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# **The Queen Elizabeth Hospital Research Expo 2019**

**Thursday 10 and Friday 11 October  
Program & Abstracts**

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# TQEH Research Expo

## Thursday 10 & Friday 11 October 2019

### **Thursday: Student Posters & Researcher Showcase**

9:15am	Poster Presentations: Laboratory Researchers
10:30am	Morning Tea
11:00am	Poster Presentations: Clinical Researchers
2:00pm	Researcher Showcase, followed by afternoon tea

### **Friday: Student Oral Presentations & Plenary Lecture**

8:15am	Honours & Summer Vacation Students
9:15 am	Junior PhD Students (Laboratory)
10:15am	Morning Tea & Trade Displays
10:45am	Senior PhD Students (Laboratory)
12:00pm	<b>Plenary Lecture: Professor John Rasko AO</b>
1:00pm	Lunch & Trade Displays
2:00pm	Clinical Research Group 1 (Clinical Trainees)
3:00pm	Clinical Research Group 2 (Clinical Higher Degrees)
4:00pm	<b>Award Presentations</b>

**Basil Hetzel Institute, Ground Floor Seminar Rooms, 37a Woodville Rd**  
more information: [www.basilhetzelinstitute.com.au](http://www.basilhetzelinstitute.com.au)

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## **TQEH Research Expo 2019**

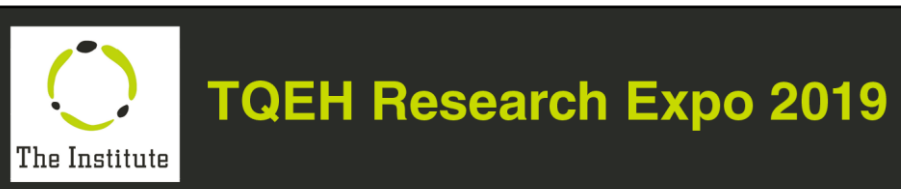
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- **Plenary lecture: Professor John Rasko AO** **p 4**
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Welcome to The Queen Elizabeth Hospital Research Expo 2019. We are delighted to again present the valuable research being conducted here at The Queen Elizabeth Hospital (TQEH) and Basil Hetzel Institute over two consecutive days. TQEH Research Expo has become a major event in the research calendar and is acknowledged as playing an important role in the professional development of the next generation of researchers. Please come along and hear about the world-class research being performed in The Institute.

This year, the Committee was delighted to receive 43 Abstracts which is a record number for this event! Twenty three students will take part in the mini-oral / poster competition on Thursday morning 10<sup>th</sup> October and twenty students will give oral presentations on Friday 11<sup>th</sup> October. Details of the program are given below. On Thursday afternoon, we will also hold the TQEH Researcher Showcase event which will be attended by donors of our major sponsor, The Hospital Research Foundation. This year, the Showcase will commence with presentations from two of our students who recently participated in the 3 Minute Thesis competition. This will be followed by a panel discussion “Challenges and Solutions to Medical Research” and details of this event are also given below.

Award presentations will follow the final oral presentations on Friday afternoon at 4pm. Please ensure to support the presenters at all the sessions!

Many people have contributed to the success of TQEH Research Expo 2019 and we would like to thank all those involved. In particular, we thank:

- Our Major Sponsor, The Hospital Research Foundation
- Other University, Hospital and Corporate Sponsors who have sponsored prizes and the catering
- Our Plenary Speaker, Professor John Rasko AO
- Chairs of the sessions

Adrian Abdo  
John Beltrame  
Tania Crotti  
Kevin Fenix  
Guy Maddern

Peter Psaltis  
Rosanna Tavella  
Deb White  
Richard Young  
Peter Zalewski



## TQEH Research Expo 2019

- Abstract judges and judges for Oral and Poster presentations

Adrian Abdo  
Christina Bursill  
Yuliy Chirkov  
Cher-Rin Chong  
Pallave Dasari  
Joanne Dollard  
Kevin Fenix  
Robert Fitridge  
Branka Grubor-Bauk  
Peter Hewett  
Catherine Hill  
Wendy Ingman  
George Kiroff  
Zlatko Kopecki

Sue Lester  
John Licari  
Mak Masavuli  
Tharshy Pasupathy  
Isuru Ranasinghe  
Katharina Richter  
Regine Süss  
Rosanna Tavella  
Damon Tumes  
Kandiah Umapathysivam  
Sarah Vreugde  
Jim Wang  
Solomon Yu  
Peter Zalewski

- Members of the Research Expo Organising Committee for the work they have put in throughout the year in planning TQEH Research Expo.

Adrian Abdo  
Rebecca Anderson  
Yuliy Chirkov  
Prue Cowled  
Gwenda Graves  
Jenny Hardingham  
Anne Hamilton-Bruce

Kathryn Hudson  
Sue Lester  
Eric Smith  
Fiona Smithson  
Rosanna Tavella  
Joanne Young

We hope that you enjoy TQEH Research Expo 2019 and find it a valuable and worthwhile activity. If you have any comments on this year's program or any ideas for the future, do not hesitate to speak to one of the members of the Organising Committee. The Committee will be happy to incorporate any feedback received when planning for 2020 commences.

### **Prue Cowled PhD**

Interim Chair, Organising Committee  
TQEH Research Expo, 2019



## **TQEH Research Expo 2019**

### **2019 TQEH Research Expo Plenary Lecture**

**12pm Friday 11 October**

**Professor John Rasko AO**

**Professor of Medicine**

**Centenary Institute, Sydney**



Professor John Rasko is an Australian pioneer in the application of adult stem cells and genetic therapy. Since 1999 he has directed the Department of Cell and Molecular Therapies at Royal Prince Alfred Hospital and the Gene and Stem Cell Therapy Program at the Centenary Institute, University of Sydney. He is the President (2018-20) of the prominent International Society for Cell & Gene Therapy.

John is a clinical haematologist, pathologist and scientist with an international reputation in gene and stem cell therapy, experimental haematology and molecular biology. In over 170 publications he has contributed to the understanding of stem cells and blood cell development, gene therapy technologies, cancer causation and treatment, human genetic diseases and molecular biology.

John serves on Hospital, state and national bodies including Chair of GTTAC, Office of the Gene Technology Regulator – responsible for regulating all genetically-modified organisms in Australia - and immediate past Chair of the Advisory Committee on Biologicals, Therapeutic Goods Administration. Contributions to scientific organisations include co-founding (2000) and past-President (2003-5) of the Australasian Gene & Cell Therapy Society; Vice President (2008-12) and President-Elect (2016-18) International Society for Cell & Gene Therapy; Scientific Advisory Committees and Board member for philanthropic foundations; and several Human Research Ethics Committees. He is a founding Fellow of the Australian Academy of Health and Medical Sciences. In 2018, the Board of the ABC honoured him as the sixtieth Boyer Lecturer. He is the recipient of national (RCPA, RACP, ASBMB) and international awards in recognition of his commitment to excellence in medical research, including appointment as an Officer of the Order of Australia.



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# TQEH Research Expo 2019

Thursday 10 October

## 9.15 – 10.30am: Mini-Oral Session for the Poster Competition

### Laboratory Researchers

Chairs: Dr Kevin Fenix and Dr Peter Zalewski

#### Abstract 6

9:15: Harrison Bolt, Mahnaz Ramezanpour, Alkis Psaltis, Peter-John Wormald, Sarah Vreugde  
The Role of FOXP3 in Sinonasal Mucosa

#### Abstract 7

9:20: James Clarke, Steven Ha, Amanda Townsend, Tim Price, Jenny Hardingham, Eric Smith  
Prognostic significance of aquaporin family members in colorectal carcinoma

#### Abstract 9

9:25: Bimala Dhakal, Fenix KA, Li MY, Drew PA, Hauben E, Voelcker N, Maddern GJ  
The effects of SFRP5 on colorectal cancer cells *in vitro*

#### Abstract 13

9:30: Michael Gouzos, Mahnaz Ramezanpour, Ahmed Bassiouni, Alkis Psaltis, P.J. Wormald and Sarah Vreugde  
A Delicate Balance: Modulating Reactive Oxygen Species after Sinus Surgery to Augment the Healing Process

#### Abstract 15

9:35: Steven Ha, James Clarke, Helen Palethorpe, Yoko Tomita, Amanda Townsend, Tim Price, Eric Smith, Jennifer Hardingham  
Determination of miR-181a and miR-21 expression as prognostic markers in colorectal cancer

#### Abstract 17

9:40: Emerance Ishimwe, Makutiro Masavuli, Eric Gowans, Branka Grubor-Bauk  
Novel vaccination approach to elicit neutralising antibodies against HIV

#### Abstract 19

9:45: Stephen Shih-Teng Kao, Mahnaz Ramezanpour, Ahmed Bassiouni, John Finnie, Peter-John Wormald, Sarah Vreugde, Alkis Psaltis  
Barrier disruptive effects of mucus isolated from chronic rhinosinusitis patients



## TQEH Research Expo 2019

### Abstract 23

9:50: Timothy Lee, Masanobu Suzuki, Mahnaz Ramezanpour, Clare Cooksley, Bola Jeong, Stephen Kao, Takayoshi Suzuki, Alkis Psaltis, Yuji Nakamaru, Akihiro Homma, Peter-John Wormald, and Sarah Vreugde  
Mucosal Zinc Depletion associates with tissue eosinophilia and collagen depletion in Chronic Rhinosinusitis

### Abstract 24

9:55: Man Ying Li, Bimala Dhakal, Guy Maddern, Ehud Hauben, XF Zhou, Kevin Fenix, Paul Drew  
Investigation of the effects of a novel orally bioavailable curcumin formulation in models of Colorectal Cancer

### Abstract 28

10:00: Maryam Nakhjavani, Palethorpe HM, Tomita Y, Smith E, Pei JV, Yool A, Price TJ, Townsend AR and Hardingham JE  
Anti-cancer properties of ginsenoside Rg3 epimers

### Abstract 31

10:05: Beula Panchatcharam, Clare M Cooksley, Mahnaz Ramezanpour, Rajan Sundaresan, Ahmed Bassiouni, Peter J. Wormald, Alkis Psaltis, and Sarah Vreugde  
Biofilms Break Barriers in Chronic Rhinosinusitis

### Abstract 34

10:10: Gohar Shaghayegh, Clare Cooksley, Kevin Fenix, Alkis James Psaltis, Peter-John Wormald, Sarah Vreugde  
Inflammatory Endotypes in Chronic Rhinosinusitis

## 10.30 – 11.00am Morning Tea

### 11.00am – 12.15pm: Mini-Oral Session for the Poster Competition Clinical Researchers

Chairs: Dr Rosanna Tavella and Dr Adrian Abdo

### Abstract 4

11:00: Bavand Bikdeli, Renuka Visvanathan, Ido Weinberg, Agustina Rivas, José Antonio Nieto, Ángel Sampériz, Mónica Loring, Fernando Javier Vázquez, Hugo Hyung Bok Yoo, Behnood Bikdeli, and Manuel Monreal  
Clinical Characteristics and Outcomes of Venous Thromboembolic Events after Hallux Valgus Surgery: Insights from the RIETE Registry

### Abstract 5

11:05: Rachel Black, Susan Lester, Catherine L. Hill, William G. Dixon  
Oral glucocorticoid use and the development of cataracts and glaucoma in patients with incident rheumatoid arthritis



## TQEH Research Expo 2019

### Abstract 8

11.10: Anupam Datta Gupta, Helen Bryden  
Botulinum toxin in healing treatment-resistant hand ulcers caused by focal spasticity-a case series

### Abstract 10

11.15: Tom Eldredge, Bills M, Jenny Myers, Jon Shenfine, Dylan Bartholomeusz, George Kiroff  
Challenges of Medical Imaging for Bile Reflux after Obesity Surgery

### Abstract 14

11.20: Nelson Granchi, Lisa Leopardi, Katarina Foley, Martin Bruening, Guy Maddern  
Surgical Coaching in the Outpatient Environment: a video-based intervention that improves surgical consultation skills

### Abstract 16

11.25: Md Monowar Hossain, David Yu, Bavand Bikdeli and Solomon Yu  
Sarcopenia and adverse post-surgical outcomes in geriatric patients group: a scoping review

### Abstract 22

11.30: Aakriti Lath, Rosanna Tavella, Ellen Rees, Lynda Tully, Margaret Arstall, John Beltrame  
Gender Differences in Post-Myocardial Infarction Angina in Australian Patients

### Abstract 27

11.35: Roger Mikaeel, Joanne Young, Eric Smith, James Kimber, Wendy Uylaki, Meghan Horsnell, Gonzalo Tapia Rico, Jenny Hardingham, Yoko Tomita, Peter J. Hewett, Jonathan Young, Darren Tonkin, Nicola K. Poplawski, Paul A. Drew, Dainik Patel, Amanda Townsend, Timothy Price  
Whole Exome Sequencing of 70 Young-Onset Colorectal Cancer Cases

### Abstract 21

11.40: Beatrice Kuang, Guilherme Pena, Kay Hon, Suzanne Edwards, Solomon Yu, Prue Cowled, Joseph Dawson, Robert Fitridge  
The prevalence and assessment of sarcopenia in diabetic foot ulcer patients



## Abstract 35

11.45: James Smyth, I Hendrix, K. Umapathysivam, C. Tufanaru, H. Grantham, G. Arendts, Renuka Visvanathan  
Roles of assessments of activities of daily living (ADL's) and frailty for transfers of nursing home (NH) residents to the emergency department (ED): a scoping review

## Abstract 41

11.50: Gabriella Venter, Joanna Tieu, Rachel Black, Susan Lester, Nieves Leonardo, Rachelle Buchbinder, Samuel Whittle, Catherine Hill  
Patient perspectives of glucocorticoid use in a cohort of patients with rheumatoid arthritis

**12.15 - 2.00pm: Lunch Break**  
(Bring your own lunch)



**TQEH Research Expo Prize Winners: 2018 [Giri Krishnan not in photo]**



## TQEH Research Expo 2019

**Thursday 10 October**

**2pm: Researcher Showcase**

Chair: Professor Guy Maddern, Director of Research, BHI, TQEH

**2.00: Introduction by Mr Paul Flynn, CEO, The Hospital Research Foundation**

**2.05: BHI 3 Minute Thesis Finalists (Faculty of Health & Medical Sciences, University of Adelaide)**

Amita Ghadge: "Why Alex Dunphy won't get breast cancer?"

Tom Eldredge: "Can we win the war on obesity?"

**2:15: Panel Discussion "Challenges and Solutions to Medical Research"**

With: Professor John Beltrame  
Professor Catherine Hill  
Ms Fiona Smithson



**Afternoon Tea  
at the conclusion of this session**





# TQEH Research Expo 2019

## Friday 11 October Student Oral Presentations & Plenary Lecture

### 8.15 - 9.15am: Honours and Summer Vacation Students

Chair: Associate Professor Tania Crotti

#### Abstract 2

8.15: Zein Amro, Andrea Yool, Katherina Richter  
Blocking Bacterial Water Channels to Prevent Growth of *Staphylococcus aureus*  
Small Colony Variants

#### Abstract 33

8.30: Ahad Sabab, Rajan Vediappan, Sha Liu, Sarah Vreugde, Steve Moratti, Alistair Jukes,  
Peter-John Wormald  
The efficacy of novel chitosan patches in a rat femoral arterial bleed model

#### Abstract 42

8.45: Vanessa Woelk, Peter Speck, Billingsley Kaambwa, Sadia Hossain,  
Isuru Ranasinghe  
Predictors of 30-day readmission costs for peripheral arterial disease patients in  
Australia: a population study.

