



2023 Newsletter #2

Welcome to our 3rd Newsletter, the Spring Edition! Congratulations, if you made it through the winter months without catching a cold. The PREVENT study reveals which viruses you may have dodged or encountered. In this newsletter, we will report some preliminary findings for the first time! Sit tight and get captivated by our thrilling program updates! If you want a chance to win a \$50 HMRI Café voucher, make sure you read to the end of the Newsletter!

PROGRAM WIDE MEETING - *** 24TH JULY 2023 ***



We had our first official program wide meeting on Monday, 24th of July. Thanks to everyone who attended. It was exciting to hear from the different themes and the seed grant recipients. We hope, you had a great time and enjoyed it as much as we did! The next meeting is planned for early next year. Keep an eye out for the Save-the-Date, which will be distributed in the next couple of months.




LEADERSHIP UPDATES AND INTRODUCTION OF A NEW THEME



Prof Nathan Bartlett and his team have joined the Infection Research Program, forming the fourth theme: Translational Virus Research. Nathan is also the new Co-Deputy Lead, together with Prof Brett Mitchell. Welcome to the program!

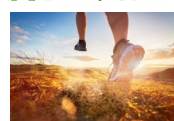


INFECTION CONTROL MATTERS - THE PODCAST

Do you love 'true crime'? So do our little program mascots. They are hooked on Prof Brett Mitchell's podcast: 'Infection Control Matters'. It's all about eliminating pathogens, preventing the spread of infections and interesting discussions around unexpected sources of infections. The podcast is available on all common platforms, including  [Spotify](#),  [Apple Podcasts](#) and  [Audible](#). Follow the links and check it out.



NewRun



PROJECT UPDATES – NEWRUN



Is running good or bad for your knees? Great question! We don't know the answer – yet! Despite providing evidence for both, a positive and negative impact of running on knee health, previous studies did not allow a definite answer. The follow-up period was too short, sample sizes too small, or a control group lacking. The NEWRUN study will address these gaps by longer-term follow-up studies. We will investigate the relationship between running and knee health by measuring the thickness of the cartilage via MRI scans in 50 volunteers over 5 years. Does regular running (5-50km per week on average) accelerate aging-related cartilage loss? Or maybe even protect it through



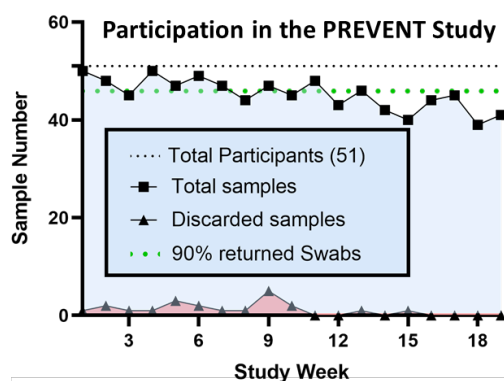
increased blood flow and strengthening of certain muscles? In addition to knee health, we will further include general health parameters such as mental health and gut health. If you would like to participate, please contact NewRun-admin@uonstaff.edu.au as soon as you can. We have received a great interest in this study and already completed 70% of this year's visits, 90% of the recruitment, and a few more candidates will be screened for eligibility. A big shout-out to Behnaz Khavari, our clinical research coordinator, for (no pun intended) running the study visits so smoothly!



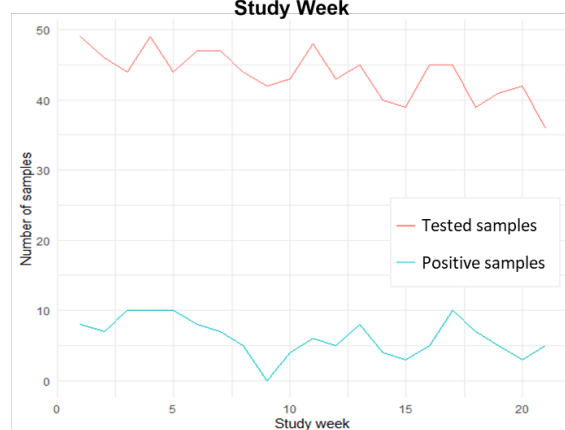
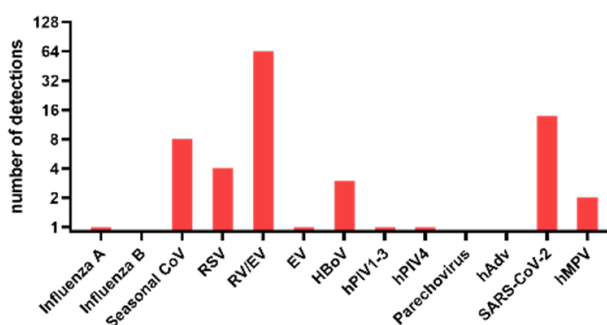


PROJECT UPDATES - THE PREVENT STUDY

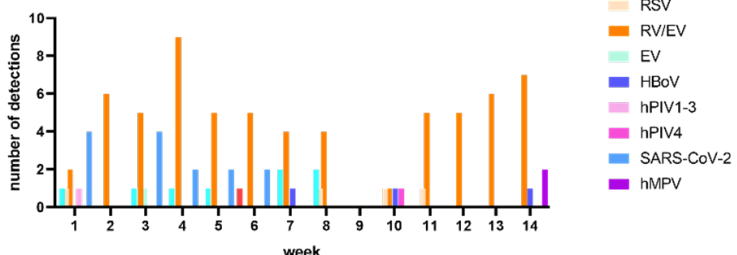
PREVENT (Pandemic RESpiratory Virus survEillaNce Trial) is a respiratory virus surveillance study to investigate which cold- and flu-causing viruses are circulating in the Newcastle and Lake Macquarie LGA over the different seasons. Participants are providing weekly nasal swabs. The first swabs were collected in the first week of June and 50 FluTrackers are currently enrolled in PREVENT. The start of the study was a great success with all participants being recruited within 24 hours after releasing the advertisement. The response rate in the first 14 weeks was over 80%. We keep our fingers crossed that everyone enrolled will continue their dedicated participation. Below is a summary of some preliminary findings. Rhinovirus (RV) and COVID-19 (SARS-CoV-2) were the most detected viruses so far. It will be interesting to see how or if this will change over the summer months.



