2) , Ani Orchanian-Cheff (3) , John Granton (2) , H.S Jeffrey Man (2) , Micheal McInnis (2) , Karen McRae (2) , Laura Donahoe (2) , Marc de Perrot (2) , Dmitry Rozenberg (2)

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INTRODUCTION: Chronic thromboembolic pulmonary hypertension (CTEPH) is characterized by thromboembolic occlusion of the pulmonary arteries, leading to symptoms such as dyspnea, chest pain, and exercise intolerance. Pulmonary endarterectomy (PEA) is the gold-standard treatment for CTEPH, while balloon pulmonary angioplasty (BPA) may be an alternative for patients at higher surgical risk. Identifying prognostic factors that affect the outcomes of PEA or BPA is crucial for optimizing treatment strategies and tailoring rehabilitation programs to improve postoperative outcomes. This systematic review investigates the prognostic roles of body composition, physical fitness, and exercise capacity in CTEPH patients undergoing PEA or BPA.

METHODS: We searched 5 databases, covering studies from inception to June 17, 2024. We included randomized controlled trials and cohort studies that evaluated the impact of body composition, physical fitness, or exercise capacity on postoperative outcomes in CTEPH patients undergoing PEA or BPA.

RESULTS: 29 studies were included. 21 (72%) studies focused on PEA, 7 (24%) on BPA, and 1(4%) incorporated both procedures, with a total of 5,443 patients. The median sample size per study was 91 [54–172], average patient age range was 57.9 years [47.9–68.8], and 55% were females. Body composition was evaluated in 52% of studies, physical fitness in 55%, and exercise capacity in 83%. Most studies examined hemodynamic and mortality outcomes. Body composition measures showed no consistent association with clinical outcomes. However, better 6-minute walk distance (6MWD) and lower baseline functional class (NYHA/WHO-FC) were frequently linked with improved outcomes. Notably, heart rate change (ΔHR) during 6MWD was the only parameter consistently associated with improved pulmonary hemodynamics.

CONCLUSION: Functional markers such as 6MWD, ΔHR, and baseline NYHA/WHO functional class are useful prognostic indicators in CTEPH. Body composition and other physical fitness metrics were not independently predictive, highlighting the need for further research to clarify their role in outcome prognostication.

FUNDING: NN and DR are supported by the Temerty Faculty of Medicine, University of Toronto. DR receives support from the Sandra Faire and Ivan Fecan Professorship in Rehabilitation Medicine.

Figure for abstract 34.

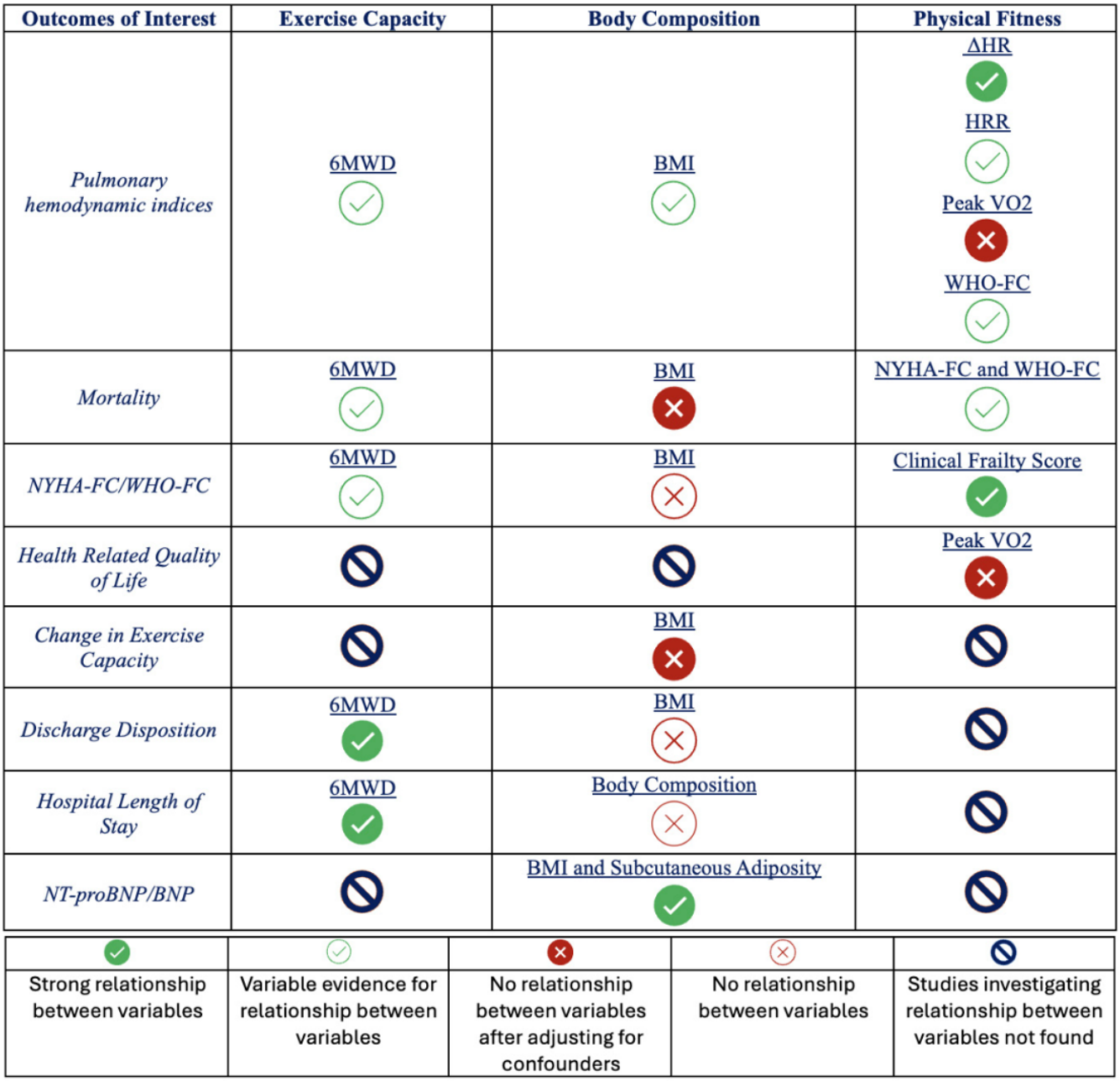

Figure 1: Associations between body composition, physical fitness, and exercise capacity parameters with CTEPH post-intervention outcomes

Abstract 35

Implementation of home-based daily spirometry in the early post-lung transplant period

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1. University Health Network. 2. University of Toronto. 3. Multi-organ Transplant Program

Introduction & Objectives: Daily monitoring of lung function in the early post-lung transplant (LTx) period can improve early detection of graft dysfunction. In-person lab testing is time and resource intensive for patients and providers. The aims of this study were to assess adherence and usability of home spirometry, and explore correlation with in-lab spirometry.

Methods: Handheld spirometers (MIR Spirobank SmartTM) were provided to LTx recipients upon hospital discharge or at their first post-transplant clinic visit. Spirometry data (FEV1, FVC, FEV1/FVC, FEF 25-75) were manually entered after a daily prompt into a custom-designed module located within the electronic medical record (EMR) patient portal (EpicTM). Results were integrated into clinical workflows for clinicians to view. Adherence was measured as the proportion of entered values vs. expected values. Usability of devices and the data entry system was assessed with a daily question during data entry and discussions with patient partners. Analyses were done to assess mean difference (t-test) and correlation coefficient between in-lab and at-home spirometry results.

Results: Data was analyzed for the initial 16 participants (87% male, 56 ± 13 years, 69% interstitial lung disease) in the first 3 months post-transplant. Median (IQR) daily adherence rate was 81 (47-91)%. All participants reported ease of use of the device and system. There was no significant difference between mean FEV1 values between groups (mean difference 0.096L ± 0.22, $p = 0.1$) with strong correlation between home and lab spirometry measurements ($r = 0.96$, $p < 0.0001$). -Conclusion: LTx recipients had a high rate of adherence and reported good usability of a home spirometry device and electronic reporting system. In-lab and home measurements had good correlation. Future directions include direct device-EMR integration and the development of alerts for abnormal or missed values to improve early detection of graft dysfunction and target opportunities to improve adherence.