#### Abstract 43

9.00: Taylor-Jade Woods, Peter Speck, Sadia Hossain, Linh Ngo, Isuru Ranasinghe,  
Billingsley Kaambwa  
Incidence of 30-day readmission and associated healthcare costs in patients  
hospitalised with atrial fibrillation: An Australian population-based study

### 9.15 - 10.15am: Junior PhD Students (Laboratory)

Chair: Associate Professor Richard Young

#### Abstract 11

9.15: Sholeh Feizi, Clare Cooksley, Clive A. Prestidge, Alkis Psaltis, Peter-John Wormald,  
Sarah Vreugde  
Treatment of bacterial airway infections with green synthesized silver/silver chloride  
nanoparticles

#### Abstract 20

9.30: Laurine Kaul, Andrew Zannettino, Regine Suess, Katharina Richter  
A new treatment combination to control staphylococci infections in hernia surgery



## TQEH Research Expo 2019

### Abstract 26

9.45

Martha Alemayehu Menberu, Andrew Hayes, Alkis Psaltis, Peter-John Wormald, Sarah Vreugde

Free fatty acids: the potential for prebiotic treatment of a dysbiotic microbiome in chronic rhinosinusitis

### Abstract 39

10.00:

Jannatul Ferdoush Tuli, Mahnaz Ramezanpour, Sha Liu, Alkis James Psaltis, Peter-John Wormald, Sarah Vreugde

Effect of *Pseudomonas aeruginosa* exoproteins on the nasal mucosal barrier in chronic rhinosinusitis

### 10.15 - 10.45am: Morning Tea and Trade Displays

### 10.45 - 11.45am: Senior PhD Students (Laboratory)

Chair: Professor Deb White

### Abstract 3

10.45:

Sarah M Bernhardt, Pallave Dasari, Danielle J Glynn, Amanda R Townsend, Timothy J Price, Wendy V Ingman

The impact of menstrual cycling on Oncotype DX Recurrence Scores in premenopausal breast cancer patients

### Abstract 12

11.00:

Amita Ghadge, Pallave Dasari, Rebecca Robker, Wendy Ingman

Impact of pubertal adiposity on breast development, breast density and breast cancer risk

### Abstract 38

11.15:

Yoko Tomita, Helen Palethorpe, Eric Smith, Maryam Nakhjavani, Amanda Townsend, Tim Price, Andrea Yool, Jenny Hardingham

Bacopasides I and II reduce endothelial cell tube formation and HT-29 colon cancer cell migration with synergy observed in inhibition of their viability

### Abstract 40

11.30:

Rajan Sundaresan VEDIAPPAN, Catherine Bennett, Ahmed Bassiouni, John Finnie, Markus Trochsler, Ryan Quarington, Claire Jones, Stephen Moratti, Alkis Psaltis, Sarah Vreugde,

Prevention of abdominal adhesions post-abdominal surgery: Assessing safety and efficacy of Chitogel with Deferiprone in a Rat Model





## TQEH Research Expo 2019

### 12.00 - 1.00pm: Plenary Lecture

**Professor John Rasko AO**

**Centenary Institute, Sydney**

**“Cell and Gene Therapy: great power brings great responsibility”**

Chair: Professor Guy Maddern

### 1.00 - 2.00pm: Lunch and Trade Displays

### 2.00 - 3.00pm: Clinical Research Group 1 (Clinical Trainees)

Chair: Professor John Beltrame

#### Abstract 18

2.00: Unyime Jasper, Renuka Visvanathan, Agathe Daria Jadcak, Solomon Yu, Joanne Dollard  
Knowledge, attitudes and strategies for reducing sedentary behaviour and increasing physical activity in hospitalised older patients

#### Abstract 29

2.15: Julia New-Tolley, Amy Reynolds, Sarah Appleton, Tiffany Gill, Susan Lester, Robert Adams, Catherine Hill  
Prevalence of gout and sleep conditions in Australian adults: 2019 Sleep Health Foundation national survey

#### Abstract 30

2.30: Linh Ngo, Anna Ali, Anand Ganesan, Richard Woodman, Andrew McGavigan, Robert Adams, Isuru Ranasinghe  
Incidence and Facility variation in complications following catheter ablation of atrial fibrillation: A nation-wide cohort study

#### Abstract 32

2.45: Oscar Russell, Susan Lester, Rachel Black, Marissa Lassere, Claire Barrett, Graeme Carroll, Lyn March, Rachelle Buchbinder, Catherine Hill  
The influence of socioeconomic factors on medication use in Australians with rheumatoid arthritis (RA): Data from Australian Rheumatology Association Database (ARAD)



## TQEH Research Expo 2019

### 3.00 - 4.00pm: Clinical Research Group 2 (Clinical Higher Degrees)

Chair: Dr Peter Psaltis

#### Abstract 1

3.00: Rachel Ambagtsheer, Elsa Dent, Renuka Visvanathan, Solomon Yu, Tim Schultz and Justin Beilby  
Diagnostic Test Accuracy of Several Common and Novel Frailty Screening Instruments Within a Primary Care Setting

#### Abstract 25

3.15: Beatriz A Martins, Renuka Visvanathan, Helen R. Barrie, Chi Hsien Huang, Eiji Matsushita, Kiwako Okada, Shosuke Satake, Suzanne Edwards  
Built Environment and Frailty: Neighbourhood perceptions and associations with frailty, experience from the Nagoya Longitudinal study

#### Abstract 37

3.30: Joanna Tieu, Seerapani Gopaluni, Mark McClure, Rona M Smith, David Jayne  
Rituximab Associated Hypogammaglobulinaemia in Autoimmune Disease: Long Term Outcomes

#### Abstract 36

3.45: Mark Thompson, Olga Theou, Robert Adams, Graeme Tucker, Renuka Visvanathan  
Frailty is a dynamic condition where repeated measurement is important for mortality prediction: findings from the North West Adelaide Health Study

### 4.00pm: Drinks, Nibbles and Prize Presentations



## ABSTRACT 1

### **Diagnostic Test Accuracy of Several Common and Novel Frailty Screening Instruments Within a Primary Care Setting**

Rachel Ambagtsheer, Dent, E., Visvanathan, R., Yu, S., Schultz, T., and Beilby, J.

National Health and Medical Research Council Centre of Research Excellence Frailty and Healthy Ageing, University of Adelaide, South Australia

**Introduction:** Frailty is a clinical syndrome in which individuals are subject to a heightened risk of negative outcomes (including falls, hospitalisation and mortality) on exposure to external stressors. It is highly prevalent among older people (10.8%). Given emerging evidence that frailty is potentially reversible, calls for more proactive screening within primary care have been advanced. However, many frailty screening instruments have not been sufficiently validated in this context.

**Research Question:** Our objective was to assess the diagnostic test accuracy (DTA) of several screening instruments to identify frailty against two widely used reference standards (Frailty Phenotype [FP, 3+ criteria] and Frailty Index [FI,  $\geq 0.21$ ]).

**Research Methods:** A prospective DTA study. We randomly recruited community-dwelling general practice patients aged 75+ years across 3 South Australian general practice sites. We assessed the Timed Up and Go [TUG], Edmonton Frail Scale [EFS], Groningen Frailty Indicator [GFI], Kihon Checklist [KC], PRISMA-7 [P7], Gait Speed Test [GST], Reported Edmonton Frail Scale [REFS] and the FRAIL Questionnaire [FQ] against the specified reference standards. DTA measures calculated were sensitivity (Se), specificity (Sp), predictive values, likelihood ratios, Youden Index and AUC.

#### **Results:**

We obtained valid data from 228 participants (median age 79y, IQR = 6y, 54.8% female). Frailty prevalence was 17.5% [FP] and 48.7% [FI]. The REFS (Se: 87.5% [73.2 - 95.8]; Sp: 75.5% [68.8 - 81.5] ; AUC:0.863) and KC (Se: 85.0% [70.2 - 94.3]; Sp: 73.4% [66.5 - 79.6] ; AUC: 0.834) met our requirements for sufficient DTA against the FP.

**Conclusions:** Two instruments – the REFS and the KC - met or exceeded our minimum criteria for sufficient diagnostic accuracy. Our results suggest that practitioners have several options for implementing frailty screening without excessive time, equipment or space requirements.

#### **LAY DESCRIPTION**

Frailty can be a serious problem for some older people. It can increase their risk of falls, hospital visits and early death. But frailty is not inevitable. In fact, research has shown that frailty is treatable. Only problem is, most people don't know that they have it, or what to do about it. GPs (doctors) can use a simple process to tell if someone is frail. But to do this, they need accurate tests. We tested some frailty tests that GPs use overseas to see if they work with Australian patients. We found two that passed the test: the Kihon Checklist and the Reported Edmonton Frail Scale.

## ABSTRACT 2

### **Blocking Bacterial Water Channels to Prevent Growth of *Staphylococcus aureus* Small Colony Variants**

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**Background:** Recurrent *Staphylococcus aureus* infections can be associated with small colony variants (SCVs). SCVs are slow growing bacteria with elevated antibiotic-resistance that can form biofilms, compromising the treatment efficacy of standard medical care. To address the need for more effective therapies against SCVs a new treatment is proposed that targets aquaporin channels (AQPs). AQPs regulate the water flow in and out of cells and have been found in mammalian cells and *Escherichia coli*. We hypothesise that *S. aureus* SCVs express AQPs and that these can be blocked by a newly synthesised AQP modulator AqB013 to prevent SCV growth.

**Methods:** To identify the presence of AQPs in *S. aureus* SCVs, polymerase chain reaction (PCR) was conducted using an *E. coli* AQP primer. The minimal inhibitory concentration (MIC) of the AQP modulator AqB013 was determined in planktonic SCVs. Bacterial growth in the presence of AqB013 was measured over 24 h. The AlamarBlue viability assay determined antibiofilm efficacy following 24 h treatment exposure to different concentrations of AqB013 (0.078 mM to 2 mM). *E. coli* ATCC 25922 was used as a control strain. Studies were done in triplicates and statistically analysed by one-way ANOVA.

**Results:** PCR results showed a band at the AQP position, suggesting the presence of a specific AQP channel in *S. aureus* SCVs that is similar to AQPZ in *E. coli*. The MIC of AqB013 was 2 mM. Bacterial growth of planktonic SCV was inhibited by AqB013 in a dose dependant manner, with 99.3% inhibition at 2 mM. AlamarBlue assays showed a significant decrease in viability of SCV biofilms at AqB013 concentrations of 0.125 mM (58% decrease) and 0.06 mM (71% decrease) ( $P < 0.0001$ ) when normalised to vehicle control (DMSO).

**Conclusion:** Our findings suggest a potential AQP channel in *S. aureus* SCVs that shares homology with *E. coli* AQPZ. If proven, a new therapeutic target can be exploited and AQP modulators could be used for treating SCV related infections.

### **LAY DESCRIPTION**

Golden Staph is a micro-organism (bacteria) that puts a burden on human health and quality of life. Following antibiotic therapy, a resistant type of these bacteria, i.e. small colony variants (SCVs) can cause recurrence of infections after months and even years. Current therapies are not effective enough, urging the need for new approaches to combat these bacteria. As water is fundamental for all life, we developed a new treatment that disrupts bacterial water channels. Our findings show that by blocking a specific water channel in SCVs we can prevent their growth, suggesting a new approach to treat infections.



## ABSTRACT 3

### **The impact of menstrual cycling on Oncotype DX Recurrence Scores in premenopausal breast cancer patients**

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**Introduction:** Oncotype DX is a genomic test used to help guide adjuvant chemotherapy treatment decisions for hormone receptor (HR)–positive breast cancers. There is a scarcity of literature on whether Oncotype DX is suitable for use in premenopausal women, where ovarian hormones estrogen and progesterone fluctuate during the menstrual cycle.

**Aim:** To determine the extent to which ovarian cycling affects Oncotype DX Recurrence Scores using paired premenopausal breast cancer samples and mouse models.

**Methods:** To investigate menstrual variation in Oncotype DX Recurrence Scores within the same tumour, paired HR-positive breast cancer samples were collected on different days of the menstrual cycle from premenopausal women (n=18), and compared to postmenopausal women (n=11). Additionally, HR-positive mammary tumours were collected from naturally cycling Mmtv-PyMt mice at either the estrus (n=25) or diestrus (n=28) phase of the ovarian cycle. The Oncotype DX gene signature was assessed through quantitative RT-PCR, and experimental recurrence scores (RS) were calculated using the Oncotype DX Recurrence Score algorithm.

**Results:** Increased discordance in RS was observed between paired samples collected from premenopausal women ( $3.2 \pm 2.5$ ; mean  $\pm$  stdev), compared to postmenopausal women ( $2.0 \pm 1.7$ ;  $p=0.04$ ), and was primarily driven by variable expression of proliferative genes. In mice, tumours collected at diestrus showed significant differences in 6/16 Oncotype DX signature genes ( $p \leq 0.05$ ), and a significant increase in their Oncotype DX recurrence score ( $21.1 \pm 2.4$ ; mean  $\pm$  SEM), compared to tumours dissected at estrus ( $15.5 \pm 1.9$ ;  $p=0.03$ ).

**Conclusion:** Oncotype DX recurrence scores are more variable in premenopausal women, and are affected by the ovarian cycle stage in mouse models. We propose that hormonal fluctuations during the menstrual cycle impact Oncotype DX Recurrence Scores, and may affect the clinical utility of this test in premenopausal women.

### **LAY DESCRIPTION**

New tests are being used to make chemotherapy treatment decisions in breast cancer. However, in premenopausal women, hormones estrogen and progesterone fluctuate during the menstrual cycle. We believe that different hormone levels could affect these chemotherapy treatment decisions. Indeed, using premenopausal breast cancer samples and several mouse models, our research shows that different levels of progesterone at the time of diagnosis can affect chemotherapy treatment decisions. We suggest that new breast cancer tests are unsuitable for use in premenopausal women, as treatment may depend entirely on the day of the menstrual cycle.

## ABSTRACT 4

### Clinical Characteristics and Outcomes of Venous Thromboembolic Events after Hallux Valgus Surgery: Insights from the RIETE Registry

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**Background:** Hallux valgus surgery (HVS) is one of the most common orthopedic procedures, often occurring in older adults. Guidelines provide inconsistent recommendations about venous thromboembolism (VTE) prophylaxis after HVS and data are scarce regarding VTE presentation and outcomes in this population. We reported the clinical characteristics and outcomes of VTE following HVS among patients enrolled in Registro Informatizado Enfermedad TromboEmbolica (RIETE), a prospective multicenter VTE registry. We compared the findings with those of other patients in RIETE.

**Methods:** Consecutive patients with VTE post HVS were included in the study. Baseline characteristics, administration of VTE prophylaxis prior to diagnosis, presenting symptoms and signs, risk factors for VTE, and 90-day outcomes including recurrent VTE, major bleeding and death were determined.

**Results:** A total of 54 patients with VTE post HVS were identified in RIETE (median age: 64 [interquartile range: 56-71] years; 85.2% female) and were compared with 74,111 VTE patients who had not undergone HVS. Among those with VTE post HVS, 63.0% had received VTE prophylaxis, in contrast to 35.6% in the rest of the RIETE cohort. Simplified Pulmonary Embolism Severity Index was zero in 66.7% of the patients with pulmonary embolism post HVS and 33.3% of other RIETE patients ( $P=0.011$ ). Compared with other VTE patients, use of estrogens was higher in HVS group (13.0% vs 5.4%,  $P=0.01$ ). All patients with VTE post HVS (100%) and most of other VTE patients (99.6%) were treated with anticoagulation, most commonly with low-molecular weight heparins. In contrast to the rest of the patients in RIETE, the absolute number of all fatal and non-fatal outcomes at 90 days was zero in the post HVS group (i.e. no deaths, no recurrence of VTE, and no major bleeding).

**Conclusions:** In a large registry of patients with VTE, all patients with VTE post HVS underwent anticoagulation. These patients had much better outcomes than the rest of VTE patients, with no deaths, recurrences or major bleeding events at 90-day follow-up.



## TQEH Research Expo 2019

### ABSTRACT 4 (continued)

#### LAY DESCRIPTION

Hallux valgus is a common problem in the feet which is corrected by surgery. A harmful complication of this surgery is development of blood clots in the thighs, legs and the lungs. As the consequences of blood clots in this situation has not been researched before, we conducted a study to assess whether people who get a blood clot after this type of surgery die more frequently compared with those who had a blood clot, but did not undergo hallux valgus surgery. Our study showed that people who get a blood clot after this surgery die less compared with others.

## ABSTRACT 5

### Oral glucocorticoid use and the development of cataracts and glaucoma in patients with incident rheumatoid arthritis

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**Background:** Cataracts and glaucoma are known glucocorticoid (GC) adverse effects. The impact of GCs on the development of cataracts and glaucoma has not been quantified.

**Aims:** To quantify the impact of GC use, dose, dose-timing and cumulative dose on the development of incident cataracts and glaucoma in patients with RA.

**Methods:** Data were from the Clinical Practice Research Datalink (CPRD), a large UK primary care database derived from electronic medical records (Jan 1992- Dec 2017). Incident RA patients were identified using a validated algorithm. Three GC exposure models assessed the impact of: 1.Current exposure, 2.Dose (prednisolone daily equivalent), current and lagged (1,3,6 months, 1&2 years) and 3.Cumulative dose, as time-varying covariates. Outcomes were analysed separately using parametric survival models. Covariates included smoking, gender and uveitis, with age used as the timescale.

**Results:** Of the 22607 patients with incident RA (median age 66, 68% female), 241 had cataracts and 164 had glaucoma on or before baseline and were thus excluded. GC use was associated with cataracts (OR 2.25, 95%CI 1.89, 2.68) and glaucoma (HR 1.60, 95%CI 1.26, 2.02). For cataracts, an increase from 0-10mg was important for current dose (OR 1.59, 95%CI 1.08, 2.33) and dose 1-year prior (OR2.08, 95%CI 1.45, 3.00). For glaucoma, a 10mg increase in GC dose was important 3-months prior (HR1.54, 95%CI 1.13, 2.10) and 1-year prior (HR1.60, 95% CI 1.20, 2.14). Compared to no use, cumulative GC doses >1000mg (OR1.63, 95%CI 1.26, 2.10) and >4000mg (OR3.15, 95%CI 2.56, 3.88) were associated with cataracts. Compared to no use, there was an increased risk of glaucoma associated with cumulative doses >4000mg (HR1.47, 95%CI 1.07, 2.02).

**Conclusions:** GC guidelines recommend patients are informed of the risks prior to treatment, however the risk of cataracts and glaucoma had not previously been quantified. This information will allow patients to make better informed GC treatment choices.

### LAY DESCRIPTION

Glucocorticoids (steroids) are a type of medication used to treat rheumatoid arthritis. Cataracts and glaucoma are known side effects of steroid use that can affect the eyes, leading to vision loss. This study was carried out to determine the size of the risk of developing these side effects in patients with rheumatoid arthritis. The findings show that steroid use doubles the risk of cataracts and increases the risk of glaucoma by 60%. An increase in steroid dose 1-year earlier, increased the risk of cataracts and glaucoma, as did cumulative doses >4000mg. These findings will help patients to make better informed choices about steroid use.



## ABSTRACT 6

### **The Role of FOXP3 in Sinonasal Mucosa**

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Chronic Rhinosinusitis [CRS] is a recalcitrant disease with multiple suggested pathoaetiologies. We hypothesise an underlying change or deficit in the innate immune system in patients with CRS. Forkhead Box Protein Three [FOXP3] is identified as an increasingly important transcription factor of the innate immune system, regulating immune activity and protecting against autoimmunity. FOXP3 has also been shown to be expressed in epithelial cells, however its role in those cells is unknown. Current research recognises mucosal membranes as critical components of the innate immune system. It is hypothesised that human nasal epithelial cells [HNECs] express FOXP3 and that HNEC FOXP3 plays a role in immune modulation in chronic sinonasal inflammatory conditions.

HNECs were collected from patients undergoing sinus surgery and grown in a monolayer or Air Liquid Interface [ALI] fully differentiated model. Immunofluorescent microscopy, immunohistochemistry, flow cytometry, quantitative PCR, and western blot were used to analyse FOXP3 in cultured cells and tissue embedded in paraffin. HNEC-ALI cultures were exposed to CD3+ cells in a dynamic in-direct co-culture. Additionally, a 3D co-culture was developed using fibroblasts seeded into a scaffold membrane, and HNECs grown and polarised in the apical chamber encouraging differentiation into an airway phenotype, allowing direct contact with Peripheral Blood Mononuclear Cells [PBMCs] cultured in the basal chamber.

FOXP3 is present in HNECs in both the nucleus and cytoplasm. HNECs from CRS patients show a threefold decreased expression of FOXP3 compared to HNECs from non-CRS patients (ANOVA and post hoc turkey,  $P < 0.05$ ). Stimulation with TGF $\beta$ 1 and IL-2 significantly increased FOXP3 expression in HNECs ( $P < 0.05$ ); and treatment with TLR3 agonist, Poly (I:C) LMW, has been shown to significantly modulate FOXP3 expression in HNECs over time. The co-culture of PBMCs with HNECs demonstrates a FOXP3 dependent change in proliferation and differentiation of CD4+ T-Regulatory Cells.

FOXP3 is expressed in sinonasal mucosal epithelial cells to a higher level in non-CRS patients compared to CRS patients. Novel co-culture methods used in this project create an *in vitro* model closer resembling the *in vivo* environment allowing assessment of the role and function of HNEC FOXP3.

### **LAY DESCRIPTION**

Chronic Rhinosinusitis [CRS], or sinus congestion, is an intrusive disease reducing sufferers' quality of life. The cause is currently unknown. It is hypothesised that it may be due to an underlying deficit in the immune system. FOXP3 is an important protein involved in dampening the immune system and protecting against autoimmunity. We discovered FOXP3 in the nose and sinus lining. To investigate the role of FOXP3 we are developing a cell culture model that more closely represents the inside of a nose. This will help us understand the role of sinus cells in diseases, and how they communicate with the immune system and white blood cells.





## ABSTRACT 7

### **Prognostic significance of aquaporin family members in colorectal carcinoma**

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**Background:** Aquaporins are a family of 13 (AQP0-12) pore-forming proteins that facilitate selective movement of water and solutes across cell membranes. Previous findings suggest AQP1 expression is associated with reduced overall survival (OS) in colorectal cancer (CRC), however prognostic significance of the other AQP family members is currently unknown. We hypothesize that functional redundancy between AQP family members may contribute to clinical outcomes.

**Aim:** To determine the prognostic significance of each AQP family member in CRC.

**Methods:** Correlations between transcript expression of each AQP family member and OS were determined in a cohort of 580 CRCs from The Cancer Genome Atlas (TCGA) using Kaplan-Meier survival curves with log-rank test. Validation of significant correlations are being performed in an independent cohort of archived CRCs from TQEH; total RNA will be extracted from cryostat cut sections of fresh frozen tissue using the AllPrep Kit (Qiagen), and relative levels of each AQP transcript determined by quantitative reverse transcription PCR using TaqMan assays (Applied Biosystems), normalising to endogenous controls using delta-delta Ct. To determine if expression of each AQP is an independent prognostic factor, multivariable Cox proportional hazards regression analyses will be performed taking into account confounders. The study was approved by TQEH HREC and all patients provided informed consent.

**Results:** Analysis of TCGA data revealed transcript expression of AQP0, 2, 4, 6, 10 and 12 was low or undetectable in all CRC. High expression of AQP7 ( $P < 0.0001$ ), and low expression of AQP8 ( $P < 0.01$ ) and 11 ( $P < 0.05$ ) was associated with decreased OS. To date amplifiable RNA has been isolated from 52 CRCs from TQEH.

**Conclusion:** Expression of AQP1, 7, 8 and 11 appear to be associated with OS in CRC. Further analysis will be required to validate these findings in an independent cohort and to determine if these AQPs are independent prognostic indicators in CRC.

### **LAY DESCRIPTION**

The aquaporins are a family of 13 proteins (AQP0-12) essential for the rapid movement of water and select solutes across cell membranes. Previous studies suggest that AQP1 may be a useful indicator of the likelihood that a patient with colorectal cancer (CRC) will survive, however currently it is not known if the other aquaporin family members contribute to patient outcomes. This study will utilize publicly available data from a large patient cohort with validation in an independent cohort from TQEH to determine if aquaporin family members are associated with outcomes in patients with CRC.

## ABSTRACT 8

### **Botulinum toxin in healing treatment-resistant hand ulcers caused by focal spasticity-a case series.**

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**Introduction:** We studied 10 patients, with long-standing treatment-resistant hand ulcers caused by focal spasticity. Patients had underlying neurological conditions with spasticity reaching a stage where the fingers unremittingly pressed into the palm resulting in skin breakdown and ulceration. These ulcers failed to respond to standard treatment causing pain and carer frustration with maintenance of hygiene. We treated them in the spasticity clinic, first with botulinum toxin (BT) injection into the spastic muscles followed by dressing and splinting.

**Methods:** We conducted pre and post BT toxin injection analysis with the following outcome measures- Visual Analog Scale (VAS) for pain, pressure ulcer grading (Ulcer) for hand ulcers, Fingertip to Palm (FTP) distance for hand opening, Carer Burden Scale (CBS) and Goal Attainment Scale (GAS).

**Results:** We noted complete healing of ulcers with improvement in pain, carer burden and other measures. We used non-parametric test (Wilcoxon sign rank test) showing significant improvements with the p values of 0.003, 0.004, 0.005, 0.004 and 0.004 respectively in VAS, Ulcer, FTP, CBS and in GAS.

**Discussion:** Focal spasticity affecting the upper limbs is a common problem frequently faced by many neurological patients. Some can develop atypical pressure ulcers of the hand causing intense suffering and stress for families and carers. Individuals with a greater degree of impairment who are placed in the residential care, constitute a vulnerable group. These patients should be referred to the multidisciplinary spasticity clinic. All patients achieved significant reduction of spasticity which allowed the hand to be opened, dressed and splinted. This resulted in complete healing of pressure ulcers, significant reduction in pain, and lessening of the carer burden.

**Conclusions:** Toning down spasticity with BT should be the first step in treating hand ulcerations caused by focal spasticity, followed by dressing and splinting.

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### **LAY DESCRIPTION**

This study is on a vulnerable group of individuals who developed spastic hand ulcers secondary to underlying neurological conditions such as stroke, multiple sclerosis etc. They deemed not suitable for structured rehabilitation due to their greater degrees of impairments and were placed in residential care facility. Their hands smelled offensive with the development of ulcerations as the untreated spastic fingers pressed hard into the palm. This caused significant suffering and carer stress as the hands could not be opened for maintenance of hygiene. They were successfully treated in the spasticity clinic.



### ABSTRACT 9

#### **The effects of SFRP5 on colorectal cancer cells *in vitro***

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Colorectal cancer (CRC) is the third most commonly diagnosed cancer and the second leading cause of cancer related death in Australia. The Wnt signaling pathway is commonly overactive in CRC. Secreted frizzled-related protein 5 (SFRP5) is an extracellular negative regulator of Wnt signaling. It is known to have tumor suppressive properties, including inhibition of tumour invasion and growth *in vitro* and *in vivo*. SFRP5 is downregulated in most cancers due to hypermethylation. The role of SFRP5 in CRC is not clearly understood. Thus, we investigated the effects of SFRP5 on the CRC cell lines MC38, SW480, SW620, HCT116 and COLO205. SFRP5 was added to cell cultures and its effects on viability, apoptosis, proliferation and cell cycle arrest were determined by crystal violet assay and flow cytometry. We found that SFRP5 inhibited the growth of CRC cell lines, with increased apoptosis and G2M arrest *in vitro*. These initial findings support the hypothesis that SFRP5 can modulate the growth of CRC cells. Further *in vitro* and *in vivo* experiments are planned to determine the potential of SFRP5 as a novel therapeutic agent in CRC.

#### **LAY DESCRIPTION**

This year alone, about 6,000 Australians will die from bowel cancer. Despite improved treatments, bowel cancer patients are still subjected to highly toxic drugs with poor clinical outcomes. Thus, there is an urgent need for new therapeutics for bowel cancer. My group has discovered that bowel cancer patients produce lower amounts of SFRP5, a protein with anti-cancer properties, compared to healthy patients. My initial findings suggest that SFRP5 can inhibit the growth of bowel cancer cells in the laboratory. I am now planning experiments to determine if SFRP5 can be used as a treatment for bowel cancer using preclinical animal studies.



### ABSTRACT 10

#### **Challenges of Medical Imaging for Bile Reflux after Obesity Surgery**

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#### **Introduction:**

Surgery for obesity alters stomach anatomy and may promote bile to reflux (BR) from the intestine into the stomach and oesophagus. Bile acts synergistically with stomach acid to damage the oesophagus and can lead to cancer. Diagnosis of BR is best made with hepatobiliary scintigraphy, a form of nuclear imaging, however the anatomical and physiological changes after obesity surgery warrant a modified scanning protocol. In this study, diagnostic challenges and proposed solutions are evaluated for using scintigraphy in this cohort.

#### **Methods:**

Scintigraphy was performed in patients who underwent either sleeve gastrectomy, Roux-en-Y gastric bypass or mini-gastric bypass. After 6-hr fast and 24-hr abstinence from opioid medications, patients received an IV injection of tracer (99mTc hepatic iminodiacetic acid). Two scans were performed: a dual anterior/posterior 60-minute dynamic study of the duodenum, stomach and oesophagus, followed by single-positron emission computed tomography with low dose CT (SPECT/CT) for 3D imaging of the abdominal anatomy. BR was quantified as the percentage of tracer found within the gastric pouch and oesophagus, compared with total tracer excretion.

#### **Results and Discussion:**

The challenge of localisation of the stomach on scintigraphy was ameliorated by adding a SPECT/CT scan for 3D reconstruction to enable accurate BR quantification. Impaired hormone-controlled gallbladder emptying, as a result of the bypassed duodenum, was addressed by ingestion of an oral 'fatty meal', stimulating jejunal cells to trigger gallbladder emptying. In bypass patients, longer scanning duration allowed time for bile to reach the site of the bypass.

#### **Conclusion:**

After obesity surgery, imaging for bile reflux requires longer scanning time, ingestion of a fatty meal, and addition of 3D CT imaging to enhance visualisation and quantification of bile reflux. Going forward, these protocol refinements will be applied to improve diagnostic yield in this cohort.

#### **LAY DESCRIPTION**

Bile helps us break down fatty food in the bowel. Weight loss surgery changes our anatomy in a way that can cause bile to move back up into the stomach and oesophagus. When this occurs, bile can damage the oesophagus and potentially cause cancer. To diagnose bile reflux, bile can be radiologically labelled so we can watch where it goes in real-time using a scanner. However weight loss surgery impacts our ability to obtain clear scan results. To get around this we have refined the established scan technique and altered the timing. Going forward, we can use this modified technique to determine if any weight loss operations increase bile reflux.



### ABSTRACT 11

#### **Treatment of bacterial airway infections with green synthesized silver/silver chloride nanoparticles**

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**Introduction:** Airway infections in Chronic Rhinosinusitis (CRS) are caused by planktonic and biofilm forms of different microorganisms. They are difficult to treat because of their emerging resistance to antibiotics. Therefore, new alternative strategies are needed to treat infections with multi-drug resistant bacteria in the context of CRS. Silver/silver chloride nanoparticles (Ag/AgCl NPs) have been proposed as safe and effective antimicrobials, however, their use is hampered by the lack of efficient production processes. We aimed to evaluate the antibacterial activity of green synthesized Ag/AgCl NPs against both planktonic and biofilm forms of clinically isolated bacteria in CRS patients.

**Methods:** Water-based eucalyptus maculate leave extracts and silver ions were used for the fabrication of AgNPs. Their size, shape and size distribution were characterized by UV-Vis spectroscopy, Transmission Electron Microscopy (TEM), and Dynamic Light Scattering (DLS), respectively. Microdilution method and Resazurin assay were used to assess antibacterial effects of Ag/AgCl NPs against planktonic and biofilm forms of bacteria, respectively. Cell toxicity was assessed by application of Ag/AgCl NPs to Human Bronchial Epithelial (HBE) cells and using standard cytotoxicity assays. Results were analysed using Graph Pad Prism 8 tests.

**Results:** Ag/AgCl NPs were rapidly produced within 5 minutes, spherical in shape and stable over 3 months with sizes ranging between 18 and 74 nm. They depicted significant dose-dependent antibacterial activity against planktonic and biofilm forms of clinical isolates from CRS patients including *Pseudomonas aeruginosa* (n=5), *Staphylococcus aureus* (n=5), *Haemophilus influenzae* (n=5) and *Streptococcus pneumoniae* (n=3) ( $p < 0.05$ ) and were non-toxic

**Conclusion:** Green synthesised AgNPs have potential to be used against planktonic and biofilm infections in the context of CRS.

#### **LAY DESCRIPTION**

Infection of nasal cavities along with sinuses which last more than 12 weeks is called Chronic Rhinosinusitis (CRS). For treatment of CRS, antibiotics acting against germs are prescribed to kill the germs. However, they are not effective because of the resistance. Consequently, researchers are exploring new medicine to kill germs one of which is silver nanoparticle. In my project, silver nanoparticle will be applied for killing germs in CRS patients which may potentially lead to the development of new treatment for CRS.





### ABSTRACT 12

#### **Impact of pubertal adiposity on breast development, breast density and breast cancer risk**

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**Introduction:** High breast density is linked to 29% of breast cancers. Puberty is a critical life stage for breast development as well as for establishment of breast density. High pubertal adiposity is associated with low adult breast density and reduced lifetime breast cancer risk. However, the biological basis of this association is unclear.

**Aim:** To understand the impact of pubertal adiposity on breast development, breast density and breast cancer risk in adulthood.

**Methods:** Pubertal adiposity is modelled in mice homozygous for a mutation in *Alms1* gene. To investigate the effect of pubertal adiposity on mammary gland development, mammary glands were collected from pubertal and adult *Alms*<sup>-/-</sup> mice (n = 10 in each group). Additionally, mammary tumours will be collected from adult *Alms*<sup>-/-</sup>-xMmtv-PyMT mice (n=30 in each group). Further, breast adipose tissue of paired high- and low- density human samples will be evaluated for differences in inflammatory factors. Statistical significance was considered at  $p < 0.05$  by using Student's t test or Wilcoxon matched-pairs rank test.

**Results:** Pubertal *Alms*<sup>-/-</sup> mice exhibit increased adiposity with larger adipocytes ( $2,205.1 \pm 109.4 \mu\text{m}^2$ ) in mammary gland compared to wildtype controls ( $1,807.1 \pm 143.9 \mu\text{m}^2$ ;  $p=0.03$ ). High adiposity led to significantly greater number of terminal end buds (TEBs) in *Alms*<sup>-/-</sup> mice ( $15.8 \pm 1.4$ ) than controls ( $9.67 \pm 1.39$ ;  $p=0.007$ ), and increased BrdU+ proliferative epithelial cells in TEBs in *Alms*<sup>-/-</sup> mice ( $2,859.1 \pm 433.3$  cells/mm<sup>2</sup>) than controls ( $1,496.1 \pm 224.8$  cells/mm<sup>2</sup>;  $p=0.01$ ). Significantly increased abundance of F4/80+ macrophages in mammary fat pad was observed in pubertal *Alms*<sup>-/-</sup> mice ( $251.9 \pm 29.3$  cells/mm<sup>2</sup>) in comparison to controls ( $113.7 \pm 14.5$  cells/mm<sup>2</sup>;  $p=0.0007$ ).

**Conclusion:** High pubertal adiposity affects breast development and can impact adult tumour development. We propose that pubertal adiposity establishes healthy breast microenvironment of low density that reduces the lifetime risk of breast cancer.

#### **LAY DESCRIPTION**

We are a society that is obsessed with weight. With super-thin celebrities serving as role-models, there is substantial pressure on teenage girls to lose weight and become thinner. But it is normal for teenage girls to gain weight during puberty. Increased weight in teenage girls lowers breast density, a significant risk factor for breast cancer, and reduces lifetime risk of breast cancer. But we do not know why increased weight in puberty lower breast cancer risk. Thus, we aim to understand how fat in teenage girls could affect breast development, breast density and breast cancer risk in adulthood.

**ABSTRACT 13****A Delicate Balance: Modulating Reactive Oxygen Species after Sinus Surgery to Augment the Healing Process**

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**Introduction:** Reactive oxygen species (ROS) are known to play a significant role in wound healing. Antibiotics have been shown to affect ROS production in nasal cells *in vitro*, but their effect in the setting of active wound healing (the period after sinus surgery, for example) remains unclear. This study analysed a broad array of antibiotics used after sinus surgery to assess their effect on wound healing and ROS production. It was hypothesised that there would be a negative relationship between ROS suppression and cell migration speed.

**Methods:** Monolayers of primary human nasal epithelial cells and fibroblasts were disrupted with a linear wound, treated with antibiotics and observed over 40 hours in a controlled environment using confocal microscopy. ROS activity and migration speed of the wound edge were measured at regular intervals. The relationship between the two parameters was analysed using mixed linear modelling.

**Results:** As hypothesised, inhibition of ROS slowed cell migration across newly formed wounds *in vitro* ( $p < 0.05$ ). Most antibiotic treatments utilised this mechanism, at least in part, to slow cell migration from 30-40 hours post injury compared to untreated cells. The ROS inhibition control treatment, mitoquinone, had the strongest effect on both parameters. This relationship was observed more reliably and profoundly in fibroblast cell lines compared with epithelial cells.

**Conclusion:** Many of the antibiotics used in rhinological practice inhibited ROS production in freshly wounded cell monolayers and created more favourable wound healing profiles, through the preferential inhibition of fibroblast migration over epithelial cells. This effect from antibiotics was not, however, as profound as a targeted mitochondrial antioxidant. These findings strengthen the notion that ROS modulation is an important mechanism for supporting optimal wound healing post-operatively.

**LAY DESCRIPTION**

There has been significant discussion recently about the role of antibiotics after surgery. Many have questioned their benefit, raising concerns about the risk of side effects and the development of drug-resistant 'super bugs'. This study shows that antibiotics have a beneficial effect on healing tissue by directly reducing inflammation. This is separate to the negative effect that we know they have on invading bacteria. By combining these two effects, they may be more beneficial after surgery than we first realized. The search continues for a medication that can achieve these same beneficial results without any unintended side effects.



### ABSTRACT 14

#### **Surgical Coaching in the Outpatient Environment: a video-based intervention that improves surgical consultation skills**

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Discipline of Surgery, University of Adelaide

##### **Purpose:**

To investigate the efficacy of a peer-based coaching intervention for improvement of surgical outpatient consultations.

##### **Methodology:**

12 qualified surgeons working at The Queen Elizabeth Hospital voluntarily participated in the coaching program. 4 senior surgeons were recruited as coaches and each coached 3 participants. For each participant, an outpatient clinic was recorded. 2 single-patient consultations were randomly selected then viewed by their coach. Recordings were assessed using the MAAS-Global Rating List (MG), forming the basis of a coaching session. The process repeated for a total of 3 sessions.