This study was supported by Boehringer Ingelheim. Boehringer Ingelheim had no role in the design, analysis or interpretation of the results in this study. Boehringer Ingelheim was given the opportunity to review the publication for medical and scientific

Abstract 36

Risk Stratification of Chronic Lung Allograft Dysfunction (CLAD) Using Combined Physiological Score

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Introduction & Objectives: CLAD is defined as a sustained (>3 months) decline in FEV1 to ≤ 80% of the highest value post-lung transplant (LTx). The early predictors of CLAD could aid in preventing CLAD progression. Oscillometry, an emerging PFT conducted during quiet breathing, has high sensitivity to lung mechanics, especially in the lung periphery where CLAD originates. We developed a combined spirometry and oscillometry "SpirOsc" score at 3 months post-LTx, demonstrating strong CLAD association within 3 years. We investigate whether 3-month SpirOsc score provides future CLAD risk assessment.

Methods: First-time double LTx recipients (Dec 2017-Dec 2021) with paired spirometry-oscillometry at 3 months post-LTx and an adjudicated CLAD status were included (n=391). Patients were censored at CLAD-onset, death if CLAD-free, or last PFT before Feb 28, 2025. The SpirOsc score consisted of: %FEV1, FEV1/FVC, R5 (resistance at 5 Hz) z-score, R5-19 (difference in the resistance between 5 to 19 Hz), and AX (area under reactance). Previously determined cutoff values were used to assign an ordinal score for each parameter if below (0) or above (1) the threshold for CLAD. The relative contributions of spirometry and oscillometry were analysed in 4 categories: category A (all normal), B (normal oscillometry-abnormal spirometry), C (abnormal oscillometry-normal spirometry), and D (all abnormal). A Cox proportional hazards model assessed the hazard ratio (HR) for CLAD adjusted for known CLAD-related factors.

Results: Peri-operative characteristics were similar between 156 CLAD and 235 CLAD-free patients, except for younger age in CLAD. CLAD patients had lower %FVC, %FEV1 and X5 (reactance at 5 Hz) z-score at 3 months post-LTx ($p<0.05$). Higher SpirOsc scores were associated with increased CLAD risk (score 5 vs 0; adjusted HR=3.18, 95%CI: 1.16, 6.26). Category D showed higher CLAD risk (adjusted HR=2.54, 95%CI: 1.36, 4.76) than category A.

Conclusions: Higher 3-month SpirOsc scores are associated with increased CLAD risk.

Abstract 37

Identifying Cough Trajectories to Predict Asthma Outcomes: Insights from Growth Based Trajectory Modelling (GBTM) and Generalized Estimating Equations (GEE) Analysis

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Background: Cough is a common symptom in early childhood, but the causes and long-term impacts can vary greatly. Some children experience occasional cough that resolves quickly, while others have more persistent or recurring symptoms.

Objectives: This study aimed to identify distinct cough trajectories from infancy to preschool using questionnaire-based data from the Canadian Healthy Infant Longitudinal Development (CHILD) Cohort Study. We then examined how these patterns relate to clinically severe respiratory outcomes such as asthma, medication use, and hospitalizations.

Methods: Group-based trajectory modeling (GBTM) was applied to parent-reported cough data from ages 3-months to 5- years. Model selection was based on BIC, AIC, posterior probabilities, and clinical interpretability. Generalized Estimating Equations (GEE) were subsequently used to assess associations between cough trajectories and respiratory outcomes, including asthma, unscheduled doctor visits, emergency department (ED) visits, hospitalizations, and respiratory medication use.

Results: A three-group model—never/infrequent, early-onset, and late-onset cough—was selected based on the lowest BIC and AIC values and median posterior probabilities >70%. Using GEEs, we found that membership in the late-onset cough trajectory was significantly associated with increased risk of unscheduled doctor visits and bronchodilator use by preschool, after adjusting for potential confounders. No significant associations were observed between early-onset cough and respiratory outcomes after adjustment.

Conclusions: Late-onset cough was associated with increased bronchodilator use and primary healthcare utilization, suggesting it may be an early marker of respiratory vulnerability. These findings underscore the importance of cough and its timing in identifying children at risk for persistent respiratory morbidity.

Abstract 38

Predicting Post-Transplant Forced Expiratory Volume in One Second using Machine Learning and Ex Vivo Lung Perfusion Data on Isolated Human Lungs

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The submitting author has requested for the abstract not to be shared given pending intellectual patents.

Abstract 39

Who uses virtual care?: A cross-sectional report of virtual care use in people living with chronic respiratory diseases

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Introduction: Virtual ambulatory care was rapidly adopted during the pandemic and continues to be popular among people with chronic respiratory diseases (CRD). Virtual care (VC) can be delivered using modern technology, such as phones or videos, to assess and communicate with patients. However, the role of VC in CRD management remains unclear.

Objective: To describe the characteristics of people living with CRD using virtual care in Ontario post-pandemic.

Methods: A population-based, cross-sectional study was conducted using the Ontario health administrative databases from ICES. All people in Ontario identified as having active asthma and/or chronic obstructive pulmonary disease (COPD) as of January 1, 2023, were followed for 1 year. The main outcome was VC use defined as 3 or more encounters (telephone or video calls) in 2023.

Results: A total of 1,074,783 people were included: 34.2% with COPD, 73.1% asthma, 7.3% both. In 2023, the total mean VC encounters was 1.73 (SD 4.10). 48% of the cohort had at least 1 VC encounter and 43% accessed VC by phone. Between groups, mean age and %females for non-VC users were 46.4 (SD 25) years and 50.7% while for VC users were 56.4 (21) years and 61.6%, respectively. Median VC encounters in non-VC users were 0 (IQR: 0-1) times/ year compared to VC-users 5 (IQR: 3-7)/ year, $p<0.001$. There were greater proportions of individuals with congestive heart failure, diabetes and hypertension in VC users. Lower neighborhood income and higher marginalization quintiles had greater proportion of visits in both groups. Greater details are reported in Table 1.

Conclusion: In 2023, people with CRD mostly used phone calls for their VC encounters. VC users were likely to be older, female with lower income and higher marginalization dimensions.

Acknowledgement: This research is supported by the Canadian Lung Association.

Figure for abstract 39:

Table 1: Characteristics of people with Asthma and COPD who did and did not use Virtual Care* in Ontario in 2023

Characteristics	Non-Virtual Care user	Virtual Care user
Age (standard deviation)	46.4 (24.6)	56.4 (20.8)
Sex (Female, n, %)	435,777 (50.7%)	132,410 (61.6%)
Rurality & Income Quintile (n, %)		
1	172,818 (20.1%)	47,506 (22.1%)
2	157,712 (18.3%)	40,961 (19.1%)
3	156,507 (18.2%)	38,697 (18.0%)
4	155,529 (18.1%)	37,897 (17.6%)
5	148,820 (17.3%)	37,364 (17.4%)
Rurality	59,284 (6.9%)	11,041 (5.1%)
Material Resources Quintile (n, %)		
1	155,008 (18.0%)	38,489 (17.9%)
2	177,867 (20.7%)	44,374 (20.6%)
3	171,107 (19.9%)	42,666 (19.8%)
4	161,597 (18.8%)	40,657 (18.9%)
5	187,366 (21.8%)	47,637 (22.2%)
Racialized and Newcomer Populations Quintile (n, %)		
1	148,929 (17.3%)	27,981 (13.0%)
2	154,360 (18.0%)	33,979 (15.8%)
3	155,697 (18.1%)	39,772 (18.5%)
4	176,312 (20.5%)	49,665 (23.1%)
5	217,647 (25.3%)	62,426 (29.0%)
Comorbidities (n, %)		
Congestive Heart Failure	56,704 (6.6%)	262,597 (12.4%)
Diabetes	133,119 (15.5%)	58,190 (27.1%)
Hypertension	285,597 (33.2%)	111,814 (52.0%)

*Virtual Care use defined as 3≤ encounters in 2023.