##### **Results:**

All participants completed the coaching program. There was a statistically significant association between the average MAAS global rating scores and coaching. Coaches of the participants whose scores improved, observed that consultation skills generally improved and that participants were receptive to coaching, implementing the strategies into their daily practice.

##### **Conclusion:**

This is the first study to show objective improvement of consultation skills in qualified surgeons after undergoing a coaching program. This supports the concept of surgical coaching as an effective tool for professional development. Assessment by blinded, independent assessors is currently underway to investigate the effect of coaching bias. Replicated studies are needed to further explore this novel educational method.

#### **LAY DESCRIPTION**

The outpatient consultation requires communication skills that are difficult to master but are essential for quality patient care. Coaching is an educational model to enhance expert performance in fields such as sport and business. 12 surgeons underwent a coaching program to improve communication skills. Each surgeon had 3 separate consults filmed over a 5-month period. Each consult video was reviewed and scored by a coach, who discussed the performance with the relevant surgeon. Overall, scores improved for the surgeons at the end of the program, indicating that coaching can be an effective way of improving communication skills in surgeons.



### ABSTRACT 15

#### **Determination of miR-181a and miR-21 expression as prognostic markers in colorectal cancer**

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**Background:** In early stage colorectal cancer (CRC) patients undergoing 'curative' resection, survival outcomes vary considerably making the decision to offer adjuvant therapy far from clear-cut. We hypothesise that high expression levels of microRNA (miR) 181a, a promoter of tumour angiogenesis, and miR-21, associated with unfavourable recurrence-free survival will provide surrogate quantitative prognostic markers for early stage CRC. The aims are to examine the expression of these two miRs in early stage CRC and to determine whether they are prognostic for survival outcomes.

**Methods:** Nucleic acids including miRs were extracted from sections of archived frozen tumour tissue from CRC patients using the AllPrep kit (Qiagen). Quantitative reverse-transcription PCR (qRT-PCR) was used to determine the levels of miR-21, miR-181a, and RNU48 control sequence. Cycle threshold (Ct) values were determined by Viia7 QuantStudio Real Time PCR instrument and expression levels of miRs were normalised to RNU48 using  $2^{-\Delta\Delta Ct}$ . To determine whether expression of the miRs is an independent prognostic marker, results will be dichotomised about the median for survival analyses using Kaplan-Meier and log rank statistic, and multivariable analyses using Cox regression analyses taking into account known prognostic factors. The study was approved by TQEH HREC and all patients gave informed consent.

**Results:** To date RNA has been isolated from 43 samples and quantified using Nanodrop. The range of RNA obtained from 10-20 10 micron sections was 22.3-665.9 ng/ $\mu$ L. The miR qRT-PCR was optimised by determining the optimal concentration of RNA in the initial poly A tailing and adapter ligation reactions and determining the optimal dilution for reverse transcription and miR-amplification reactions.

**Conclusion:** Sufficient RNA was obtained from archived frozen tissue sections for reliable amplification of miR 181a and miR-21. Survival analyses will be performed when all the RT-PCR studies are completed.

#### **LAY DESCRIPTION**

In early stage CRC, patients undergo surgery to remove the tumour however survival outcomes vary considerably making the choice to offer therapy post-surgery unclear. Biomarkers are needed to help with this decision. MicroRNAs (miRs) are small non-coding nucleic acids that regulate expression of genes involved in cancer. Levels of miR-181a and miR-21 in early stage tumours will be measured to determine if they are predictive for a patient's survival outcome post-surgery. Knowledge of the potential for cancer recurrence and metastatic disease will prompt closer follow-up of these patients and allow earlier intervention with chemotherapy.

## ABSTRACT 16

**Sarcopenia and adverse post-surgical outcomes in geriatric patients group: a scoping review**

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Geriatric Medicine, TQEH

**Background:** Sarcopenia is associated with adverse outcomes in cancer, chemotherapy, solid organ transplants, intensive care and medical patients. It has also been proven to increase mortality, hospital length of stay and complications in the perioperative period in adult patients. However, there are limited studies that examined the association of post-surgical outcomes and sarcopenia in patients aged 65 years and older.

**Objective:** This scoping review aimed to examine the relationship between post-surgical outcomes and sarcopenia in patients aged 65 years and older.

**Methodology:** EMBASE and Medline databases were searched for sarcopenia, perioperative period and post-surgical outcomes. The articles were screened based on our exclusion and inclusion criteria. Finally, the identified studies were reviewed systematically as per the Joanna Briggs Institute (JBI) Methodology for Scoping Reviews, and conclusions were drawn based on the findings of the review.

**Results:** A total of nine hundred articles were found from a literature search on Embase and MEDLINE with the keywords. After duplicates removal and application of the inclusion and exclusion criteria, eight articles were included for this study. All studies defined sarcopenia as low muscle mass but did not include physical function or muscle strength as the parameter of sarcopenia. Five out of eight studies found higher early or late mortality in low muscle mass group. Moreover, low muscle mass was associated with high mortality in emergency surgeries, the reduced long term survival rate in open elective surgeries, and the increased length of hospital stay in endoscopic surgeries.

**Conclusion:** The current review suggests that low muscle mass is associated with adverse post-surgical outcomes in the elderly. It remains to be determined if applying the definition of sarcopenia as per the international consensus of sarcopenia will affect the association of adverse post-surgical outcomes and sarcopenia.

**LAY DESCRIPTION**

Scoping review is a strategy to map literature in a specific area. This is particularly useful for emerging and complex topics. Sarcopenia is a common condition associated with aging defined as progressive loss of skeletal muscle strength, mass and function. Sarcopenia can lead to physical disability, functional impairment and mortality, and it is associated with adverse outcomes in various surgical settings. However, in elderly patients, a limited number of studies have examined this association. This is the first systematic review which showed that sarcopenia is associated with the various adverse post-surgical outcomes in the elderly.



**ABSTRACT 17****Novel vaccination approach to elicit neutralising antibodies against HIV**

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Globally, 37 million individuals are infected with human immunodeficiency virus (HIV). There is no vaccine that can prevent HIV infection, while therapeutic options are lifelong and do not protect from re-infection. Vaccination remains the most successful and cost-effective strategy to prevent future infections. An ideal HIV vaccine should elicit protective neutralizing antibodies (NAb) to HIV. HIV-infected individuals who are co-infected with non-pathogenic GB virus type C (GBV-C) have shown prolonged survival compared with those infected with HIV alone and GBV-C envelope protein (E2) elicits NAb against HIV. Therefore, the aim of this study is to develop novel DNA-based GBV-C E2 vaccines to generate neutralising antibodies against HIV.

To develop an optimal DNA vaccine, different forms of secreted GBV-C envelope genes (sE1 and sE2) fused to an oligomerisation domain known as IMX313P were cloned into the pVAX plasmid using NEBuilder HiFi DNA Assembly Cloning Kit. Fusion of vaccine antigens to IMX313P results in self-assembly into soluble heptameric structures after expression, resulting in increased immunogenicity and protective efficacy, when compared to the same dose of monomeric antigen. The following vaccine constructs were made: pVax-sE1-V5-IMX313P, pVax-sE2-IMX313P, pVax-sE1/E2-IMX313P, pVax-sE2(aa.27-72)-V5-IMX313P, pVax-sE2(aa.276-292)-IMX313P. Antigen expression was assessed by immunofluorescence and Western blotting. Groups of Balb/c mice were immunised intradermally with different DNA vaccines 3 times, at three-week intervals (50-µg/dose). Serum from vaccinated mice will be collected to measure anti-E2 antibody levels by ELISA. The ability of each vaccine to elicit broadly NAb against five different HIV strains will be measured by an *in vitro* neutralization assay in collaboration with Prof Purcell at the University of Melbourne. The outcome of these studies will pave the way for the development of more effective HIV vaccines in the future.

**LAY DESCRIPTION**

HIV remains a major global public health problem, with 1.8 million new infections annually. A vaccine against HIV is necessary, particularly in low-income countries, where the infection rate is the highest. Individuals co-infected with HIV and GBV-C virus have shown prolonged survival compared with those only infected with HIV. This project aims to use GBV-C proteins to develop a novel DNA vaccine against HIV. With this novel approach, we hope to develop an inexpensive and novel DNA-based vaccine that can help in the development of an effective HIV vaccine.

## ABSTRACT 18

### **Knowledge, attitudes and strategies for reducing sedentary behaviour and increasing physical activity in hospitalised older patients**

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Older adults spend up to 99% of their time in hospital sitting or lying (sedentary) with very little physical activity (PA). This contributes to a longer length of hospital stay and poor outcomes such as worsening frailty. Very little is known about the perspectives of hospitalised older patients about sedentary behaviour (SB). Exploring consumer perspectives assists the co-design and development of strategies to reduce SB and improve PA in hospital.

#### **Aims**

The aims of this study of older inpatients are to explore their:

- Knowledge of and attitudes to SB and PA;
- Willingness to change their SB and increase PA;
- Views as to what would be required to help them change their SB and improve PA

#### **Methods**

Semi-structured interviews were conducted with 22 patients aged 65 years and older on an orthopaedic and a geriatric medicine ward at The Queen Elizabeth Hospital. Data collection and analysis was conducted in accordance with grounded theory methodology.

#### **Results**

Older patients are unfamiliar with the term sedentary behaviour. They described SB as being physically and mentally inactive. They are somewhat aware that being sedentary is detrimental to their physical and or mental health. Older people reported they were willing to move more if they felt safe and supported. They reported barriers to PA such as a fear of falling, lack of confidence, physical limitations, lack of activities, lack of support, busy staff and the ward environment. Older patients report that group activities, education and encouragement from staff, goal setting with or without objective feedback and family members/staff support are strategies that could improve their PA and reduce SB in hospital.

#### **Discussion/Conclusion**

Older people have some understanding of the harmful effects of SB and are willing to undertake PA but would like to feel safe and supported.

#### **LAY DESCRIPTION**

Research shows that older patients mostly sit or lie in bed when hospitalised, which can impact on their health. This study sought to understand older patients perspectives about being inactive and their willingness to move more. Patients reported several barriers to moving more in hospital such as lack of engaging activities, busy staff, fear of fall, uncoordinated activities and physical problems. They suggested that having group activities, getting education from staff, support from staff/family members and being allowed to set personal goals about their activity would encourage more activity in older patients during hospital admission.

## ABSTRACT 19

### **Barrier disruptive effects of mucus isolated from chronic rhinosinusitis patients**

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#### **Introduction**

Mucus isolated from Chronic Rhinosinusitis (CRS) patients has been previously demonstrated to have elevated levels of inflammatory cytokines and neutrophil activity compared to healthy mucus samples. However, the direct effect of nasal mucus on the mucosal barrier and its relation to CRS disease phenotype and severity is not known.

#### **Hypothesis/ Research Question**

It is hypothesised nasal mucus from CRS patients has a negative effect on nasal mucosal barrier function when compared to healthy mucus

#### **Methods**

Mucus samples were collected from the nasal cavities of CRS patients and healthy controls and applied to air-liquid interface (ALI) cultures of primary human nasal epithelial cells. Membrane integrity and function was assessed via transepithelial electrical resistance (TER) and cilia beat frequency (CBF). Cell toxicity, and inflammatory response were investigated.

#### **Results**

122 mucus samples obtained from 35 healthy controls, 48 CRS without nasal polyps (CRSsNP) and 39 CRS with nasal polyps (CRSwNP) were applied to ALI cultures. Healthy control mucus applied to ALI cultures demonstrated higher TER and CBF when compared to CRS mucus and negative controls. Elevated interleukin 6 and 8 was observed following the application of CRS mucus when compared to healthy control mucus.

#### **Conclusion**

Healthy mucus appears to have a protective effect on mucosal barrier function when compared to CRS mucus. Further research is required to identify the components of healthy control mucus and CRS mucus to account for these differences.

#### **LAY DESCRIPTION**

Chronic rhinosinusitis (CRS) is a commonly reported illness amongst the Australian population with significant effects on quality of life. Nasal mucus from CRS patients has been associated with increased levels of inflammation. This study aimed to investigate if nasal mucus from CRS patients has damaging effects to the cells within the sinuses.

Healthy mucus appears to have a protective effect on the sinus mucosa. Chronic rhinosinusitis mucus is associated with increased inflammation of the sinuses and cell death. Further research is needed to identify differences in mucus composition to account for the detrimental effects of CRS mucus.



## ABSTRACT 20

### **A new treatment combination to control staphylococci infections in hernia surgery**

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**Background:** Staphylococci are associated with hernia mesh infections affecting 8 million people worldwide. Typically, an infection requires mesh removal, which often leads to recurrence of hernia and higher mortality. Standard treatment frequently fails due to the rise of antibiotic-resistance and the formation of biofilms (i.e. bacterial clusters embedded in a protective matrix). This urgently calls for new antibacterial treatments and investigations on the unknown presence of biofilms in hernia mesh infections.

**Hypotheses:** 1) Biofilms form on meshes of hernia patients. 2) The combination of diethyldithiocarbamate (DDC) and copper (Cu) has antibiofilm activity.

**Methods:** The biofilm killing (BK) of DDC and Cu was determined in 3 methicillin-resistant *S. aureus* (MRSA) and 1 *S. epidermidis* (SE) strain via the AlamarBlue assay. To assess synergy of DDC-Cu and antibiotics, checkerboard assays were performed in biofilms. Tissue samples of hernia patients were analysed by fluorescence in-situ hybridization and confocal microscopy to detect biofilms. Statistical analysis was performed via two-way ANOVA.

**Results:** Monotherapy with a) DDC had no antibiofilm effect and b) Cu had up to 21% BK in MRSA and 7% BK in SE. The DDC-Cu combination showed significant antibiofilm activity compared to DDC and Cu alone (MRSA1: 99% BK,  $P < 0.0001$ ; MRSA2: 95% BK,  $P < 0.05$ ; MRSA 3: 99% BK,  $P < 0.01$ ; SE: 87% BK,  $P < 0.05$ ). In MRSA biofilms DDC-Cu showed synergy and near synergy with fluoroquinolones, tetracyclines, glycopeptides and aminoglycosides and additive effects with  $\beta$ -lactam antibiotics. Microscopy indicated the presence of staphylococci biofilms on hernia meshes.

**Conclusion:** The results suggest that DDC-Cu is a promising new strategy against staphylococci. By enhancing the activity of multiple antibiotic classes standard medical care could regain treatment efficacy against antibiotic-resistant strains. Microscopy studies will be continued to assess the role of biofilms in hernia mesh infections.

### **LAY DESCRIPTION**

Hernia is when parts of an organ squeezes through a hole in the belly, which can be life-threatening if left untreated. Usually a mesh is implanted to fix this problem, but the mesh can be infected by superbugs like Golden Staph resulting in surgery for mesh removal, recurrence of hernia and higher death rates. As many antibiotics lost their power to kill superbugs, new treatments are urgently needed. We developed a new way to destroy Golden Staph by feeding them a toxic cocktail of 2 compounds: one gives them a hangover, while the second knocks them out. This boosts the strength of antibiotics against resistant bacteria and could save lives.

## ABSTRACT 21

### **The prevalence and assessment of sarcopenia in diabetic foot ulcer patients**

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#### **Purpose**

Sarcopenia is associated with a higher risk of major adverse cardiovascular events and mortality in patients with diabetic foot disease. The prevalence of sarcopenia in people aged  $\geq 65$  years in the general population of South Australia is 7.6%, but in the diabetic foot ulcer population it remains unknown. Moreover, it is difficult to perform mobility-based sarcopenia assessments of patients with foot ulceration. Our project aims to identify both the prevalence of sarcopenia and assess hand grip strength as a measurement of sarcopenia in this population.

#### **Method**

A prospective cohort of fifty-nine patients with diabetic foot ulcers was identified over a twelve-month period from January 2018 in multidisciplinary foot clinics within South Australia. Recent CT scans were examined at the most caudal level of the L3 vertebra. Psoas area was normalised for patient height with sarcopenia defined as total psoas area (TPA)  $< 385 \text{ mm}^2/\text{m}^2$  for females and  $< 545 \text{ mm}^2/\text{m}^2$  for males. The hand grip strength was measured using a hand dynamometer with low grip strength defined as  $< 20 \text{ kg}$  for females and  $< 30 \text{ kg}$  for males. The grip strength measurement correlation with TPA was assessed using a linear and binary logistic regression model.

#### **Results**

The median age of all patients was 71 (interquartile range, 67-82) with 75.9% identified as male. The prevalence of sarcopenia in our cohort of South Australian diabetic foot ulcer patients was 15.8%. For patients aged  $\geq 65$  years old, the prevalence was 17.9% and affected one-quarter of men. Low hand grip strength correlated with TPA measurements of sarcopenia (odds ratio, 1.04 (95% CI 1.01, 1.08);  $P = 0.022$ ).

#### **Conclusion**

The prevalence of sarcopenia amongst diabetic foot ulceration patients remains significantly higher than the general population. Assessment of sarcopenia using the hand grip strength test is an accurate, easier and cheaper test compared to medical imaging techniques in a cohort unable to perform gait speed analysis.

#### **LAY DESCRIPTION**

Sarcopenia is the presence of low muscle strength and size, which has been linked with poor outcomes and survival in the diabetic foot ulcer population. We found that 2.5x more people with diabetic foot ulcers are affected by this disease compared to the rest of South Australia. This disease affected one quarter of men aged  $\geq 65$  years old. Grip strength is a simple handheld test, which accurately identifies sarcopenia in a group of patients whose diagnosis normally may be limited by the inability to perform more rigorous physical testing.



## ABSTRACT 22

### Gender Differences in Post-Myocardial Infarction Angina in Australian Patients

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#### Background:

Post-myocardial infarction (MI) angina is increasingly recognised as an important patient-focused outcome, however there is no Australian data evaluating this clinical endpoint. This study aimed to (i) identify the proportion of MI patients with post-infarct angina at 4 weeks after hospitalisation and (ii) determine if gender differences exist in angina symptoms at hospitalisation and 1-month post-infarct.

#### Methods:

Patients from Lyell McEwin Hospital diagnosed with MI and undergoing coronary angiography were consented to participate in a quality of life (QoL) follow-up assessment. The Seattle Angina Questionnaire (SAQ) measuring angina frequency, physical limitation and overall QoL was administered in hospital and at 4 weeks via telephone. The proportion of male and female patients experiencing angina at baseline and 1 month was compared using Pearson's Chi-Squared test. Cross-sectional comparisons between SAQ domain scores for males and females were done using t tests.

#### Results:

During a 3-month recruitment period, 30 MI patients were consented (mean age  $69 \pm 10$  years, 23% females). At baseline, 77% of patients reported angina in the previous 4 weeks and this was similar between males and females (78% vs 73%,  $p > 0.05$ ). Although not statistically significant, females had lower SAQ scores for physical limitation ( $58 \pm 15$  vs  $82 \pm 6$ ,  $p = 0.09$ ) and overall QoL ( $30 \pm 10$  vs  $42 \pm 5$ ,  $p = 0.27$ ) indicating poorer functioning but similar angina frequency scores ( $83 \pm 7$  vs  $82 \pm 4$ ,  $p = 0.93$ ). At 1 month, the proportion of females with post-infarct angina was 67% vs 50% in males ( $p = 0.47$ ). The SAQ responses showed that females had lower scores compared to men on all domains (not statistically significant): physical limitation ( $92 \pm 8$  vs  $98 \pm 1$ ,  $p = 0.16$ ), angina frequency ( $82 \pm 7$  vs  $87 \pm 4$ ,  $p = 0.54$ ) and QoL ( $73 \pm 15$  vs  $84 \pm 5$ ,  $p = 0.34$ ).

#### Conclusion:

Over half of MI patients report ongoing angina symptoms in the first 30-days. This preliminary analysis suggests females may be at higher risk for post-infarct angina.

#### LAY DESCRIPTION

In Australia, no studies have examined how many patients continue to have chest pain after hospitalisation for a heart attack and if there are any gender differences in this outcome. This study hence asked patients who presented to hospital with a heart attack to complete a questionnaire on their chest pain symptoms, and at 4 weeks later for follow-up. Overall, over half of the patients reported ongoing chest pain symptoms at 1 month post hospitalisation (54%). In males this was 50% and in females, chest pain symptoms occurred in 67% which suggests that females may be more likely to have chest pain after having a heart attack compared to men.

## ABSTRACT 23

### **Mucosal Zinc Depletion associates with tissue eosinophilia and collagen depletion in Chronic Rhinosinusitis**

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Chronic rhinosinusitis (CRS) is a chronic inflammatory condition of the paranasal sinuses and linings of the nasal passages. Its pathophysiology is complex with studies showing zinc deficiency, tissue eosinophilia, immune dysfunction and impaired wound healing all playing major roles. However, the significance of decreased zinc levels and its effects on these other factors is unknown.

Our study aimed to identify links between serum, mucous and tissue zinc levels in the context of CRS, especially in relation to collagen content and eosinophil infiltration. We hypothesized that given the current literature; zinc deficiency may also have downstream effects on cytokine and collagen synthesis.

Zinc levels were measured from serum, mucous and tissue samples in 3 cohorts of patients including; chronic rhinosinusitis with nasal polyps (CRSwNP), chronic rhinosinusitis without nasal polyps (CRSsNP) and controls. Cultures of both Human Nasal Endothelial Cells and primary fibroblasts were exposed to zinc deplete and non-deplete media and assessed for differences in cell toxicity, inflammatory cytokine expression and collagen synthesis. We then measured tissue zinc levels and correlated them with Metallothionein-3 (MT3) expression, collagen and inflammatory cell infiltration on histology and Tissue Micro Array.

CRSwNP patients expressed both increased mucus zinc levels ( $P=0.0243$ ) and reduced tissue zinc levels ( $P=0.0023$ ). We further demonstrated a statistically significant correlation between these zinc levels; reduced collagen formation ( $R=0.41$ ,  $P=0.013$ ), increased eosinophil counts ( $R=-0.40$ ,  $P=0.0374$ ) and reduced MT3 expression ( $R=0.44$ ,  $P=0.007$ ). ELISA assays also displayed significantly higher levels of inflammatory cytokines in zinc-depleted cells compared to controls.

Zinc deficiency in patients with CRS likely plays a pivotal role in its pathogenesis through promotion of pro-inflammatory cytokine expression, impaired collagen synthesis and downstream effects.

### **LAY DESCRIPTION**

Chronic rhinosinusitis is an inflammatory condition of your nose characterized by a blocked/runny nose, decreased smell and facial pain. Previous research has identified low Zinc, one of many elements in your body, as a contributing factor to the development of this condition. Our study aimed to link this finding with other known factors including inflammation and poor wound healing. Exposing nasal tissue samples to normal and low concentration zinc solutions and assessing the inflammatory response and tissue structure after showed us that low zinc does have a negative effect on these processes, likely providing potential treatment targets.



### ABSTRACT 24

#### **Investigation of the effects of a novel orally bioavailable curcumin formulation in models of Colorectal Cancer**

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Colorectal cancer (CRC) is the second most common cause of cancer-related death in Australia. Liver metastases are the most common and major cause for death, in this cancer. The five-year survival rate for patients with liver metastases is 30%. Thus, the development of effective drugs for treatment would be of significant clinical value. Curcumin (CUR) has been widely studied as a potential anti-cancer drug. CUR is reported to regulate molecular pathways associated with cell-cycle arrest and apoptosis. However, CUR has poor water solubility and bioavailability. Our group has developed Solu-CUR, a novel formulation of CUR. It uses Soluplus as a vehicle, which greatly increases CUR aqueous solubility, intestinal absorption and bioavailability. The aim of this project is to investigate the effects of Solu-CUR against CRC cell lines *in vitro* and *in vivo*. We treated 10 CRC cell lines (MC38, Colo205, Colo320, Colo320DM, HCT116, HT29, SW48, SNU-C2B, SW480, SW620) with Solu-CUR, or equivalent concentrations of native CUR in DMSO, or Soluplus or DMSO alone. At the concentrations tested, both Solu-CUR and native CUR reduced cell numbers by up to 60% compared to controls. We are investigating reasons for differences observed in the extent of the reduction between the CUR formulations, and between the different cell lines. We are establishing a mouse model to determine the effect of treatment with Solu-CUR on CRC liver metastatic disease.

#### **LAY DESCRIPTION**

Colorectal cancer (CRC) is the second leading cause of cancer death in Australia. Liver metastases is common and has a poor survival. Curcumin is reported to be effective against cancer cells, but poor solubility reduces the amount of drug which reaches a cancer. Soluplus-curcumin increases the solubility of curcumin, and can be taken orally. By increasing the concentration of curcumin reaching the cancer it may improve survival in patients with metastatic CRC. We show that Soluplus-curcumin reduces the rate that cancer cells grow, and plan to measure how its effect as a treatment in mice with liver metastases.



## ABSTRACT 25

### **Built Environment and Frailty: Neighbourhood perceptions and associations with frailty, experience from the Nagoya Longitudinal study**

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**Introductions:** Frailty is a state of reduced physiological reserves and increased vulnerability to endogenous and exogenous stressors. Neighbourhood environments are being recognized as factors that can influence older adults health, physical activity and wellbeing, and can play an important role towards the development and progression of frailty.

**Aim:** Investigate if frailty is associated with neighbourhood perceptions, and which environmental attributes are associated with frailty, in Nagoya, Japan.

**Methods:** Cross-sectional analysis of 2017 wave of the Nagoya Longitudinal Study-Healthy Elderly, a cohort of community-dwelling older adults. Neighbourhood perceptions were assessed with the Neighbourhood Environmental Walkability Scale (NEWS), which includes eight subscales (residential density, land use mix diversity, land use mix access, street connectivity, walking/cycling facilities, aesthetics, traffic and crime safety) and a composite index. Frailty was assessed using a frailty index (range 0 to 1). Univariate and multivariable linear regression models were performed to investigate associations of socio-demographic correlates and frailty index level on the dependent variables of environmental perception. The final model was adjusted for age, gender, education, marital status, social isolation, economic status and physical activity.

**Results:** Data for 370 participants were analysed, with 50.8% classified as robust, 37.3% as pre-frail and 11.9% as frail. In multivariable linear analysis, frailty was associated with NEWS composite index ( $P < 0.001$ ), land use mix diversity ( $P=0.004$ ), land use mix access ( $P=0.045$ ), street connectivity ( $P=0.031$ ), walking/cycling facilities ( $P=0.020$ ), aesthetics ( $P=0.032$ ) and crime safety ( $P=0.002$ ), after adjustment for covariates.

**Discussion:** Increasing frailty levels had a linear association with worsening neighbourhood perceptions, across several themes. This study introduces a novel aspect of the frailty-environment relationship, that older adults with increasing frailty have poorer perceptions of their neighbourhood, which could lead to further constriction of their life-space, less social and physical engagement with neighbourhood and potentially worsen their frailty status.



## TQEH Research Expo 2019

### ABSTRACT 25 (continued)

#### LAY DESCRIPTION

Where a person lives can make a difference to how healthy he or she is ageing? Some older adults can develop a syndrome called frailty, and signs and symptoms include walking slowly, losing weight, having difficulty doing tasks such as climbing stairs and/or carrying heavy weights. We found out that older adults with frailty are more likely to perceive their neighbourhood as less walkable, with worse traffic and crime safety and more difficulty to access shops. Older adults with frailty might be more vulnerable to the neighbourhood they live in, and that could have a negative impact on their health.

## ABSTRACT 26

### **Free fatty acids: the potential for prebiotic treatment of a dysbiotic microbiome in chronic rhinosinusitis**

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#### **Introduction**

Nasal microbiome imbalance or dysbiosis has recently been implicated in the pathophysiology of recalcitrant CRS. Commensal bacteria frequently found in the human sinonasal cavity require an exogenous free fatty acid nutrient to thrive. Hence, free fatty acid based growth-promoting agents (prebiotics) may help restoring the balance of a dysbiotic microbiome in CRS patients.

#### **Hypothesis**

Free fatty acid nutrients can enhance the growth of commensal bacteria but can negatively affect nasal pathogens in planktonic and biofilm form.

#### **Aim**

To determine the effect of Tween80 and Oleic acid on the growth of common nasal bacteria and their antibacterial & anti-biofilm activity against nasal pathogens.

#### **Methods**

Bacterial strains isolated from the sinonasal cavities were treated with various concentrations of Tween80 and Oleic acid and grown in nutrient-poor and nutrient-rich media, followed by determining bacterial growth by measuring optical density over 24 hours. In addition, the effect of Tween80 and Oleic acid on *S. aureus* and *P. aeruginosa* biofilm formation was tested using Alamar-blue assays and results were statistically analyzed using two-way analysis of variance.

#### **Results**

At least 22 sinonasal clinical isolates including the commensals *C. accolens*, *C. propinquum*, *C. pseudodiphthericum* and *S. epidermidis* and the pathogens *S. aureus* and *P. aeruginosa* were analysed. Tween80 and oleic acid at low concentrations (0.125 and 0.0625%) significantly promoted the growth of commensals particularly *C. accolens* in a nutrient poor environment ( $p < 0.05$ ). Moreover, Tween80 and oleic acid (1-0.125%) reduced the formation of *S. aureus* biofilms whereas oleic acid, in particular at 0.0625 & 0.03125% concentrations significantly reduced already established *S. aureus* biofilms ( $p < 0.05$ ).

#### **Conclusion**

This study indicated Tween80 and oleic acid promoted the growth of nasal commensal bacteria and reduced *S. aureus* biofilms supporting their potential as prebiotics for modulating dysbiosis in CRS.

#### **LAY DESCRIPTION**

Nasal microbiome imbalance or dysbiosis has recently been implicated in the pathophysiology of recalcitrant CRS. Commensal bacteria frequently found in the human nasal cavity requires an exogenous free fatty acid nutrient to thrive. Hence, free fatty acid based growth-promoting agents (prebiotics) may help restoring the balance. In this study, treatment of nasal clinical isolates both commensals and pathogens with various doses of free fatty acids such as Tween80 and Oleic acid significantly stimulated the growth of commensals and reduced the formation of biofilms supporting their potential as prebiotics for modulating dysbiosis in CRS.



## ABSTRACT 27

### Whole Exome Sequencing of 70 Young-Onset Colorectal Cancer Cases

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**Background:** In recent years, evidence suggests that there is a rising trend of colorectal cancer (CRC) in young adults in the USA, Australia and many other countries without a well-known cause being reported. This is a serious health concern because YOCRC results in increasing burden of disease through long term morbidity and life years lost. Young adults with CRC often present with advanced stages of the disease with increased prevalence of aggressive histopathological features, and frequently receive aggressive chemotherapies. Up to 50% of the cases have a family history with the disease, suggesting a germline genetic role.

**Aim:** The aim of this study was to perform whole-exome sequencing, on blood DNA from young adults with CRC, to determine the proportion with known actionable mutations, as well as to discover new genes for CRC in young adults.

**Methods:** Seventy unrelated young individuals with CRC (ages 18 to 55 years, 59% or 41/70 female) were recruited in the South Australian Young Onset CRC Study (SAYO). All patients underwent a face-to-face interview and their detailed family history was recorded. Evaluation of all tumours for MMR deficiency was performed by microsatellite instability testing and/or immunohistochemical analysis, exome sequencing was performed for 70 patients.

**Results:** Twenty-five of 69 (36%) patients had a family history with CRC, and 12/69 (17%) had a first-degree relative with CRC. Seven of 63 (11%) cases had a MMR deficient cancer, three of these had confirmed lynch syndrome, and a further four cases had lynch-like syndrome. Sex of 69 (9%) had serrated polyposis syndrome (SPS). Three of 70 had BRCA2 pathogenic germline mutation. One RNF43 and two biallelic MUTYH mutations were found in three individuals. Both the RNF43 and one of the biallelic MUTYH mutation carriers had no evidence of polyposis.

**Conclusion:** There is a need to identify young individuals at increased risk for CRC in the general population so that prevention strategies can be instituted. Eight of 70 (11.4%) young adults with CRC carry actionable germline mutations.

### LAY DESCRIPTION

Colorectal cancer (CRC) is rising in Australian young adults without a well-known cause being reported. Young adults with CRC present at advanced stages of the disease and they thus suffer considerable mortality and morbidity in their most productive time of life, impacting on education, career, family life, and physical and mental health in the survivors. There is a need to identify young individuals at increased risk for CRC in the general population. Though lifestyle risk factors may be involved, almost half number of the cases have a family history with the disease suggesting a germline genetic cause in developing this malignancy.



## ABSTRACT 28

### Anti-cancer properties of ginsenoside Rg3 epimers

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Ginsenoside Rg3 (Rg3), extracted from *Panax ginseng*, has two epimers: 20(S)-Rg3 (SRg3) and 20(R)-Rg3 (RRg3). The aim of this study was to investigate the efficacy of these epimers individually and in combination, in *in vitro* models of breast cancer growth, migration, invasion and angiogenesis. Breast cancer cell lines (MDA-MB-231, HCC1143, DU4475, MCF7, BT474 and T47D) and endothelial cell lines (HUVEC, 2H11 and 3B11) were studied. Only SRg3 (100  $\mu$ M) inhibited the proliferation of MDA-MB-231 among all the cell lines ( $p < 0.0001$ ), while the combination doses (SRg3+ RRg3: 50+25, 25+12.5 and 12.5+6.2  $\mu$ M) inhibited the proliferation of endothelial cell lines ( $p < 0.0001$ ). The mechanism for inhibition of proliferation, tested with flow cytometry, was cell cycle arrest in G0/G1 and not induction of apoptosis. RRg3 (50  $\mu$ M), stereo-specifically inhibited the cell invasion in spheroid invasion assay by 78% ( $p = 0.0001$ ) and cell migration in wound closure assay by 22% ( $p = 0.001$ ). Both epimers inhibited cell migration in transwell assay by 70% ( $p < 0.0001$ ). The combination doses showed even better efficacy in inhibition of migration in both transwell and loop formation assays. The combination doses also significantly inhibited the wound closure and loop formation in endothelial cells. At 50+25  $\mu$ M loop formation was completely inhibited ( $p < 0.0001$ ). Molecular docking showed that Rg3 had a high binding score (-9 kJ/mol) with aquaporin 1 (AQP1) and oocyte swelling assay showed that SRg3, stereoselectively, inhibited the water channel of AQP1. The expression of AQP1 is correlated with cancer cell migration, invasion and angiogenesis and amongst our cell lines, MDA-MB-231 showed the highest transcript expression of AQP1 (tested with RT-PCR). This could, in part, explain a mechanism of action of Rg3 in this cancer model. Further steps are designed to investigate the mechanisms Rg3 in inhibition of angiogenesis and tumour growth, and the efficacy of Rg3 in *in vivo* models.

### LAY DESCRIPTION

The key challenge with breast cancer is to stop the spread of the cancer to other sites in the body and prevent new blood vessel formation needed to sustain the growing cancer. In this study, we have tested two related compounds extracted from the ginseng plant. In breast cancer cell models, we have shown that the combination of these two compounds significantly inhibits the growth, movement and migration of breast cancer and completely prevents new blood vessel formation. These results indicate the potential of these compounds for future testing in animal models and in human clinical trials to treat breast cancer.



## ABSTRACT 29

### **Prevalence of gout and sleep conditions in Australian adults: 2019 Sleep Health Foundation national survey.**

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**Background:** Population studies have shown an association between gout and obstructive sleep apnea (OSA)

**Objective:** To determine the relationship between gout and sleep conditions in an Australian community sample.

**Setting:** Representative population-based sample.

**Participants:** Australian adults ≥18 years

**Methods:** A cross-sectional national online panel survey assessed self-reported doctor-diagnosed OSA, insomnia (according to International Criteria for Sleep Disorders-3 criteria) and behavioural sleep problems. Participants self-reported physician-diagnosed gout and other health conditions. Possible undiagnosed OSA was estimated using self-reported frequent loud snoring and witnessed apneas. Analysis was performed by logistic regression and reported as age and sex adjusted odds ratios (OR).