Abstract 40

Prefrontal cortex activity and variability in respiratory muscle activation during concurrent inspiratory loading and cognitive task performance

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Introduction & Objectives: Inspiratory threshold loading (ITL) increases ventilatory demands and may impair cognition during dual-tasking, suggesting shared neural networks between respiratory and cognitive control. Consequently, ITL dual tasking may not only impair cognition, but also impact respiratory muscle function due to competition for shared neural resources. This study aimed to investigate the effects of ITL-cognitive dual-tasking on prefrontal cortex (PFC) activity, cognitive performance, and respiratory muscle activity.

Methods: Twenty-seven healthy participants (14 females; mean age = 23.9 ± 2.7 years) were recruited. Participants performed three randomized 3-minute tasks: inspiratory threshold loading (ITL; 20 cmH2O); the Stroop Colour-Word Test (SCWT); and their combination (ITL+SCWT). Functional near-infrared spectroscopy (fNIRS) was used to assess bilateral medial and dorsolateral PFC activity, quantified by the slope of the change in oxygenated hemoglobin over time. Respiratory muscle activity was assessed using surface electromyography (EMG) on the sternocleidomastoid (SCM), scalene (SA), parasternal intercostal (PI), and diaphragm/intercostals (Dia/IC). Cognitive performance was assessed based on SCWT accuracy and reaction time.

Results: PFC activity was greater during ITL+SCWT compared to ITL alone across all regions ($p = 0.002$). ITL+SCWT resulted in greater reaction time and percentage error than SCWT alone ($p < 0.001$). Greater variability (coefficient of variation) in EMG activation duration was observed in the SCM ($p = 0.012$), SA ($p = 0.010$), and Dia/IC ($p = 0.041$).

Conclusion: ITL+SCWT resulted in greater PFC activity, cognitive performance decrements, and greater variability in the duration of respiratory muscle activation. Further research is warranted to explore the impact of dyspnea on cognition and respiratory muscle function during multitasking in individuals with respiratory disease.

Supported by: NIH grant (PR), Mitacs (UM), and CIHR (MVH).

Abstract 41

A machine learning algorithm to quantify smoking damage in donor lungs

Lielle Ronen (1-3), Serena Hacker MSc (1, 2, 4), Lorenzo Del Sorbo MD (1, 2, 5), Shaf Keshavjee MD (1-3, 6), and Andrew T. Sage PhD (1-3, 10)

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The submitting author has requested for the abstract not to be shared given pending intellectual patents.

Abstract 42

Investigating photoacoustic imaging as a novel method of monitoring edematous lung injury

Rajiv Sanwal (1,2), Chris Faeth (2,3), Katie Leung (4), Callum Frazer (5), Eno Hysi (2,3), Warren L. Lee, (1, 2, 6)

1. Department of Laboratory Medcine and Pathobiology, Faculty of Medicine, University of Toronto. 2. Keenan Research Center, St. Michael's Hospital. 3. Department of Medical Biophysics, Faculty of Medicine, University of Toronto. 4. Department of Chemical Engineering, University of Waterloo. 5. Faculty of Science, University of Waterloo. 6. Interdepartmental Division of Critcal Care Medicine, University of Toronto.

Acute respiratory distress syndrome (ARDS) is a major cause of morbidity and mortality. Excessive lung inflammation, often from pneumonia or sepsis, causes severe pulmonary edema and a reduction in gas exchange, leading to hypoxia and death. Imaging of ARDS relies on chest X-rays/CT scans which possess several limitations: there is exposure to ionizing radiation, a lack of real-time monitoring, lack of physiological information, and requires patient transport.

To address this problem, we propose the use of photoacoustic imaging (PAI) as a novel lung imaging modality. Briefly, a laser is used to illuminate the lungs and interacts with molecules in tissue (e.g. hemoglobin) to produce an acoustic response which is detected by a transducer. Notably, the wavelength of the excitatory laser can be changed to assess different qualities such as oxy- and deoxy-hemoglobin content, providing physiological readouts of lung function. Using a murine pneumonia model, we imaged mice pre- and post-infection to assess the capacity of PAI to measure edematous lung injury. Lungs were collected post-mortem for injury confirmation and PAI images were analyzed to measure oxygen saturation.

Using PAI, we measured changes in acoustic response between healthy and fluid-filled lung tissue. Data from different wavelengths revealed increases in deoxyhemoglobin and decreases in oxyhemoglobin after lung infection. Lung injury was confirmed using histology and wet/dry analysis. Using a scanning apparatus, we also generated 3D images of fluid-filled lungs using both ultrasound and photoacoustics, providing a map to identify the most edematous lung regions. Finally, preliminary data from a pig pneumonia model illustrated the feasibility of PAI when scaled up to larger animal models.

Altogether, these data demonstrate that PAI has high potential to be a new clinically valuable tool in ARDS monitoring leading to earlier interventions and improved outcomes.

We would like to thank the research vivarium staff for their expertise and assistance. This work is supported by an NFRF-Explorations grant and an Ontario Graduate Scholarship

Abstract 43

Characteristics of a first episode of acute lung allograft dysfunction (ALAD) and the risk of chronic lung allograft dysfunction (CLAD) following lung transplant

Julie Semenchuk (1,2), Gregory Berra (1,2), Meghan Aversa (1,2), Ella Huszti (1,2), Rasheed Ghany (1,2), Tereza Martinu (1,2), Stephen Juvet (1,2)

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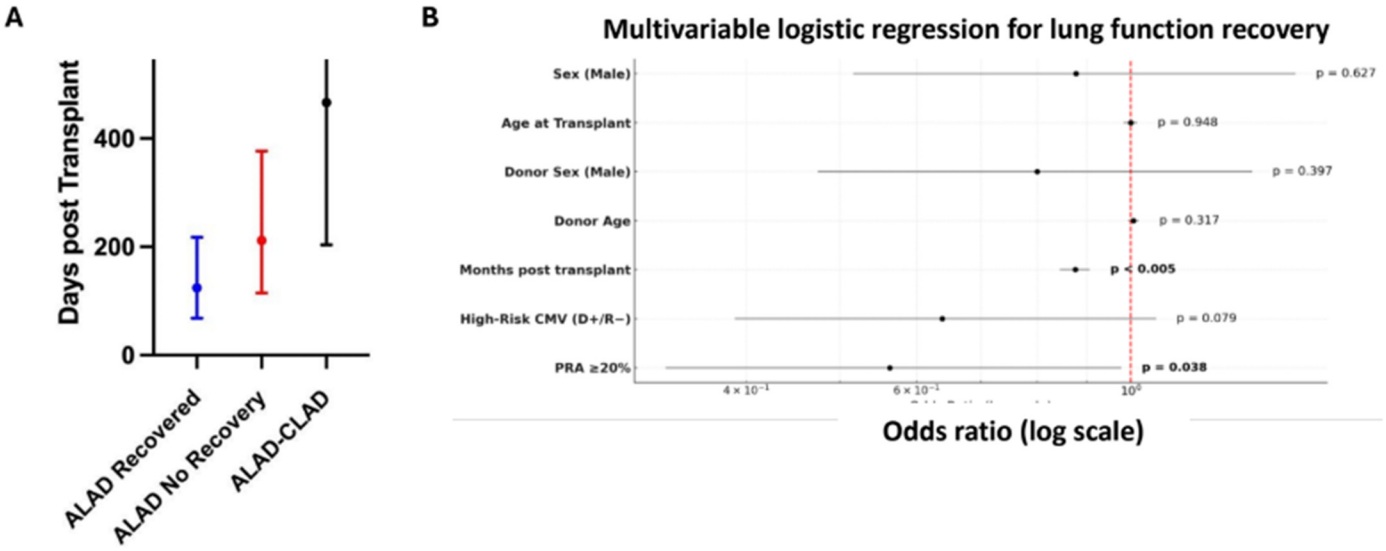
Purpose: ALAD has no formal definition, and an ISHLT consensus statement is under development. ALAD has been associated with underlying cellular changes, highlighting the need to define this entity clinically. In this study, our goal was to examine the trajectory of lung function after ALAD and explore risks associated with progressive lung function decline.