**Results:** From a total of 2044 respondents, 1948 (95.3%) provided a yes/no response when asked about gout. Respondents with gout (126, 6.5%) were more likely to be male than female (11.2% v 2.0%,  $p < 0.01$ ), and were more frequently diagnosed with heart disease, diabetes, heartburn/reflux and hypertension than those without gout ( $p < 0.01$ ). They were also more likely to report OSA (22.2% v 5.3%; OR 3.8, [95% CI 2.3, 6.3]), insomnia (17.5% v 6.6%, OR 4.6 [2.7, 7.8]), and have possible undiagnosed OSA (16.7% v 9.3%; OR 2.9 [1.7, 5.0]). People with gout were additionally more likely to report worry about their sleep (OR 2.2 [1.5, 3.3]), pain disrupting sleep most nights (OR 1.9 [1.2, 3.0]), and making errors at work in the past 3 months due to sleepiness (OR 3.0 [1.6, 5.9]).

#### **Conclusion:**

Gout is associated with higher frequency of sleep disorders, including OSA. Furthermore, the consequences of poor sleep including reduced work productivity and safety have been associated with gout in our study. This suggests that sleep disorders need to be addressed in people with gout.

#### **LAY DESCRIPTION**

The aim of this study was to determine if a relationship between gout and sleep disturbance exists. To answer this, we performed a national, online survey of 2044 Australian adults. We found that people with gout were more likely to have obstructive sleep apnea and insomnia. Furthermore, they were more likely to report worry about their sleep, pain interrupting their sleep, and more errors at work due to sleepiness. Therefore, gout and poor sleep appear to be linked, and this may result in diminished work productivity and safety.

## ABSTRACT 30

### **Incidence and Facility variation in complications following catheter ablation of atrial fibrillation: A nation-wide cohort study**

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**Introduction:** Catheter ablation of atrial fibrillation (AF) is a rapidly disseminating procedure which poses certain risk of complications. The incidence of procedural complications is uncertain, and the extent to which complication rates may vary among institutions, however, has not been systematically evaluated.

**Aim:** We assessed the incidence and facility variation in complications after AF ablation using population-wide data.

**Methods:** We included patients aged  $\geq 18$  years with a primary diagnosis of AF undergoing catheter ablation between 2010-15 in Australia and New Zealand. The primary outcome was major complications occurring in hospital or up to 30-days after discharge. A hierarchical generalized linear model was used to estimate the hospital-specific risk-standardised complication rate (RSCR).

**Results:** A total of 20,902 patients undergoing an AF ablation were included (mean age  $62.1 \pm 11.6$  years; 29.2% female) from 75 hospitals with 43 performing  $\geq 25$  procedures during the study period. A major complication occurred in 6.76% patients (4.78% in-hospital, 2.28% post-discharge and 0.28% experienced both). Bleeding (3.76%) and pericardial effusion (0.88%) were the most common complications. Procedure-related deaths occurred infrequently (0.14%). Among 43 hospitals that performed  $\geq 25$  procedures, the median RSCR was 6.79% and RSCR varied from 4.09% to 11.68% with 5 hospitals significantly different from the national average. There was no association between a centre's ablation volume and its RSCR (correlation coefficient  $r \sim 0.0$ ,  $p = 0.654$ ).

**Conclusions:** Major complications following AF ablation are common and vary nearly 3-fold among institutions independent of ablation volume and differences in patients' and procedural characteristics, which suggests disparities in care quality. Complication rates should be reported at a facility-level to make procedural complications fully transparent and standardise care.

### **LAY DESCRIPTION**

Catheter ablation of AF is an intervention used to treat atrial fibrillation and it was the fastest growing cardiovascular procedure in Australia with an annual increase of 30.8% from 2000-10. However, AF ablation can cause major complications and uncertainties exist about how common these complications are and whether the risk of complications varies among hospitals. We found that 6.76% of patients undergoing AF ablation experienced a major complication and most importantly, this risk varied by nearly three-fold (4.09% - 11.68%) among hospitals, which suggests variation in care quality.

## ABSTRACT 31

### **Biofilms Break Barriers in Chronic Rhinosinusitis (CRS)**

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#### **Background:**

Staphylococcus aureus biofilms contribute to persistent inflammation in Chronic Rhinosinusitis (CRS). *S. aureus* produces exoproteins that disrupt the nasal epithelial barrier, however, their effect on the mucosal barrier structure and function and how that relates to severity of disease remains unknown. We investigate the effect of exoproteins from clinical isolates of *S. aureus* from CRS patients in planktonic form and as biofilms on the nasal epithelial barrier in relation to severity of disease.

#### **Methods:**

Clinical isolates from 39 CRS patients with *S. aureus* grown as planktonic and biofilm form were concentrated and applied to Air Liquid Interface (ALI) cultures. Tissue samples were stained with Haematoxylin and Eosin to assess inflammation. Transepithelial Electrical Resistance (TEER), permeability of FITC-dextran and Lactate Dehydrogenase (LDH) cytotoxicity were measured and correlated with disease severity scores and tissue inflammation. Structure of tight junctions (TJs), expression of protein Zona Occludens-1 (ZO-1) and claudin-1 were detected by immunofluorescence (IF) and electron microscopy (EM). Statistics using paired Wilcoxon signed rank test and Spearman correlation to compare disease severity scores was performed.

#### **Results:**

*S. aureus* biofilm exoproteins differed between isolates, significantly correlated with levels of inflammation on histopathology and showed a dose-dependent reduction of TEER, cell viability, and increased permeability ( $P < 0.001$ ) when compared to equal concentrations of exoproteins derived from planktonic cultures. Discontinuity in ZO-1 and claudin-1 immunofluorescence was confirmed as disrupted TJs on EM.

#### **Conclusion:**

Exoproteins from *S. aureus* biofilm disrupt the mucosal barrier and their concentrations correlate with levels of inflammation. Anti-toxin therapies and targeted barrier protection could be avenues of novel therapies in CRS.

### **LAY DESCRIPTION**

Golden staph causes sinusitis (stuffy nose, facial pain & loss of smell) a common disease but difficult to treat. This bug roams free (planktonic) on human skin and nose, but when threatened for survival they become stealthy (biofilms). Human nose has natural barrier that prevent these bugs from entering, however Golden staph evades the defense causing disease and resist treatment. My study investigated both form of bugs from 39 patients with sinusitis to understand the human nasal defense structure and how the 2 different forms evade it. This understanding will enable us to innovate ways to eliminate these bugs and bring relief to patients.

## ABSTRACT 32

### **The influence of socioeconomic factors on medication use in Australians with rheumatoid arthritis (RA): Data from Australian Rheumatology Association Database (ARAD)**

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**Aim:** To determine the effect of socio-economic status (SES) on medication use in Australian patients with RA

**Methods:** The Australian Rheumatology Association Database is an observational, longitudinal biologic DMARD (disease modifying anti-rheumatic drug) registry collecting patient-reported safety and other outcome data from RA patients. SES was measured by: (1) participants' highest educational level (less than high school, high school or tertiary education); (2) population quintiles of the Index of Relative Socio-Economic Advantage and Disadvantage (IRSAD) using postcode data (higher score denotes higher SES). Analysis was performed by multivariable, random effects, panel logistic regression with additional covariates of age, sex and disease duration. Results were interpreted as ordinal (linear and quadratic) trends in the predicted marginal, covariate adjusted, probabilities of medication use.

**Results:** 3247 RA patients (73% female, mean age 56 years, mean disease duration 13 years) were included. Higher education was associated with a reduced probability of conventional synthetic DMARD (csDMARD) use (linear slope -2.2% (95% CI -3.2, -1.2),  $p < 0.001$ ), but a greater probability of NSAID use (linear slope 1.8% (95% CI 0.5, 3.0),  $p = 0.004$ ). Higher IRSAD scores were associated with less biologic DMARD use, which was most notable for the highest two quintiles ( $p$  linear=0.017,  $p$  quadratic=0.003), and less opioid use (linear slope -2.4% (95% CI -3.9, -0.9),  $p = 0.0004$ ). Prednisolone use was not associated with either SES variable.

#### **Conclusion:**

Lower SES, measured at area level, was associated with greater use of biologic DMARDs and opioids in RA patients. In contrast, lower education levels were associated with greater probability of csDMARD use but no effect on bDMARDs. These findings are consistent with previous studies reporting poorer disease outcomes in RA patients with low SES. However, the lack of interchangeability of different measures of SES requires further exploration.

#### **LAY DESCRIPTION**

We assessed the effect of socio-economic status (SES) on medication use in Australian patients with RA. Medication use according to participants' SES was assessed by using a large database of surveys completed by RA patients over time. We found that lower SES as determined by participants' area of residence was associated with greater use of opioid and biologic disease modifying antirheumatic drugs (DMARDs), whereas lower education levels were associated with greater probability of conventional synthetic DMARD and reduced anti-inflammatory medication use. These results point to a variation in healthcare by participants' SES.



**ABSTRACT 33****The efficacy of novel chitosan patches in a rat femoral arterial bleed model**

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Intraoperative bleeding is the leading cause of death during surgery. It can distort the surgeon's visual field and increase the risk of complications. Previously, chitosan patch has proven to be an effective haemostat, but whether modifying the chitosan patch can improve its efficacy, remains unanswered. In this study, chitosan patches were modified using polyethylene glycol (PEG) or F127 surfactant to enhance flexibility or platelet/erythrocyte trapping ability of chitosan, respectively. Using *in vitro* and *in vivo* models, this project aimed to test the hypothesis that modified chitosan patch is more efficacious than non-modified chitosan, gauze and commercial haemostats Surgicel and FloSeal. Sixty 8-10 weeks old Wistar Albino rats underwent femoral artery dissection and isolation. A standardized 0.4mm arterial injury was created and the rats were randomized to receive 1 of 6 haemostats (Chitosan, Chitosan/F127 (CF), Chitosan/PEG (CP), Surgicel, FloSeal, or gauze). The outcome measures were, bleeding time and total blood loss. Upon completion of the experiment, blood samples were taken from each rat and applied to the haemostats under lab conditions to test their erythrocyte and platelet aggregation abilities in isolation. The mean bleeding time for the Chitosan group was 125s, which was significantly lower than FloSeal (174s), CF (204s) and Gauze (382s) ( $p<0.05$ ), but not Surgicel (174s) or CP (188s). Gauze had the highest bleeding time compared to the other groups ( $p<0.001$ ). There were no significant differences in the total blood loss between the groups ( $p=0.65$ ). *In vitro* experiments found Chitosan and CP patches to exhibit similar erythrocyte and platelet aggregation ability ( $p=0.43$  and  $p=0.93$ , respectively), which were significantly higher than the other groups ( $p<0.05$ ). In conclusion, non-modified chitosan patch is equally or more efficacious than commercial haemostats and modifying the chitosan patch with PEG or F127 surfactant, does not increase its efficacy.

**LAY DESCRIPTION**

Bleeding during surgery can distort the surgeon's vision and increase the risk of complications. Chitosan patch has been shown to effectively stop bleeding during surgery, but whether changing the chemical or physical structure of chitosan patch can increase its clotting ability, remains unknown. In this study, we modified the structure of the chitosan patch by either adding polyethylene glycol or surfactant F127 to increase its flexibility or blood trapping ability, respectively. Lab and animal experiments were used to test the patches. The results showed, unmodified chitosan patch is better than modified patches, at stopping bleeds.



## ABSTRACT 34

### Inflammatory Endotypes in Chronic Rhinosinusitis

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**Introduction:** Chronic rhinosinusitis (CRS) is a highly prevalent inflammatory disease of the upper airway that afflicts about 9.2% Australians. In contrast to the classical phenotypic classification of CRS patients into those with (CRSwNP) and without (CRSSNP) nasal polyps, endotyping categorizes disease variants based on their underlying pathophysiologic mechanisms. It is hypothesized that CRS patients differ in their immunological endotypes in relation to the risk for disease progression, recurrence and comorbid conditions.

**Method:** The study aims to analyse tissue from 50 patients. Sinonasal tissue was harvested at the time of sinus surgery from CRS patients and controls and processed into a single cell suspension. To characterize the Th2 and non-Th2 inflammatory patterns in CRS patients, the expression of CD3, CD4+, CD8+, IFN- $\gamma$ , IL-4, IL-17A and FOXP3 was studied using multi-colour flow cytometry. The frequency of B cell subpopulation was also investigated using flow cytometric analysis of CD19, CD24, CD27, CD38, CD138 and IgD cell surface markers. One-way analysis of variance (ANOVA) was used for multiple comparisons, where  $p < 0.05$  was considered to be statistically significant.

**Result & Conclusion:** Analysis is under way and we expect to observe differences in IL-4+ T-cells and INF- $\gamma$ + T-cells in CRSwNP and CRSSNP as well as in FOXP3+ T regulatory cells. We will also investigate changes in the frequency of naïve and memory B cells. With the emergence of biologics, endotyping and key markers identification may enable personalized pharmacotherapy for recalcitrant CRS.

### LAY DESCRIPTION

Chronic rhinosinusitis occurs when the lining of the sinuses gets infected or irritated, become swollen, and create extra mucus. Approximately 10% of CRS patients suffer from recalcitrant disease which is unresponsive to medical and surgical treatments. A better definition of the disease is an unmet clinical need to allow for more selective and mechanistically rational treatment.

## ABSTRACT 35

### **Roles of assessments of activities of daily living (ADL's) and frailty for transfers of nursing home (NH) residents to the emergency department (ED): a scoping review.**

James Smyth.\* I.Hendrix.\*\* K.Umapathysivam.# C.Tufanaru.## H.Grantham.^ G.Arendts.^ R.Visvanathan.#,+

\*Department of Emergency Medicine, The Queen Elizabeth Hospital (TQEH). \*\*Pharmacy, TQEH. #Adelaide Geriatrics Training and Research with Aged Care Centre (G-TRAC), School of Medicine, University of Adelaide. ##Australian Institute of Health Innovation, Macquarie University, NSW. ^Curtin University. ^^Emergency Medicine, University of Western Australia. +Aged and Extended Care Services, TQEH.

**Background:** Nursing home (NH) residents have high levels of needs; transfers to the emergency department (ED) carry potentially avoidable risks of complications and demands on resources.

**Aims and hypotheses:** The aims of this scoping review were to map evidence and seek gaps on the following research questions:

- What are the roles of pre-hospital activities of daily living (ADL's) and frailty assessments at the NH in deciding to transfer?
- What are the the roles of the assessments after transfer in ED decision making?

#### **Methods:**

4 databases (CINAHL, Embase, Pubmed, Scopus) were searched on these inclusion criteria:

- Population: NH residents (65 years or older).
- Concept: ADL's and frailty assessments.
- Context: transfer to the ED.

Abstracts of references found were then screened by two independent reviewers. Full text screening, references selection and analysis followed.

#### **Results:**

846 abstracts were found. 38 references were selected. The majority of the NH residents transferred was female and aged in the 80's. Most of the ADL and frailty assessments were done at the NH rather than at the hospital.

**Discussion:** Findings related to the research questions were grouped for discussion into either associations or interventions.

#### **Associations:**

- more disabled residents transferred and admitted more frequently;
- frailty also associated with transfers.

**Interventions** (including ADL's or frailty assessments) with positive outcomes of less transfers and admissions:

- presence of a nurse practitioner at the NH;
- telemedicine assessment of NH residents from the hospital;
- collaborative quality improvement program between hospital and NH staff.

Overall, the principal lacune in the evidence map was reference to both less frequent assessments in the ED and then use in decision making.

**Conclusions:** The main evidence gaps related to ADL and frailty assessments done less often in the ED as well as their roles in ED decision making. The assessments' roles in decisions could also be researched further with regards to the status at the time of emergency.



### ABSTRACT 35 (continued)

#### LAY DESCRIPTION

NH residents have high levels of needs related to frailty; transfers to the ED are frequent and carry risk. The aims of this literature review were to find evidence on the roles of pre-hospital ADL's and frailty assessments at the NH in deciding to transfer elderly residents and in ED decision making after arrival. 38 publications from 846 found in the searches were selected by meeting the aims. Overall the main evidence gaps to follow up related to the assessment being done and used less often in the ED for decision making. Residents with greater disability are transferred to the ED and admitted to wards more frequently.

## ABSTRACT 36

### **Frailty is a dynamic condition where repeated measurement is important for mortality prediction: findings from the North West Adelaide Health Study**

Mark Q Thompson (1,2), Olga Theou (1,2,3), Robert J Adams (4), Graeme R Tucker (2), Renuka Visvanathan (1,2)

1. National Health and Medical Research Council (NHMRC) Centre of Research Excellence: Frailty and Healthy Ageing, University of Adelaide, South Australia 2. Adelaide Geriatrics Training & Research with Aged Care (G-TRAC) Centre, Adelaide Medical School, Faculty of Health and Medical Sciences, University of Adelaide, South Australia 3. Division of Physiotherapy and Medicine, Dalhousie University, Canada 4. The Health Observatory, Faculty of Health and Medical Sciences, University of Adelaide, South Australia

Frailty is a state of decreased physiological reserve and vulnerability to stressors. Frailty places individuals at greater risk of adverse health outcomes, however, it is a dynamic condition and may not always lead to decline.

**Aims:** The aim of this study was to measure frailty state transitions, and to determine the relationship between frailty status (at baseline and follow-up) and mortality using both the Frailty Phenotype (FP) and Frailty Index (FI) in the North West Adelaide Health Study,

**Methods:** analysis of a population-based cohort of community-dwelling older adults (n = 909, mean age 74.4 (SD 6.2) years, 55% female). There was a mean 4.5 years between baseline and follow-up. Mortality was matched to official death records with a minimum of 10 years follow-up.

**Results:** Improvement in frailty state was common for both tools (FP 15.5%; FI 7.9%). The majority remained stable (FP 44.4%; FI 52.6%), and many transitioned to a worse level of frailty (FP 40.1%; FI 39.5%). For both measures, baseline frailty was a significant predictor of mortality up to 10 years, with initially good predictive ability (AUC 0.8-0.9) decreasing over time. Repeated measurement at follow-up resulted in good prediction compared to lower (AUC: 0.6-0.7) discrimination of equivalent baseline frailty status. In a multivariable model, frailty measurement at follow-up was a stronger predictor of mortality compared to baseline. Frailty change for the Continuous FI was a significant predictor of decreased or increased mortality risk based on corresponding improvement or worsening of score (HR = 1.04, 95%CI = 1.02-1.07, p = .001).