Methods: This was a retrospective cohort study of lung transplant (LT) recipients from 2014-2019 with a minimum of three FEV1 measurements and a first ALAD episode within two years post-LT. ALAD was defined as a decline in FEV1 of 10% or more from the highest FEV1 in the preceding 120 days (reference value). Lung function trajectory was graphed and grouped into “ALAD-recovered” if a subsequent FEV1 returned to within 10% of the reference value, “ALAD-no recovery” if subsequent FEV1 did not improve, and “ALAD-CLAD”, if ALAD date aligned with CLAD onset.

Results: A total of 950 LT recipients were screened. Of the 832 that met criteria for analysis, 689 (82.8%) had ALAD in the first two years post-LT. Of these, 570 (83%) were ALAD-recovered, 92 (13%) ALAD-no recovery, and 27 (4%) had an ALAD-CLAD. In the ALAD-recovered cohort, lung function recovered within 3 months for 548 (96%) patients. The median time to ALAD was lowest for ALAD-recovered at 124 days (IQR 68, 218) and highest for ALAD-CLAD at 466 days (204, 558) (Fig A, $p<0.001$). In multivariable logistic regression models, months post transplant (OR 0.876, CI 0.845, 0.907) and pre-transplant sensitization defined as PRA>20% (OR 0.563, CI 0.330, 0.978), were associated with lack of lung function recovery following ALAD (Fig B).

Conclusion: ALAD is common in the first two years post-LT with most patients recovering lung function. Individuals with later-onset ALAD and elevated pre-transplant PRA > 20% may benefit from more intensive monitoring and early intervention.

Figure for abstract 43.



Abstract 44

Trends in Pulmonary Exercise Testing Utilization after the COVID-19 Pandemic in Ontario: A population-cohort study

Javier Silva-Valencia (1,2), Karen Tu (1,3), Rahim Moineddin (4), Debra A. Butt (1,5), Braden O'Neill (1,6), Anthony Train (1,7), Jessica Gronsbell (1,8), Andrea Gershon (1,2)

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Introduction & Objectives:
Pulmonary exercise testing, including six-minute walk tests, exercise oximetry, and independent exercise assessments, are critical tools for managing chronic respiratory and cardiac conditions, evaluating treatment response, and determining long-term oxygen therapy needs. During the COVID-19 pandemic, testing was reduced to limit viral spread. This study aimed to evaluate post-pandemic trends of pulmonary exercise testing utilization in Ontario overall and across demographic groups.

Methods:
We conducted a population-based cohort study using Ontario administrative data between April 2015 and December 2023 to evaluate pulmonary exercise testing before, during, and after the COVID-19 pandemic. We used an Auto-Regressive Integrated Moving Average Model (ARIMA) model and incidence rate ratios to evaluate recovery trends. Subgroup analysis examined if trends were similar in different groups.

Results:
During the study period, 505,902 tests were performed for 362,888 individuals. As of December 2023, testing rates were still 21% below pre-pandemic levels (IRR 0.79, 95%CI 0.70-0.89). Recovery was lower in males (IRR 0.76, 95%CI 0.66-0.86), individuals living in lower socioeconomic status neighborhoods (IRR 0.71, 95%CI 0.58-0.86), and rural residents (IRR 0.71, 95%CI 0.62–0.83). Northern Ontario saw the most pronounced shortfall compared to other regions, with testing rates one-third of pre-pandemic levels (IRR 0.33, 95% CI 0.26–0.43).

Conclusion:
More than three years after the pandemic began, pulmonary exercise testing rates have yet to return to pre-pandemic levels, with certain groups disproportionately affected. This highlights a significant and ongoing disruption in diagnostic capacity and quality of care for people with respiratory and cardiac diseases.

Abstract 45

Have Pulmonary Function Testing Rates Recovered Post-COVID-19 Pandemic?: A Population-based Study

Javier Silva-Valencia(1,2), Karen Tu (1,3), Krystle Amog (1,4), Rahim Moineddin (5), Debra A. Butt (1,6), Jessica Gronsbell (1,7), Braden O'Neill (1,8), Anthony Train (1,9), Andrea Gershon (1,2)

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Introduction & Objectives: Pulmonary Function Tests are critical in diagnosing and managing respiratory conditions such as chronic obstructive pulmonary disease and asthma. However, because they generate aerosols, they were restricted in laboratories and offices during the COVID-19 pandemic to prevent virus spread. We aim to determine whether Pulmonary Function Test capacity had returned to pre-pandemic levels overall and across demographic groups in a large North American cohort.

Methods: We conducted a population-based cohort study in individuals aged 7 and older from 2015 to 2023 in Ontario, Canada, using provincial health administrative data. Incidence rate ratios (IRR) were used to compare observed rates to rates that would have been expected if the pandemic had never occurred and to assess whether test utilization returned to pre-pandemic levels. Subgroup analyses were conducted across various demographic characteristics.

Results: There were 8,302,872 tests performed on 2,683,844 people during the study period. As of December 2023, testing rates were still 27% lower than they were prior to the pandemic (IRR 0.73, 95% CI 0.63 – 0.87). Recovery was lower in males (IRR 0.72, 95%CI 0.62–0.86), those aged 18-65 (IRR 0.68, 95%CI 0.59–0.82), urban residents (IRR 0.72, 95%CI 0.62–0.86), and individuals of lower socioeconomic status (IRR 0.68, 95%CI 0.59–0.81).

Conclusion: More than three years after the pandemic onset, pulmonary function test rates in Ontario still have not recovered to pre-pandemic levels, with certain groups more affected than others. This points to a possible worse quality of care and disparities in care for people with respiratory disease.

Abstract 46

Evaluation of online videos and websites on inspiratory muscle training for individuals with chronic lung disease

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Introduction & Objectives: Inspiratory muscle training (IMT) is an effective rehabilitation modality for individuals with chronic lung disease, and can improve dyspnea, exercise capacity, and quality of life. Individuals commonly access online health information as a source of instruction and education; however, no studies have evaluated the quality of IMT resources. Thus, the study objectives are to evaluate the content, reliability, quality, and comprehensibility of IMT-related videos and websites for individuals with chronic lung disease, and determine the characteristics of these online resources.

Methods: The search term "(respiratory muscle training) OR (inspiratory muscle training)" was used to evaluate the first 200 YouTube videos and 200 Google websites to determine if they met the study's inclusion criteria: educational or instructional online resource on IMT for individuals with any chronic lung disease. Two reviewers independently evaluated videos and websites using validated scoring systems including modified DISCERN, Global Quality Scale (GQS), PEMAT understandability and actionability, until consensus reached. A content table comprising key IMT components was also scored.

Results: 40 videos and 14 websites were included. Majority of videos (50%) and websites (64%) were uploaded by for-profit organizations. The average content score (out of 25) was low for videos and websites: 7.7+/-4.4 and 11.4+/-5.3, respectively (p=0.01). Videos and websites scored poorly on modified DISCERN (out of 5): 2.0 IQR[1.0–3.0] and 3.5 IQR[2.0–4.0], respectively (p=0.001). Similarly, GQS scores (out of 5) were low for videos and websites: 2.0 IQR[2.0–3.0] and 3 IQR[2.8–3.3], respectively (p=0.003). Videos and websites did not meet the minimum threshold score of >70% set by PEMAT tool for actionability, but did for understandability.

Conclusion: There are a limited number of IMT-related videos and websites for individuals with chronic lung disease. Our findings highlight the need for high-quality, evidence-based online resources, as IMT is an important rehabilitation modality for individuals with chronic lung disease.

This work was funded by the Sandra Faire & Ivan Fecan Professorship in Rehabilitation Medicine, Canadian Institutes of Health Research (PJM 185763), and Comprehensive Research Experience for Medical Students (CREMS) Program.

Abstract 47

A mouse model for pre-transplant administration of regulatory T cells (Tregs) to donor lungs followed by lung transplantation (LTx)

Yamato Suzuki, Betty Joe, Sumiha Karunagaran, Mingyao Liu, Tereza Martinu, Shaf Keshavjee, Stephen Juvet.

Lung Transplant Program and Latner Thoracic Research Laboratories, Toronto General Hospital Research Institute, University Health Network, University of Toronto, Toronto, ON, Canada

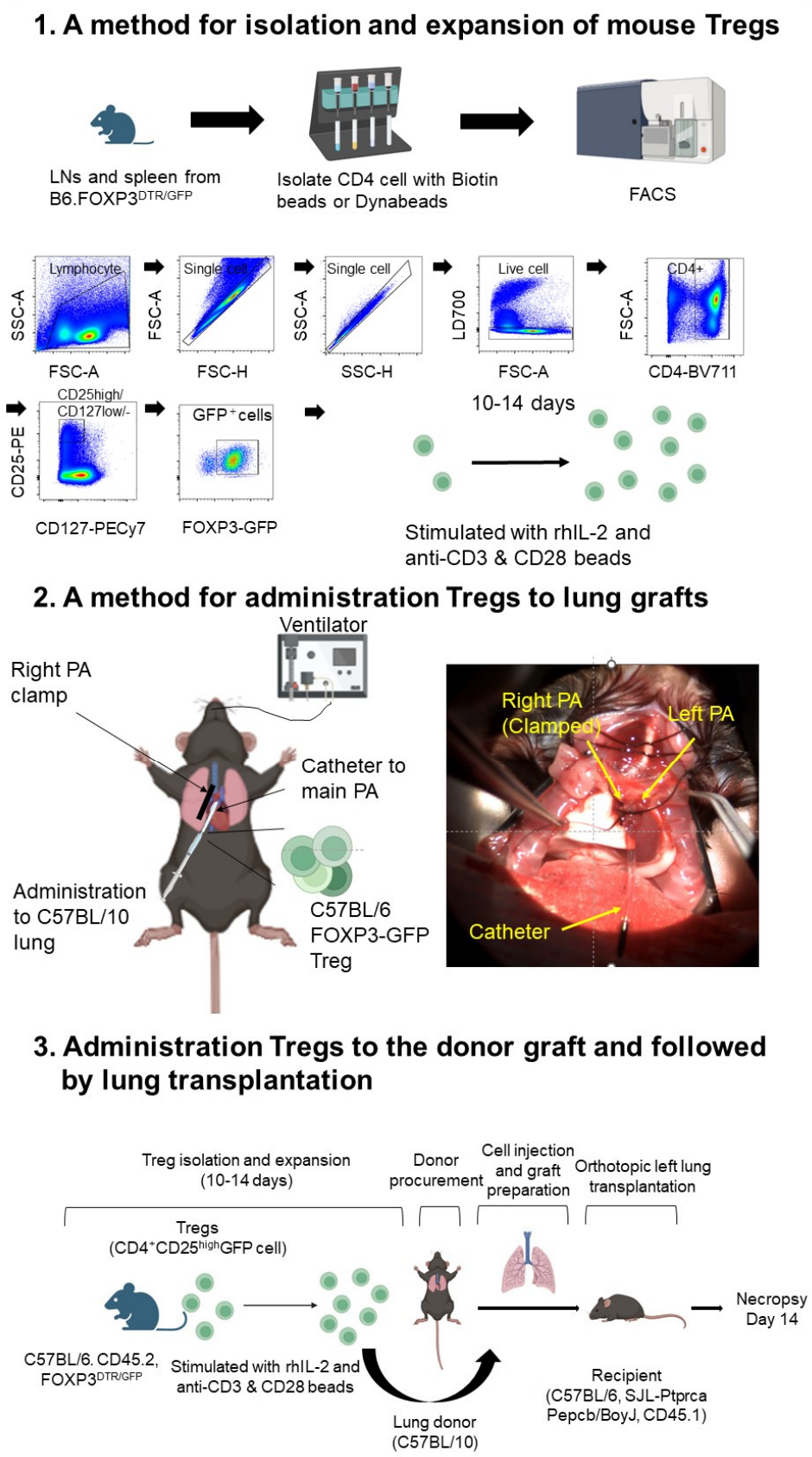
Background: Tregs can modulate graft rejection by suppressing T cell activation. In previous studies, we delivered Tregs to rat lungs using Ex Vivo Lung Perfusion (EVLP) prior to LTx, resulting in inhibition of conventional T cell activation at day 3 and increased graft $FOXP3^+$ cells at day 7 post-LTx. This study aims to establish a mouse model for Treg administration to donor lungs, prior to implantation, followed by LTx. Success of a mouse model will allow the use of transgenic mice to test the effects and mechanisms of pre-LTx-administered Tregs on inhibiting lung allograft rejection and fibrosis.

Methods: Tregs were isolated from C57BL/6 (B6) FOXP3 DTR/GFP/J mice. Lymph node and spleen CD4+ T cells were enriched by magnetic negative selection. $GFP^+CD4^+CD25^+$Tregs were sorted using fluorescence-activated cell sorting and activated with anti-CD3 and anti-CD28 beads with 104 units/mL recombinant human interleukin-2. After 10 days in culture, 9.0×10^6 GFP^+ Tregs were administered to the left lung of C57BL/10J (B10) donor mice via the pulmonary artery after lung flush preservation. Flow cytometry and microscopy were performed on lungs 1.5 hours post-administration to assess Treg presence. In a separate group of B10 donor lungs, 4.1×10^6 Tregs were administered, then lungs were transplanted into B6 recipients, followed by flow cytometry analysis 1-day post-LTx (Fig. A).

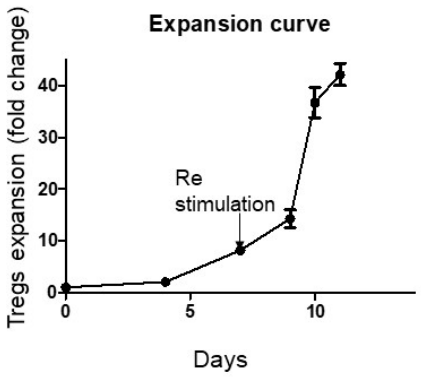
Results: Flow cytometry revealed that 1.5 hours post-administration, 6.4×10^5 cells (7.1% of administered Tregs) in the lung, representing 9.7% of live $CD45^+$ cells (Fig. B). Immunofluorescence showed GFP^+Tregs were localized primarily in the capillaries (Fig. C). In the LTx experiment, 1.0×10^5 cells (2.4% of administered Tregs) persisted in the graft 1 day post-LTx (1.8-2.7% of live $CD45^+$ cells) (Fig. D).

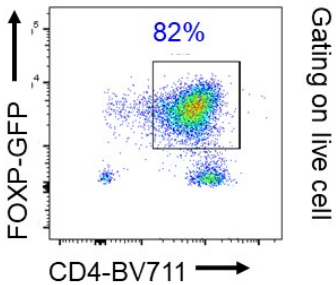
Conclusion: Tregs were successfully administered to donor lungs prior to LTx and persisted at least 1-day post-LTx. We continue to study their long-term persistence and functional role in promoting graft acceptance.

Figure for abstract 47.