**Conclusions:** Frailty was a dynamic process where improvement was possible. Frailty measurement is a good predictor of mortality up to 10 years, however, recency of frailty measurement is important for improved prediction. A regular review of frailty status is required in older adults.

### **LAY DESCRIPTION**

Frailty is a dynamic condition where improvement is possible, and the majority of individuals remain stable. Frailty measurement is a significant predictor of mortality up to 10 years, with predictive strength best immediately after measurement and gradually decreasing over time. A more recent repeated measurement of frailty improves prediction. This suggests that a regular review of frailty status is required in older adults.

## ABSTRACT 37

### **Rituximab Associated Hypogammaglobulinaemia in Autoimmune Disease: Long Term Outcomes**

Joanna Tieu (1,2), Seerapani Gopaluni (2), Mark McClure (2), Rona M Smith (2), David RW Jayne (2)  
(1) Discipline of Medicine, University of Adelaide; (2) Department of Medicine, University of Cambridge

#### **Background:**

Despite a low incidence of hypogammaglobulinemia (HG) in clinical trials using rituximab (RTX), HG occurs in follow-up of patients with autoimmune disease.

Immunoglobulin replacement therapy (IRT) is used to reduce infection rates but there is a paucity of data on its efficacy and impact on longer-term outcomes.

We examined the characteristics of patients with RTX associated HG in autoimmune disease, and their long-term outcomes with IRT.

#### **Methods:**

Patients attending a Vasculitis and Lupus clinic, who received RTX for autoimmune disease between 2004 and 2012, with an immunoglobulin G (IgG) <7g/L on at least 2 occasions were included in this retrospective review. Patients were categorised into nadir IgG subgroups of <3g/L, 3 to <5g/L and 5 to <7g/L. Differences between nadir IgG subgroups were assessed by Chi-squared tests. Trends across subgroups confirmed by Somer's D tests. Continuous variables were compared using Kruskal-Wallis and Wilcoxon sign ranked tests.

#### **Results:**

Of 142 patients, 101 (71.1%) had ANCA-associated vasculitis, 18 (12.7%) systemic lupus erythematosus and 23 (16.2%) other diagnoses. Most received RTX for relapsing (69.3%) or refractory (25.0%) disease. Mean follow-up was 97.2 months from first RTX. Median time to IgG <5g/L was 22.5 months [interquartile range (IQR) 3.0 to 61.5] and to IgG <3g/L was 24.5 months [IQR 4.0 to 80.8]. Previous cyclophosphamide and glucocorticoid use 12 months post-RTX increased the likelihood of IgG <5g/L or requiring IRT at 60 months' follow-up. IRT was commenced in 29 patients, most (65.5%) with an IgG <3g/L. Median duration from first RTX to IRT was 71.0 months [IQR 26.5 – 89.0]. IRT was associated with lower infection rates but not severe infections (requiring intravenous antibiotics or hospital admission).

#### **Conclusion:**

RTX associated HG is progressively identified with longer term follow-up. In patients with recurrent infection, use of IRT was associated with a reduction in infection burden.

#### **LAY DESCRIPTION**

Rituximab is a medication targeting a part of the immune system called B cells. Although clinical trials haven't shown any effects on one of the jobs of B cells, making immunoglobulins that help protect against infection, this has been seen in practice. This study looked at the characteristics of patients with autoimmune disease who developed low immunoglobulins after Rituximab. This study found that low immunoglobulins were often only found years after Rituximab was started. In people who were experiencing recurrent infections, replacing immunoglobulins reduced the risk of infections, but not severe infections that lead to hospital stays.





### ABSTRACT 38

#### **Bacopasides I and II reduce endothelial cell tube formation and HT-29 colon cancer cell migration with synergy observed in inhibition of their viability**

Yoko Tomita\*† ‡, Palethorpe H\*, Smith E\*, Nakhjavani M\*†, Townsend AR\*‡, Price TJ\*‡, Yool A†, Hardingham JE\*†‡

\*Molecular Oncology Group, Basil Hetzel Institute, The Queen Elizabeth Hospital, Woodville South 5011, †Discipline of Physiology, School of Medicine, University of Adelaide, Adelaide 5005, ‡Department of Medical Oncology, The Queen Elizabeth Hospital, Woodville South 5011

**Background:** Bacopasides I (Bac I) and II (Bac II) are triterpene saponins isolated from a medicinal plant *Bacopa monnieri*. While some triterpene saponins exhibit anti-cancer effect, that of Bac I and II are not well described and their synergy has never been investigated. This study assessed synergy of Bac I and II in inhibiting viability of endothelial and colon cancer cells, and examined anti-tube formation and anti-migratory effect of combined Bac I and Bac II on these cells.

**Methods:** IC<sub>50</sub> of Bac I and II and their synergy were assessed on viability of 2H-11 and HT-29 using crystal violet. Tube formation and migration assays were performed with combined Bac I and II on 2H-11 and HUVEC, and HT-29, respectively. For migration assay, circular wound was made on a cell monolayer and wound closure was monitored. Angiogenesis assay was performed on endothelial cells grown on matrigel and the number of tubes formed was counted. IC<sub>50</sub> was estimated using GraphPad Prism and one-way ANOVA was used for statistical analysis.

**Results:** IC<sub>50</sub> of Bac I and II were 106 (95% CI 99-113) and 13μM (95% CI 12-13) for 2H-11 and 98 (95% CI 83-116) and 21μM (95% CI 19-23) for HT-29. With Bac II 5μM present, IC<sub>50</sub> of Bac I was 10 (95% CI 8-11) for 2H-11 and 7μM (95% CI 6-7) for HT-29. Their synergy was confirmed for both cell lines on isobologram. Combination treatment at 5/5μM reduced tube formation by 82% for 2H-11 ( $p < 0.0001$ ) and 73% for HUVEC ( $p < 0.0001$ ), compared to vehicle, where Bac I 10μM and Bac II 5μM individually did not inhibit their tube formation. Combined Bac I and II at 12.5/7.5 μM reduced migration of HT-29 by 75% compared to vehicle ( $p < 0.0001$ ).

**Conclusion:** The findings indicate Bac I and II exhibit synergistic cytotoxicity on endothelial and colon cancer cells and combined treatment may impair colon cancer growth via inhibiting tumour cell migration and tumour angiogenesis with less toxicity than monotherapy. Further evaluation of Bac I and II in animal tumour models is suggested.

#### **LAY DESCRIPTION**

Bacopasides I and II are extracts of a herbal plant *Bacopa monnieri*, used as traditional medicine in parts of the world. Several structurally similar chemicals have anti-cancer effect and hence we examined anti-cancer effect of Bacopasides I and II in cell culture. The result showed together Bacopaside I and II stopped growth of blood vessel and cancer cells more than the sum of their separate effect. Combined Bacopasides I and II also reduced tube formation of blood vessel cells and movement of colon cancer cells. Bacopasides I and II have a potential to be new colon cancer treatment and combining them may allow us to use less of each drug.



### ABSTRACT 39

#### **Effect of *Pseudomonas aeruginosa* exoproteins on the nasal mucosal barrier in chronic rhinosinusitis**

Jannatul Ferdoush Tuli, Mahnaz Ramezanzpour, Sha Liu, Alkis James Psaltis, Peter-John Wormald, Sarah Vreugde

Otolaryngology, Head and Neck Surgery, The University of Adelaide

**Introduction:** Chronic rhinosinusitis (CRS) is one of the most common chronic respiratory conditions in the current world. *P. aeruginosa* infections and biofilms are often implicated in severe recalcitrant CRS, particularly in the context of cystic fibrosis (CF). Mucosal barrier disruption can be exacerbated by bacterial secreted products and is one of the major contributors to airway inflammation, however the role of *P. aeruginosa* in this process is not known.

**Aim:** To determine the effect of exoproteins produced by *P. aeruginosa* clinical isolates from CF and non-CF patients in planktonic and biofilm form on mucosal barrier structure and function.

**Methods:** Exoproteins from *P. aeruginosa* isolates of CRS patients in planktonic and biofilm form were collected and protein concentration measured by nano orange protein assay. Biofilm metabolic activity was measured using Alamar Blue assays. Different concentrations of exoproteins were applied to air-liquid interface (ALI) cultures of primary human nasal epithelial cells (HNECs) and membrane integrity was evaluated by transepithelial electrical resistance (TEER) over time, passage of fluorescently labelled dextrans and immunofluorescence. Cytotoxicity assays were performed to measure cell viability.

**Results:** Exoproteins of 40 *P. aeruginosa* isolates of CRS patients (15 CF and 25 non-CF) were harvested in late stationary phase and from 48-hour biofilms. Biofilm metabolic activity was higher in CF than in non-CF isolates ( $p < 0.05$ ). Exoproteins from planktonic cultures had a dose- and time-dependent detrimental effect on mucosal barrier structure with a reduction in TEER and increased permeability of FITC-dextrans ( $p < 0.05$ ) without affecting cell viability.

**Conclusion:** *P. aeruginosa* exoproteins isolated from planktonic forms disrupt the mucosal barrier and could contribute to the mucosal inflammation in CRS patients.

#### **LAY DESCRIPTION**

*P. aeruginosa* is one of the major microbes responsible for recalcitrant infection in CRS and cause persistent lung infection in Cystic fibrosis. Exoproteins secreted from bacteria can rupture mucosal barrier and toxins enter into the cell to initiate inflammation and infection. The aim of my study is to understand the mechanism and effect of bacterial exoproteins that are produced by *P. aeruginosa* in planktonic and biofilm form on mucosal barrier structure and function. The findings of my study will enhance the understanding of *P. aeruginosa* infection in CRS and CF leading to explore therapeutic approaches.



## ABSTRACT 40

### **Prevention of abdominal adhesions post-abdominal surgery: Assessing safety and efficacy of Chitogel with Deferiprone in a Rat Model**

Rajan Sundaresan VEDIAPPAN\*, Catherine Bennett\*, Ahmed Bassiouni\*, John Finnie\*\*, Markus Trochsler\*\*\*, Ryan Quarington\*\*\*\*, Claire Jones\*\*\*\*, Stephen Moratti\*\*\*\*\*, Alkis J Psaltis\*, Sarah Vreugde\*, Guy Maddern\*\*\*, PJ Wormald\*

\* Department of Surgery - Otolaryngology Head and Neck Surgery, The University of Adelaide, Australia, \*\*SA Pathology and Adelaide Medical School, The University of Adelaide, Adelaide, Australia, \*\*\*Department of Surgery, The University of Adelaide, Australia, \*\*\*\*Department of Biomechanics Laboratory, Spinal Research Group & Centre for Orthopaedic and Trauma Research, \*\*\*\*\*Department of Chemistry, Otago University, Dunedin, New Zealand

**Background:** Adhesions are often considered an inevitable consequence of abdominal and pelvic surgery, jeopardizing the medium and long-term success of these common procedures. Numerous strategies have been tested to reduce adhesion formation, however, to date, no surgical or medical therapeutic approaches can abrogate adhesions after abdominal surgery. This study tested the safety and efficacy of Chitogel complexed with Deferiprone and/or Gallium Protoporphyrin in different concentrations to prevent adhesion formation after abdominal surgery.

**Materials and Methods:** 64 adult (8-10 week old) male Wistar albino rats underwent midline laparotomy and caecal abrasion and 48 rats underwent caecal abrasion with enterotomy and suturing, followed by topical application of Kaolin to induce adhesions. The abrasion model rats were randomized to receive 4 ml saline, Chitogel or Chitogel with Deferiprone (5, 10 or 20 mM) along with Gallium Protoporphyrin (250µg/mL). The abrasion with enterotomy rats were randomised to receive 4 ml saline, Chitogel or Chitogel with Deferiprone (1 or 5 mM). At day 21 rats were euthanized, and adhesions graded macroscopically by an investigator blinded to the treatment groups, using pre-determined adhesion scores and microscopically using histopathology by a blinded pathologist and tensile strength testing.

**Results:** Chitogel with Deferiprone 5 mM and GaPP reduced adhesion formation significantly ( $p < 0.01$ ) on macroscopic evaluation and histology ( $p < 0.05$ ) in an abrasion model. Chitogel with Deferiprone 5 mM and 1 mM reduced adhesion significantly ( $p < 0.05$ ) in a rat model of colon abrasion and enterotomy. Deferiprone-Chitogel did not weaken the wound and sutured site and had better tensile strength than naïve caecal tissue.

### **LAY DESCRIPTION**

Scars and adhesions are unpleasant result of aberrant wound healing in humans. This is quite so often after abdominal surgery causing pain and can be life threatening. Bowels can get entangled in these adhesions causing bowel obstruction, a serious complication. My research focused on a new gel made from products of shrimp and prawn-Chitogel. This gel when applied into the abdomen after surgery has the ability to coat the bowel and prevent adhesions by quickening clot and slowing the scar. Our investigation in rats proved that a Chitogel based product could help in controlling the wound healing and thereby decrease adhesions significantly.



## ABSTRACT 41

### **Patient perspectives of glucocorticoid use in a cohort of patients with rheumatoid arthritis**

Gabriella Venter (1,2), Joanna Tieu (1,2), Rachel Black (1,2,3), Susan Lester (1,2), Nieves Leonardo (1), Rachelle Buchbinder (4), Samuel Whittle (1,2), Catherine L Hill (1,2,3).

(1) Rheumatology Unit, The Queen Elizabeth Hospital, Woodville, (2) Discipline of Medicine, University of Adelaide (3) Rheumatology Unit, Royal Adelaide Hospital, (4) Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University. (5) Monash Department of Clinical Epidemiology, Cabrini Institute, Melbourne, Victoria,

**Objective:** Prednisolone is effective in managing symptoms of rheumatoid arthritis (RA) but has predictable and common adverse effects. We explored patient perspectives of prednisolone use in RA.

**Methods:** RA patients registered with the Australian Rheumatology Association Database (ARAD) who had recently completed an ARAD questionnaire were invited to participate in an online survey. Responses were linked to demographics, medications, quality of life, and disability scores. The Beliefs about Medicine Questionnaire (BMQ) measured patient beliefs on a scale from 1 to 5, with higher scores indicating stronger beliefs. Free-text responses outlining reasons for stopping or declining prednisolone were analysed with NVivo 12 to identify themes for refusal, cessation, and adverse effects and to quantify the proportion of respondents identifying with each theme.

**Results:** The survey response rate was 79.6% (803/1009). Current use was reported in 251 (31.3%) respondents and previous use in 432 (53.8%). Compared to previous users, current users were older, had higher self-reported pain and disease activity scores, and lower quality of life and function scores ( $p \leq 0.001$ ). Current users also had higher BMQ scores for prednisolone-specific necessity (3.6 vs 1.7,  $p < 0.001$ ) and concerns (2.7 vs 2.3,  $p < 0.001$ ). Free-text responses cited concern about adverse effects in 12/17 (70.6%) who declined prednisolone. Key themes for cessation in free-text responses from previous users included adequate disease control (30.3%), adverse effects (25.2%), and predetermined short-term use (21.3%). The most common adverse effects were weight gain (27.5%), osteoporosis (14.7%), and neuropsychiatric issues (13.8%).

**Conclusions:** In our cohort, RA patients taking prednisolone strongly believed it was necessary yet were also concerned about its use. Overall, disease control, adverse effects, and balancing short-term benefits with long-term risks were important considerations for patients using prednisolone.

### **LAY DESCRIPTION**

Prednisolone is a medication that can quickly control symptoms of rheumatoid arthritis, but often comes with harmful side effects. We surveyed a group of people with rheumatoid arthritis about their experience of, and thoughts about, prednisolone. We found that patients taking prednisolone strongly believed they needed it to manage their disease but were worried about the side effects from taking it. Side effects were also a common reason for stopping or never starting prednisolone, and patients thought that balancing short-term benefits with long-term risks was important in deciding whether or not to use prednisolone.

## ABSTRACT 42

### **Predictors of 30-day readmission costs for peripheral arterial disease patients in Australia: a population study.**

Vanessa Woelk (1), Peter Speck (1), Billingsley Kaambwa (2), Sadia Hossain (3), Isuru Ranasinghe (3)  
(1) College of Science and Engineering, Flinders University (2) Health Economics, College of Medicine and Public Health, Flinders University (3) Health Performance and Policy Research Unit, Basil Hetzel Institute, The University of Adelaide

**Introduction:** Peripheral arterial disease (PAD) is a common and debilitating cardiovascular condition affecting over 200 million people worldwide (1). When left to manifest, severe blockages to blood flow can result in chronic pain, non-healing ulcers and infections resulting in limb amputation. The global prevalence and economic burden of hospital readmissions are extremely high for PAD, but this has not been thoroughly evaluated in Australia.

**Aim:** To determine the rate, cost and predictors of costs of unplanned 30-day readmissions for patients admitted to Australian hospitals following a primary diagnosis of PAD.

**Methods:** We included patients aged  $\geq 18$  years who were admitted to an Australian hospital with a primary diagnosis of PAD and an unplanned readmission, using data from July 2011-June 2015. Diagnosis related group cost data were inflated to 2019 AUD and a generalised linear model used to determine predictors of low or high 30-day readmission costs.

**Results:** Of patients who had an initial hospital admission for PAD, 10.84% ( $n=6932$ ) had an unplanned readmission within 30 days of discharge. Our cohort had a median (interquartile range) readmission cost of \$9,883 (\$5,201-15,371) and an overall economic burden of over \$90.25 million. Patient factors including vascular disease with complications ( $p<0.000$ ), renal failure ( $p<0.003$ ) and protein-calorie malnutrition ( $p<0.020$ ) were associated with higher readmission costs. Patients who underwent surgical revascularisation ( $p<0.043$ ) at index admission, or had previously undergone a lower limb amputation ( $p<0.002$ ), also had higher readmission costs.

**Conclusion:** More than 1 in 10 patients hospitalised for PAD experience an unplanned readmission to hospital within 30 days of discharge, with each event costing the Australian healthcare system \$9,883. Reducing unplanned readmissions and addressing patient factors associated with increased readmission costs may reduce the economic burden of PAD and improve quality of care.

1. Fowkes FGR, Rudan D, Rudan I, Aboyans V, Denenberg JO, McDermott MM, et al. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. *The Lancet*. 2013;382(9901):1329-40.