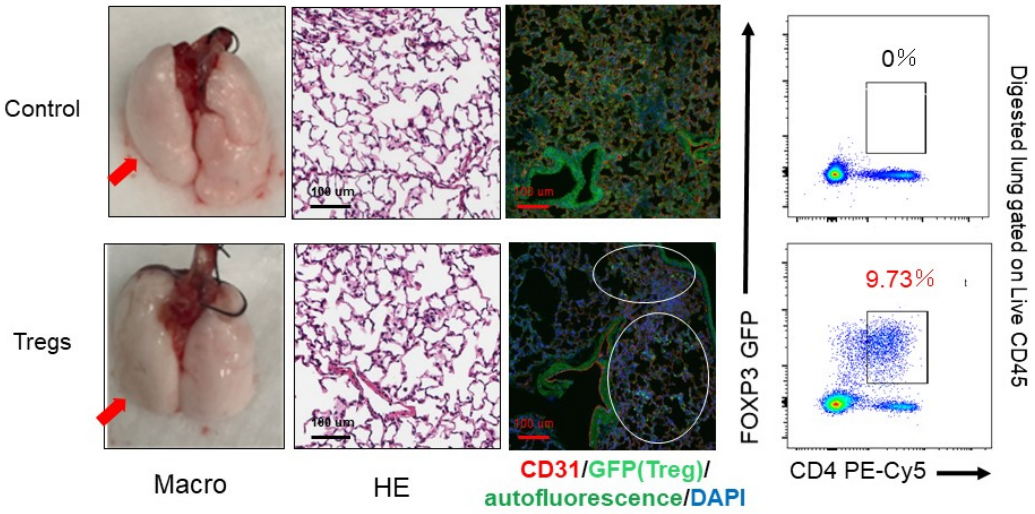


1. Tregs were expanded while maintaining GFP expression

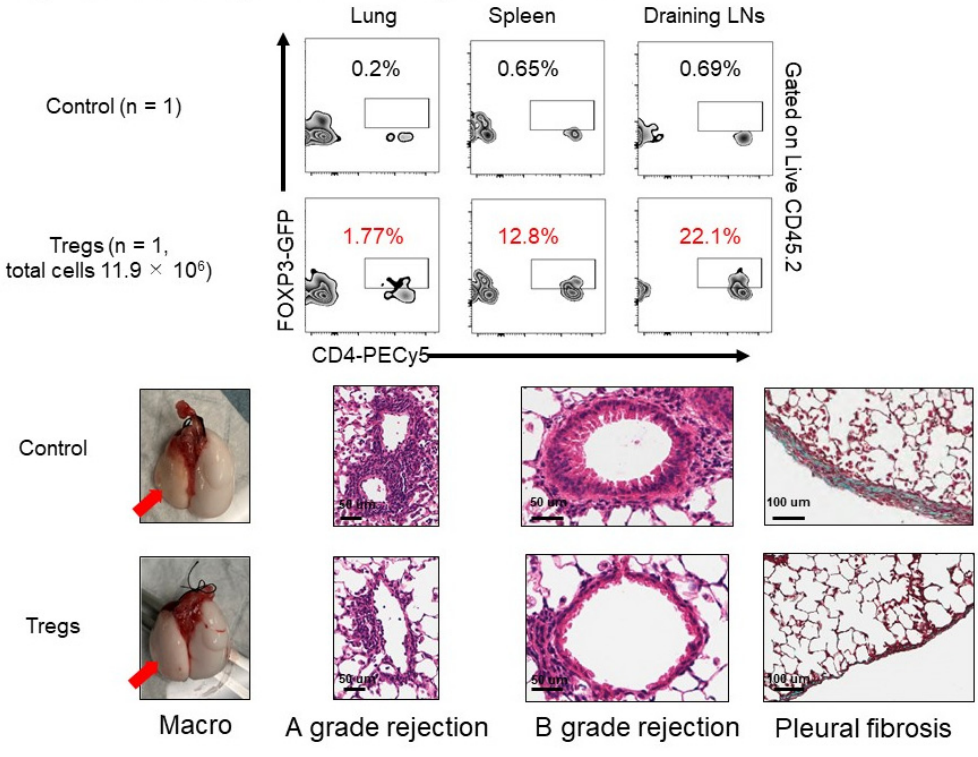




2. Tregs were administered to the donor graft without causing obvious lung injury



3. Tregs were retained in the lung graft and secondary lymphoid organ in 14 days after LTx



Abstract 48

Comparative Effectiveness of Electronic Cigarettes and Pharmacotherapy for Smoking Cessation: A Systematic Review and Bayesian Network Meta-analysis of Randomized Trials

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Background: Electronic cigarettes (e-cigarettes) are commonly used as an aid for smoking cessation, but their comparative effectiveness versus conventional pharmacotherapies remains uncertain. This study aimed to perform a network meta-analysis of randomized controlled trials (RCTs) evaluating the effectiveness of e-cigarettes compared to conventional pharmacotherapies for smoking cessation.

Methods: We conducted a systematic review and Bayesian network meta-analysis of RCTs. We searched Embase, Psychinfo, Cochrane CENTRAL, and Web of Science for RCTs comparing approved or e-cigarettes to standard care, no treatment, or behavioral treatment. The primary outcome was biochemically confirmed continuous smoking cessation. We used Bayesian random-effects network meta-analysis for data synthesis.

Results: A total of 309 RCTs including 143,823 patients were analyzed. E-cigarettes increase smoking cessation compared to placebo (OR 2.50, 95% Crl: 2.00 to 3.20) (high certainty). E-cigarettes probably increase smoking cessation compared to control interventions (OR 2.50, 95% Crl: 2.00 to 3.13) (moderate certainty) and compared to nicotine replacement therapy (NRT) (OR 1.39, 95% Crl: 1.11 to 1.72) (moderate certainty). E-cigarettes probably increase smoking cessation compared to bupropion (OR 1.43, 95% Crl: 1.11 to 1.82) (moderate certainty). The effect of e-cigarettes compared to bupropion combined with NRT is very uncertain (OR 1.27, 95% Crl: 0.86 to 1.82) (very low certainty). E-cigarettes probably reduce smoking cessation compared to the combination of e-cigarettes with NRT (OR 0.60, 95% Crl: 0.35 to 1.11) (moderate certainty). E-cigarettes may reduce smoking cessation compared to the combination of e-cigarettes with varenicline (OR 0.46, 95% Crl: 0.15 to 1.16) (low certainty). Compared to varenicline alone, e-cigarettes may not significantly improve smoking cessation rates (OR 0.92, 95% Crl: 0.68 to 1.19) (low certainty). E-cigarettes may also not significantly differ in effectiveness compared to varenicline combined with bupropion (OR 0.66, 95% Crl: 0.36 to 1.25) (low certainty) or varenicline combined with NRT (OR 0.67, 95% Crl: 0.40 to 1.14) (low certainty).

Conclusion: Our network meta-analysis suggests that e-cigarettes increase smoking cessation compared to placebo, and probably compared to control interventions, NRT, and bupropion. However, the effectiveness of e-cigarettes compared to combination therapies, including NRT and varenicline, remains uncertain.

Abstract 49

Post-Lung Transplant (LT) Longitudinal Bronchoalveolar Lavage (BAL) Profiling Reveals Prognostic Autoantibodies (AABs) with Pathogenic Potential in Chronic Lung Allograft Dysfunction (CLAD)

Daniel Vosoughi (1), Ke Fan Bei (1), Shaf Keshavjee (1), Tereza Martinu (1), Stephen Juvet (1)

1. Toronto Lung Transplant Program, University Health Network

Introduction: We identified novel AABs strongly associated with future CLAD. It remains unknown whether AABs exhibit distinct longitudinal dynamics that might likewise carry prognostic value, and whether they bind cognate cell-surface antigens of pathogenic relevance.

Methods: BAL AABs were profiled by antigen microarray. Surfactant protein-D (SP-D), secreted by alveolar-type-II (AT2) cells, was measured by ELISA. Post-LT samples were retrospectively collected at 3, 6, 12, 18, and 24-months (m) post-LT from 79 patients who developed CLAD before 5 years (CLAD; n=28) or remained CLAD-free for at least 5 years (noCLAD; n=51). AAB scores were developed as previously described (PMID: 39971216). Next, explanted lung tissue from CLAD (n=12; BOS, n=5; RAS, n=7), IPF (n=3), COPD (n=3), and donor (n=5) patients were analysed by flow cytometry. Plasma samples paired to CLAD tissue (n=11) were profiled for AABs.