### **LAY DESCRIPTION**

Peripheral arterial disease (PAD) is a common cardiovascular condition. In particular, frequent unplanned readmissions add a considerable expense to treatment plans and are considered a marker of poor quality of care. Despite this, few Australian studies have evaluated the frequency of PAD readmissions, nor investigated predictors of frequent and costly readmissions. We found that 10.84% of PAD patients are acutely readmitted to hospital within 30-days, with a median cost of \$9,883. Reducing unplanned readmissions by focusing on identified predictors of costs may offer a significant opportunity to reduce healthcare costs.



### ABSTRACT 43

#### **Incidence of 30-day readmission and associated healthcare costs in patients hospitalised with atrial fibrillation: An Australian population-based study**

Taylor-Jade Woods\*, Peter Speck\*\*, Sadia Hossain^, Linh Ngo^, Isuru Ranasinghe^, Billingsley Kaambwa\*

\*Flinders University College of Medicine and Public Health; \*\*Flinders University College of Science and Engineering; ^The University of Adelaide, Basil Hetzel Institute for Translational Research

**Introduction:** Recent Australian policy reform has targeted reducing unplanned hospital readmissions to minimise patient harm and avoidable healthcare costs, yet the 30-day readmission rate for patients hospitalised with atrial fibrillation (AF) in Australia is unknown. The direct healthcare costs of these readmissions and factors influencing these costs are also unknown.

**Aim:** To identify the 30-day readmission rate for patients hospitalised for AF, the cost of those readmissions and predictors of costs.

**Methods:** We used hospitalisation data from all public and most private hospitals in Australia to identify patients aged  $\geq 18$ y hospitalised with a primary diagnosis of AF between July 2011- June 2015. The primary outcome was an unplanned readmission within 30-days of discharge and associated costs. Generalized linear modelling was used to identify predictors of readmission costs. All costs were reported in 2019 AUD.

**Results:** There were 199,886 AF hospitalisations. Of these, 26,680 (13.87%) resulted in an unplanned readmission within 30-days. Readmitted patients had a mean age of  $72 \pm 12$  y; median 50.83% were female and readmissions had a median length of stay (LOS) of 2 days. The median cost of a readmission was \$7,009 (interquartile range [IQR] \$3,771 - \$10,235). Factors associated with increased readmission costs included female gender ( $p < 0.001$ ), older age ( $p < 0.001$ ), longer index LOS ( $p < 0.001$ ), and comorbidities such as diabetes ( $p < 0.05$ ), congestive heart failure ( $p < 0.001$ ), and major depressive/bipolar/paranoid disorders ( $p = 0.032$ ). Cardiac device implantation ( $p < 0.001$ ), catheter ablation ( $p < 0.001$ ), and cardioversion ( $p = 0.03$ ) were associated with reduced readmission costs.

**Conclusion:** Unplanned readmissions after hospitalisation for AF are common and costly to the health system. Efforts to reduce readmission costs should target high-risk patients who are female, older and have multiple comorbidities.

#### **LAY DESCRIPTION**

Australian policy reform focuses on reducing unplanned readmissions, yet the 30-day readmission rate, associated costs and factors driving these costs among AF patients in Australia are unknown. Using nationwide hospitalisation data, we found that around 1 in 7 AF patients were unexpectedly readmitted to hospital within 30 days. These readmissions were costly at about \$7,000 per readmission. Older patients, females and patients with multiple comorbidities had higher costs. Guideline-recommended intervention such as cardioversion, catheter ablation, and cardiac device implantation were associated with lower readmission costs.





# TQEH Research Expo 2019

## TQEH Research Day Prize Winners: 1992 – 2018

### 2018

<b>Honours/Summer Student</b>	Ashley Twigger
<b>Junior Laboratory PhD Student</b>	Giri Krishnan
<b>Senior Laboratory PhD Student</b>	Lisa Cherian
<b>Clinical Trainee</b>	Rachel Goggin
<b>Clinical Higher Degree Student</b>	Anupam Gupta
<b>Poster Prize</b>	Namfon Pantarat
<b>Best Lay Description</b>	Rachel Goggin
<b>Ivan De La Lande Award</b>	Clementine Labroschiano

### 2017

<b>Honours/Summer Student</b>	Sean Mangion
<b>Junior Laboratory PhD Student</b>	Sathish Paramasivan
<b>Senior Laboratory PhD Student</b>	Christopher DeFelice
<b>Clinical Trainee</b>	Fiona Chan
<b>Clinical Higher Degree Student</b>	Mian Ooi
<b>Poster Prize</b>	Alexandra Shoubridge
<b>Best Lay Description</b>	Maddison Archer

### 2016

<b>Honours/Summer Student</b>	Bahador Assadi-Khansari
<b>Junior Laboratory PhD Student</b>	Vahid Atashgaran
<b>Senior Laboratory PhD Student</b>	Dijana Miljkovic
<b>Clinical Research Group 1</b>	Ben Thurston
<b>Clinical Research Group 2</b>	Scott Ellis
<b>Poster Prize</b>	Vasilios (Bill) Liapis
<b>Best Lay Description</b>	Vasilios (Bill) Liapis

### 2015

<b>Honours Student</b>	Aashray Gupta
<b>Junior Laboratory PhD Student</b>	Vasilios (Bill) Liapis
<b>Senior Laboratory PhD Student</b>	Aneta Zysk
<b>Junior Clinical Researcher</b>	Zoe Kopsaftis
<b>Senior Clinical Researcher</b>	Kristin Carson
<b>Poster Prize</b>	Ben Thurston
<b>Best Lay Description</b>	Kati Richter

### 2014

<b>Honours Student</b>	Tammy Willsmore
<b>Junior Laboratory PhD Student</b>	Kati Richter
<b>Senior Laboratory PhD Student</b>	Bill Panagopoulos
<b>Clinical Research Group 1</b>	Shailaja Nair
<b>Clinical Research Group 2</b>	Harshani Jayasinghe
<b>Poster Prize: Junior</b>	Alice Du
<b>Poster Prize: Senior</b>	Helen Palethorpe
<b>Best Lay Description</b>	Aneta Zysk

### 2013

<b>Honours Student</b>	Zacki Malik
<b>Junior Laboratory PhD Student</b>	Vikram Padhye
<b>Senior Laboratory PhD Student</b>	Amanda Drilling
<b>Clinical Research Group 1</b>	Tharshy Pasupathy
<b>Clinical Research Group 2</b>	Shailaja Nair
<b>Poster Prize</b>	Shalini Sree Kumar
<b>Best Lay Description</b>	Tamsin Garrod

### 2012

<b>Honours Student</b>	Sathish Paramasivan
<b>Junior Laboratory PhD Student</b>	Erin Swinstead
<b>Senior Laboratory PhD Student</b>	Irene Zinonos
<b>Clinical Research Group 1</b>	Neil CW Tan
<b>Clinical Research Group 2</b>	Rachel Dreyer
<b>Poster Prize</b>	Michael Collins
<b>Best Lay Description</b>	Tessa Gargett

### 2011

<b>Honours Student</b>	Sam Biermann
<b>Junior Laboratory PhD Student</b>	Amenah Jaghoori
<b>Senior Laboratory PhD Student</b>	Irene Zinonos
<b>Clinical Higher Degrees</b>	Elsa Dent
<b>Clinical Research</b>	Scott Graf
<b>Poster Prize</b>	Yang Du
<b>Best Lay Description</b>	Michael Djukic

### 2010

<b>Honours Student</b>	Joshua Woenig
<b>1<sup>st</sup> year PhD Laboratory</b>	Camille Jardeleza
<b>2<sup>nd</sup> year PhD Laboratory</b>	Joshua Jervis-Bardy
<b>3<sup>rd</sup> year PhD Laboratory</b>	Sam Boase
<b>Clinical Higher Degree</b>	Rachel Dreyer
<b>Poster Prize</b>	Sumithra Krishnan
<b>Best Lay Description</b>	Chris Lauder



# TQEH Research Expo 2019

## 2009

Honours Student	Raymond Yu
Junior Laboratory PhD Student	Kanchani Rajopadhyaya
Senior Laboratory PhD Student	Darling Rojas
Clinical Higher Degree	Andrew Foreman
Allied Health-Pharmacy	Nicole Such
Poster Prize	Shaundee Sen
Best Lay Description	Michael Collins

## 2008

Honours Group 1	Krishna Jeyaraman
Honours Group 2	Kanchani Radjopadhyaya
PhD Basic Science Jnr	Tyson Matthews
PhD Basic Science Snr 1	Christine Ball
PhD Basic Science Snr 2	Victoria Kopetz
Nursing & Allied Health	Hayley Vasileff
Higher Degrees Clinical	Rowan Valentine
Poster Prize	Andrew Foreman
Best Lay Description	Boris Fedoric

## 2007

Honours student	Tyson Matthews
PhD Basic Science Jnr	Darling Rojas & Boris Fedoric
PhD Basic Science Snr	Nicola Leung
PhD Snr Clinical	Shilpa Prasad
Higher Degrees Clinical	Tong Le
Nursing & Allied Health	Hayley Vasileff
Undergraduates Vacation	Julia Kirby
Poster Prize	Alicia Chan

## 2006

Honours student	Darling Rojas
PhD Basic Science	Deirdre Zander
PhD Basic Science	Christine Ball
PhD Clinical 1	Alkis Psaltis
PhD Clinical 2	Achim Beule
Nursing & Allied Health	Wendy McInnes
Undergraduates Vacation	Khanh Tran
Poster Prize	Rosanna Tavella

## 2005

Honours Group 1	Boris Fedoric
Honours Group 2	Nick Mabarrack
PhD Junior Laboratory	Rebecca Dragovic
PhD Senior Laboratory	Theresa Hickey
PhD Clinical	Alkis Psaltis
Nursing & Allied Health	Peter Cheung
Undergraduates Vacation	Amellia Laidlaw
Poster Prize	Cadence Minge

## 2004

Honours Group 1	Kara Cashman
Honours Group 2	Joanne Reed
PhD Junior Laboratory	Rebecca Dragovic
PhD Senior Laboratory	Harshita Pant
PhD Clinical	Wai Lim
PhD Population Health	Mark Kohler
Medical Student	Anthony Pisanello
Poster Prize	Theresa Hickey

## 2003

Honours Group 1	Maggie Centenera
Honours Group 2	Claire Seymour-Griffin
PhD Junior Laboratory	Ben Davies
PhD Senior Laboratory	Madelyn Zawitkowski
PhD Clinical	Jim Jannes
PhD Population Health	Katie Kandelars
Poster Prize	Melanie Bagg

## 2002

Honours	Deborah Marrocco
PhD Junior Laboratory	Ashley Newland
PhD Senior Laboratory 1	Cassandra Woihe
PhD Senior Laboratory 2	Madelyn Zawitkowski
Higher Degree Clinical	Matt Worthley
Higher Degree Surgical	Charles Morrison
Medical Student	Sasa Todorovic
Poster Prize	Lien Ho

## 2001

Honours	Ashley Newland
Higher Degree Jnr	Cassandra Woihe
Higher Degree Snr	Al Truong Tran
Higher Degree Clinical	Matt Worthley
Higher Degree Surgical	Fiona Court
Advanced Fellowship Trainee	Anita Lee
Medical Student	Aiden Burrell
Poster Prize	Greg Roach

## 2000

Honours Group 1	Ilse Dahn
Honours Group 2	Melanie Sutton
Higher Degree Group 1	Samantha Yates
Higher Degree Group 2	Tina Bianco
Higher Degree Clinical	Merlin Thomas
Nursing & Allied Health	Libby Birchmore
Medical Student	Victoria Tay
Poster Prize	Nicole Lamond

## 1999

**Honours**  
**Higher Degree Group 1**  
**Higher Degree Group 2**  
**Higher Degree Clinical**  
**Advanced Fellowship Trainee**  
**Nursing & Allied Health**  
**Medical Student**

Tenielle Webb  
 Ai Truong Tran  
 Damien Hussey  
 Denise Roach  
 Justin Evans  
 Terry Jones &  
 Dorothy Pannell  
 Edmund Tse &  
 Ru-Siang Cheng

## 1998

**Honours**  
**Higher Degree Group 1**  
**Higher Degree Group 2**  
**Higher Degree Clinical**  
**Advanced Fellowship Trainee**  
**Nursing & Allied Health**  
**Medical Student**  
**Poster Prize**

Ai Truong Tran  
 Sarah Swinburne  
 Damien Hussey  
 Sarah Downie  
 Alan Wigg  
 Robyn Clark  
 Rae-Wen Chang  
 Lucia Sabordo

## 1997

**Honours**  
**Higher Degree Group 1**  
**Higher Degree Group 2**  
**Higher Degree Clinical**  
**Advanced Fellowship Trainee**  
**Nursing & Allied Health**  
**Medical Student**

Samantha Yates  
 Lisa Butler  
 Michael Texler  
 Dorothy Keefe  
 Andrew Luck  
 Simon Stewart  
 Nan Williams

## 1996

**Honours**  
**Higher Degree Group 1**  
**Higher Degree Group 2**  
**Higher Degree Clinical**  
**Advanced Fellowship Trainee**  
**Nursing & Allied Health**  
**Medical Student**  
**Poster Prize**

Anthony Kiosoglous  
 Jennifer Hardingham  
 Guy Patrick  
 Christopher Zeitz  
 Alan Wigg  
 Julie Lucker  
 Michael Osborn  
 Matthew Callaway

## 1995

**Honours**  
**Higher Degree Group 1**  
**Higher Degree Group 2**  
**Higher Degree Clinical**  
**Advanced Fellowship Trainee**  
**Medical Student**

Antiopi Varelias  
 Guy Patrick  
 Andreas Evdokiou  
 Christopher Zeitz  
 Toby Coates  
 Rohini Sharma

## 1994

**Honours**  
**Higher Degree Group 1**  
**Higher Degree Group 2**  
**Advanced Fellowship Trainee**  
**Medical Student**

Lucia Sabordo &  
 Linda Dadds  
 Rebecca Ritchie &  
 James Moore  
 Guy Patrick  
 David Campbell  
 I-Wen Chu

## 1993

**Basic Science**  
**PhD/MD**  
**In Training**  
**Clinical**  
**Medical Student**

Dean Bacich  
 Cui Lan Zhang  
 Jennifer Hardingham  
 Dorothy Keefe  
 Kenneth Ooi

## 1992

**Basic Science**  
**PhD/MD**  
**Clinical**

Yi Zhang  
 Warwick Grooby  
 David Campbell



TQEH Research Expo Prize Winners: 2018 [Giri Krishnan not in photo]



## **TQEH Research Expo 2018**

### **TQEH Research Day Plenary Lectures: 1992 - 2019**

- 2019: Professor John Rasko AO – Centenary Institute, Sydney**  
“Cell and Gene Therapy: great power brings great responsibility”
- 2018: Professor Peter Rathjen – The University of Adelaide**
- 2017: Hon. Mark Butler MP – Australian Labor Party**  
“The Politics of Ageing”
- 2016: Professor Anne Kelso AO – NHMRC**  
“Medical research: why we mustn’t stop now”
- 2015: Professor Steve Webb – Royal Perth Hospital, University of Western Australia & Monash University**  
“Pushing or pulling over the evidence-practice gap”
- 2014: Professor Brendan Crabb – Burnet Institute**  
“Malaria in the 21<sup>st</sup> century”
- 2013: Professor Tanya Monro – The University of Adelaide**  
“From theoretical physics to solutions in health and defence: a transdisciplinary journey”
- 2012: Professor Barry Brook – The University of Adelaide**  
“Future climate extremes and how to avoid them!”
- 2011: Professor Steve Wesselingh - SAHMRI**  
“Health Reform and Medical Research: Building better links between medical research and health care delivery to improve health outcomes”
- 2010: Professor David Allen - The University of Sydney**  
“Duchenne muscular dystrophy; connecting the gene to the disease”
- 2009: Professor David Vaux - La Trobe University**  
“Ten rules for the presentation and interpretation of data in publications”
- 2008: Dr Bob Irving - Nanotechnology Victoria**  
“Nanotechnology - Opportunities and Challenges at the Smallest Frontier of Science”
- 2007: Jenni Metcalfe - President Australian Science Communicators**  
“A Schizophrenic Life: the Career of a Science Communicator”
- 2006: Dr Rob Morrison - Science Communicator**  
“Trust me, I’m a Science Communicator”



## TQEH Research Expo 2018

- 2005: Professor Rob Norman - The University of Adelaide**  
"The reproductive revolution: How The Queen Elizabeth Hospital led the field"
- 2004: Robyn Williams - Australian Broadcasting Corporation**  
"How modern medicine changed the world - some anniversaries"
- 2003: Dr Sarah Robertson - The University of Adelaide**  
"Facing Challenges and Finding Solutions in Reproductive Medicine"
- 2002: Professor John Chalmers - The University of Sydney**  
"Enhancing Health and Medical Research in the Teaching Hospital Environment"
- 2001: Professor Peter Rathjen - The University of Adelaide**  
"Regenerative medicine using stem cells: Medicine for the new millennium"
- 2000: Professor Grant Sutherland - The University of Adelaide**  
"The human genome project: Applications to medical research"
- 1999: Dr Philip Reece - Biota Holdings**  
"Biota and Relenza: New drug discovery in Australia"
- 1998: Professor Colin Matthews (Moderator) - The University of Adelaide**  
Speakers: Dr Tim Kuchel, Dr David Turner, Dr John Chandler  
"And Man-made Dolly: The ethics of cloning"
- 1997: Dr Julian Cribb - CSIRO**  
"The origin of AIDS"
- 1996: Dr Deane Hutton - Science Communicator**  
"20:20 vision – Living in the 21<sup>st</sup> Century"
- 1995: Professor Mike Tyler - The University of Adelaide**  
"Frogs – the new frontier for natural products pharmacology"
- 1994: Dr Gael Jennings - Australian Broadcasting Corporation**  
"Communicating research via the medium of television"
- 1993: Dr Mark Wahlqvist - Monash University**  
"Salt intake and the non-pharmacological treatment of hypertension"
- 1992: Professor David Jarrett - The Queen Elizabeth Hospital**  
"The place of research in the face of a shrinking medical budget"
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