Results: Ten BAL AABs were elevated over time in CLAD. BAL AABs were associated with future CLAD at 12, 18, and 24-m post-LT (Fig.1A). Among these, IgG anti-GRP78 levels spike at 12-m, (Fig.1B), more so in early CLAD (≤ 24-m, Fig.1C), and coincided with a marked decline in SP-D levels (Fig.1D). GRP78 is known to translocate to the cell surface under conditions of stress. AT2 cell-surface GRP78 was significantly elevated in BOS, and more so in RAS – the more severe CLAD phenotype – as well as in IPF (Fig.2A). Plasma IgG anti-GRP78 levels were strongly negatively correlated with GRP78+ AT2 cells (Fig.2B), possibly reflecting depletion, and positively correlated with intragraft IgG+ class switched memory B-cells (Fig.2C).

Conclusion: BAL AABs appear prognostically useful. IgG anti-GRP78 levels spike concurrent with SP-D decline, possibly reflecting AAB-mediated AT2 cell injury. Presumably, allograft stress may induce AT2 cell-surface GRP78 translocation, driving a GRP78-directed B-cell response and enabling AAB-GRP78 ligation, leading to injury, death, and clearance as a conceivable mechanism of CLAD and pulmonary fibrosis.

Figure for abstract 49.

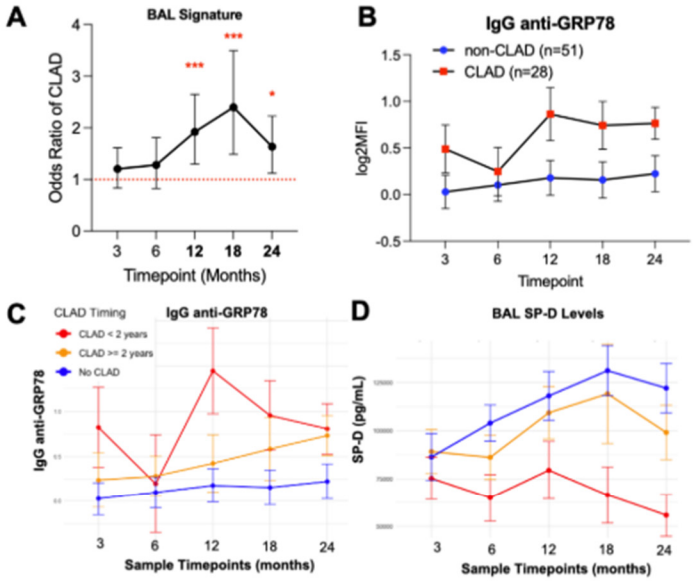

Figure 1. BAL AABs are associated with future CLAD and a decline in AT2 cell function. A) Odds ratio of future CLAD by 5 years using patient specific AAB scores calculated using the top 4 IgG AABs in CLAD BAL. Logistic regression. B) Longitudinal dynamics of BAL IgG anti-GRP78 in patients who developed CLAD by 5 years compared to patients who remained CLAD-free by 5 years. C) Longitudinal IgG anti-GRP78 and (D) BAL SP-D levels further stratified by early (≤ 2 years) and later (≥ 2 years) CLAD.

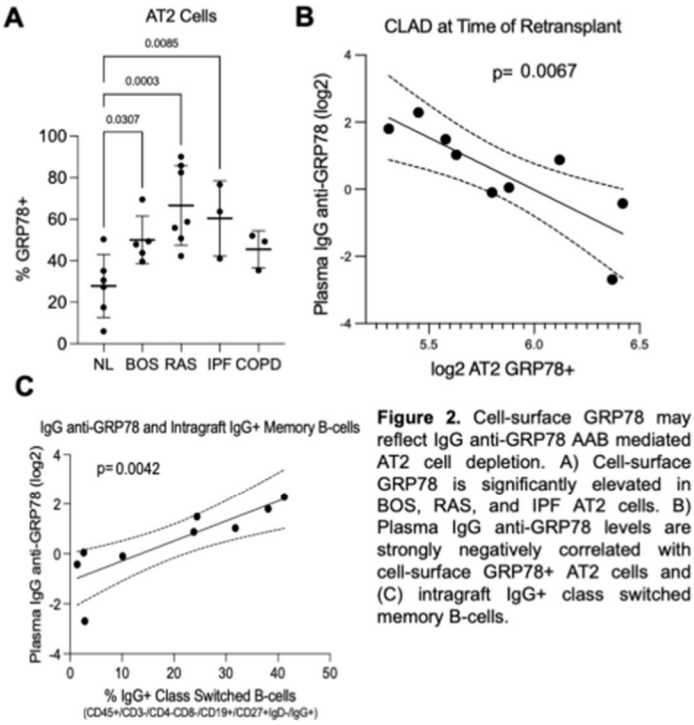

Figure 2. Cell-surface GRP78 may reflect IgG anti-GRP78 AAB mediated AT2 cell depletion. A) Cell-surface GRP78 is significantly elevated in BOS, RAS, and IPF AT2 cells. B) Plasma IgG anti-GRP78 levels are strongly negatively correlated with cell-surface GRP78+ AT2 cells and (C) intragraft IgG+ class switched memory B-cells.

Abstract 50

COPD Action Plans: An Analysis

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Background: Chronic obstructive pulmonary disease (COPD) affects 10% of adults over 40. Personalized action plans (APs), recommended in international guidelines, improve quality of life and reduce hospitalizations, yet remain underused by patients and primary care providers. To assess whether the APs themselves contribute to this low uptake, we analyzed commonly used APs for their development, evaluation methods, content, and format.

Methods: We collected English-language COPD APs from: 1) internet search; 2) international COPD guidelines; 3) pulmonary/COPD organizations and experts; 4) trials identified in a previous Cochrane review of randomized controlled trials (RCTs) of COPD self-management; and 5) an updated literature search (Cochrane Airways Trials Register, CENTRAL, MEDLINE, EMBASE, Clinicaltrials.gov and World Health Organization International Clinical Trials Registry Platform databases). We evaluated development and validation methods, and completed duplicate document analysis for content, format, and reading level of identified APs. Results were summarized descriptively.

Results: We identified 59 unique COPD APs from seven countries. Only seven (12%) reported development methods, with one including patients in development. Of 54 APs not from RCTs, only four had been evaluated (as part of larger complex interventions). In terms of AP content, while general descriptors and instructions were similar, there was significant variability in practical instructions, for example medication options, doses, and duration. Formatting was inconsistent, and APs met a mean of 5.2/8 clinical education design principles. The average Flesch-Kincaid grade level was acceptable across plans.

Conclusion: COPD APs are strongly recommended across guidelines but are rarely implemented. Our novel analysis of internationally available COPD APs reveals that there are several intrinsic factors related to their development, evaluation, content, and format that may be contributing to this care gap. A user-preference based COPD AP with expert consensus on content and human factors optimization of format should be developed and evaluated.

Supported by: Division of Respirology, Department of Medicine, University of Toronto.

Abstract 51

Benefit and safety of long-term proton pump inhibitor use in lung transplant recipients

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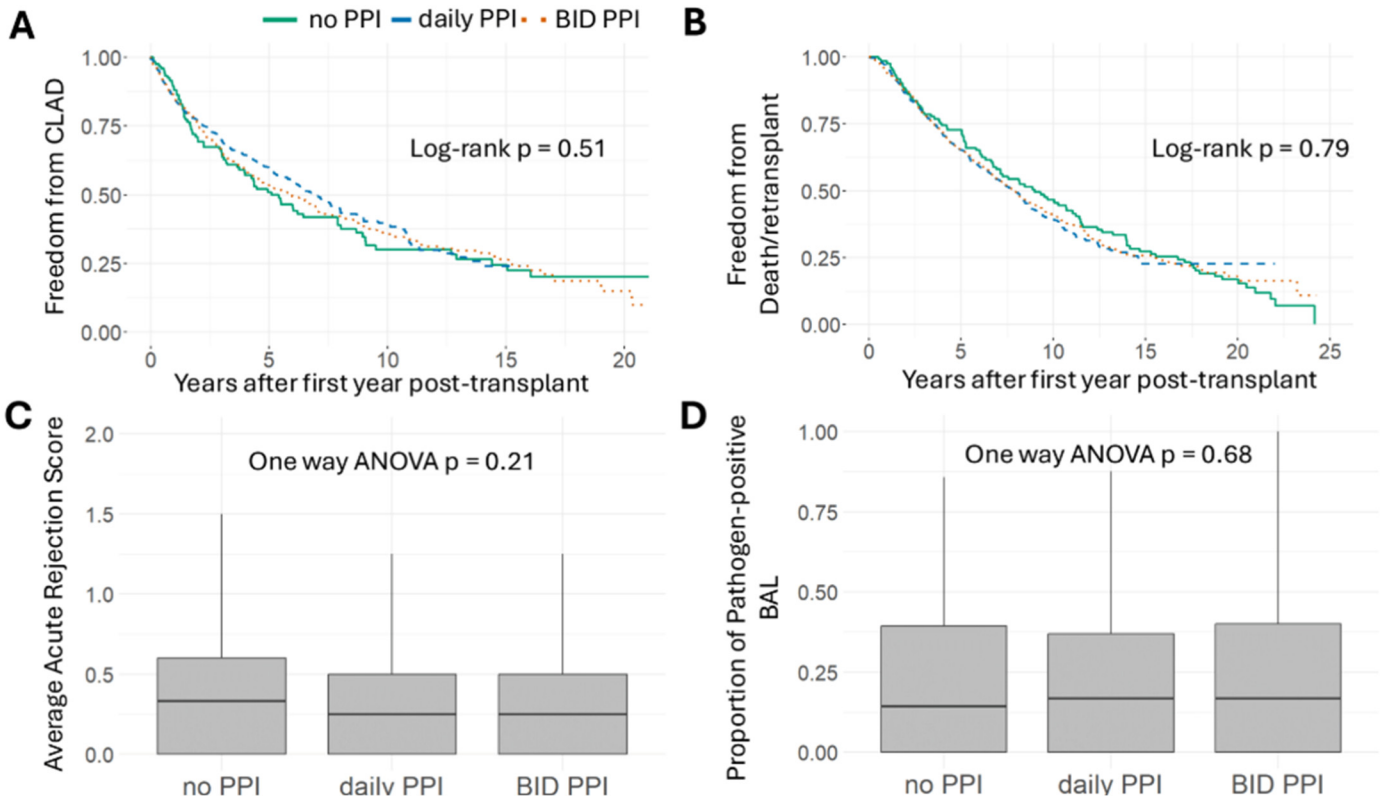
Background: Gastroesophageal reflux is thought to drive microaspiration and is a known risk factor for poor outcomes following lung transplantation (LT). Although proton pump inhibitors (PPI) are commonly used for symptomatic treatment of gastroesophageal reflux, it remains unclear whether they modify the underlying risk of microaspiration. Recent studies have raised concerns over the safety of long-term PPI use, including potentially increased risk of pneumonia. We assessed long-term PPI use and association with key clinical outcomes in LT recipients.

Methods: This single-center retrospective cohort study included all adult first LT recipients from 1999 to 2018 who were alive and chronic lung allograft dysfunction (CLAD)-free at 1-year post-transplant. PPI use in the first year post-LT was determined from electronic medical records, with long-term use defined as ≥8 continuous weeks.

Results: Among 1308 included patients, 121 (9%) patients were not on PPI, 562 (43%) patients were on daily PPI, and 625 (48%) patients were on twice daily PPI. Patients on PPI were older and from a later era. There were no differences in time to CLAD or death/retransplant in unadjusted Kaplan Meier models and adjusted Cox proportional hazards models for age, sex, era, LT type, and cytomegalovirus serology mismatch. In the first year post-LT, the A score (average of acute cellular rejection A-grades across transbronchial biopsies) and the proportion of bronchoalveolar lavage positive for clinically-significant pathogens were similar between groups.

Conclusion: Long-term PPI use and dose in the first year post-LT was not associated with acute rejection, bronchoalveolar lavage pathogen positivity, CLAD or death/retransplant. Despite a lack of clear benefit, long-term PPI use was highly prevalent. It is reassuring that long-term PPI use, even at twice daily, does not appear to worsen major outcomes. However, given their common use, we plan to evaluate their appropriateness and other clinically-relevant endpoints in LT recipients.

Figure for abstract 51.



Abstract 52

Digital twins of ex vivo human lungs enhance preclinical therapeutic evaluation

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Introduction and Objectives: Digital twins show great potential in transplant medicine for evaluating new therapies to repair injured donor organs. Ex vivo lung perfusion (EVLP) sustains donor lungs before transplantation and generates real-time, multi-modal data, offering a unique opportunity to train machine learning models to forecast lung function and create digital twins of human lungs. We developed a digital twin model of ex vivo lungs and validated its clinical utility to evaluate therapeutic efficacy of donor lung treatments.

Methods: Lung physiology, biochemistry, proteomic and metabolomic biomarkers, transcriptomics, and imaging features were derived from n=1000 EVLP cases performed at our centre (2008-2024). Multi-modal time-series forecasting models were trained with k-fold cross-validation using tree-based XGBoost and deep learning-based gated recurrent unit models to forecast lung functional parameters at future time points with mean absolute error and mean absolute percentage error as model evaluation metrics. As a proof-of-concept to validate the clinical utility of digital lungs, therapeutic efficacy (pulmonary arterial pressure, PAP) and safety (edema) of a thrombolytic treatment were evaluated using the digital twins of n=16 EVLP cases with suspected pulmonary emboli.

Results: The digital lung model accurately predicted donor lung function for over 75 functional parameters during EVLP, with an average accuracy of 96.4% compared to the observed values. The digital twin approach identified treatment-induced reductions in PAP without causing lung edema in thrombolytic-treated lungs, tailored to each individual case.

Conclusion: Using real-world data, we validated digital twin models for preclinical therapeutic evaluation, showing that they enable direct comparisons between treated organs and their virtual counterparts. This advancement supports precision medicine, enhances preclinical assessments, and accelerates clinical trials in respirology research.

Abstract 53

Compensatory Anti-Ferroptosis Responses in Human Lung Cells Exposed to EVLP Perfusate Steen Solution

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Purpose: Ex-vivo lung perfusion (EVLP) with Steen solution can support the donor lungs for several hours and has greatly improved donor lung assessment and utilization. However, Steen solution has limited nutrients and lacks cytoprotective components. This study aims to examine the effect of Steen solution on basic cellular functions and identify mechanisms of injury to target with nutrients and therapeutics. We hypothesized that Steen solution exposure to cells leads to activation of ferroptosis - an iron-mediated programmed cell death.

Methods: Human bronchial epithelial cells and human pulmonary microvascular endothelial cells were cultured to sub-confluence at 37℃ and then exposed to either Steen solution or culture for 2, 4, 24 and 48h. Antioxidant and protein levels related to ferroptosis were examined with enzymatic assay and western blotting, respectively.

Results: Glutathione levels were significantly depleted in BEAS-2B cells incubated in Steen solution compared to DMEM after 24h. Glutathione peroxidase 4 activity, which attenuates lipid peroxidation, was significantly decreased in Steen solution after 48h. However, no difference in protein levels was observed. SLC7A11 protein, involved glutathione synthesis, was increased in Steen solution after 48h. No significant changes in protein levels of the antioxidative transcription factors NRF2 was observed after 48h, however, its regulator, KEAP1, significantly decreased in both cell types. FTH1 (ferritin heavy chain, a ferroxidase enzyme) protein levels were significantly increased, while the levels of NCOA4, modulator for FTH1 degradation were decreased.

Conclusions: Steen led to impaired anti-oxidative function in both cell types, which may reduce protection against ferroptotic mechanisms. Prolonged exposure results in compensatory changes towards anti-ferroptosis.

Thanks to the Division of Respirology and the Latner Thoracic Surgery Research Laboratories for this opportunity.