Total number of detected viruses



Weekly numbers of detections



PROJECT UPDATES - ROADMAP



Program lead Prof Josh Davis received an NHMRC grant worth \$4.7M for the ROADMAP study, an adaptive platform trial running over 5 years to investigate and identify the best management strategy for prosthetic joint infections. Congratulations on this outstanding achievement!

The pre-trial activities are in full swing. There are now weekly meetings, either with the Global Trial Steering Committee, the Domain Specific Working Groups, or the stats team. We also finalised the recruitment process for the Newcastle-based staff positions, which will commence early next year. It is exciting to see the committees and working groups growing, the protocols and appendices taking shape, and, step by step, getting closer to the commencement of the trial.

ACHIEVEMENTS

Deputy lead Prof Brett Mitchel received an MRFF Clinical research grant (\$1.5 million) to help prevent healthcare associated pneumonia. A multi-centre randomised controlled study will evaluate if increased frequency and quality of oral care will reduce the incidence of healthcare associated pneumonia. Click [here](#) to access the full article. Brett further received the **Sigma Nursing - 2023 International Nurse Researcher Hall of Fame Award**. Click [here](#) to read more. Congratulations, Brett!





Congratulations, Dr Sarah Browning (ECR representative of the Infection Prevention Theme) and **A/Prof Laurens Manning** (CIB of the ROADMAP grant) for being highlighted in an article from Childs-Kean et al., which chose the top 10 papers relevant to outpatient parenteral antimicrobial therapy (OPAT): A Bundle of the Top 10 OPAT Publications in 2022, published in *Open Forum Infectious Diseases*, 2023.



Sarah's study investigated the occurrence of adverse events (AEs) in a large cohort of adults admitted to the OPAT service over 10 years. One key finding was that AEs were more likely to occur in the first 2 weeks of intravenous antibiotic therapy. Longer treatment duration did not increase the risk of AEs. While OPAT AEs were common, the incidence of major AEs was low. Click [here](#) for the full article.

Laurens's trial compared short (2 weeks) versus standard (6 weeks) duration of parenteral antibiotics for prosthetic joint infections managed with DAIR (debridement, antibiotics and implant retention procedure), using a DOOR (desirability of outcome ranking) approach. His findings provide supporting evidence that an early transition from parental to oral antibiotics may be beneficial in some patients with PJI managed with DAIR. Click [here](#) for the full article.



RECENT PAPERS FROM OUR PROGRAM

In each edition of this newsletter, we will highlight a few recent publications by our affiliates, and relevant to the aims and themes of our program. Please let us know about *your* recent papers.

1st theme: Severe bacterial Infections

[Design Characteristics and Recruitment Rates for Randomized Trials of Peri-Prosthetic Joint Infection Management: A Systematic Review](#)

(L Manning, B Allen and **JS Davis**, September 2023, *Antibiotics*)

→ Systematic review about RCTs investigating the management of prosthetic joint infections (PJIs), their recruitment rates and primary endpoints.

→ 15 RCTs with a total of 1743 participants with PJI have been reviewed. The trials were characterised by slow recruitment rates and heterogeneous endpoint assessment, highlighting the need for informed international guidelines. To meet recruitment goals, PJI trials should be conducted globally at multiple high-recruiting sites.

[A multi-site, international laboratory study to assess the performance of penicillin susceptibility testing of *Staphylococcus aureus*](#)

(A Henderson, ..., **JS Davis** et al., June 2023, *Journal of Antimicrobial Chemotherapy*)

→ A high proportion of *S. aureus* has been reported to be penicillin susceptible, yet clinical practice guidelines have not been updated and still assume high levels of resistance. Penicillin susceptibility tests have been found to have high error rates and routine testing for penicillin susceptibility has been discontinued.

→ This study compared two laboratory penicillin susceptibility testing methods and found that EUCAST was superior to CLSI. Interestingly, some isolates were susceptible to penicillin despite testing positive for the *blaZ* resistance gene. The clinical relevance of these organisms remains unclear.

2nd theme: Infection Control & Prevention

[A randomised controlled trial investigating the effect of improving the cleaning and disinfection of shared medical equipment on healthcare-associated infections: the CLEAning and Enhanced disiNfection \(CLEEN\) study](#)

(K Browne, ..., **BG Mitchell**, February 2023, *Trials*)

→ Many new infections are acquired at the hospital or other health-care settings. The CLEEN study will investigate whether additional cleaning of shared medical equipment reduces the occurrence of





healthcare-associated infections (HAIs). It will be conducted over 13 weeks in 10 wards of one large Australian hospital. The primary outcome is the reduction of HAIs. Secondary outcomes include the thoroughness of equipment cleaning and the cost-effectiveness of the intervention.

[Multimodal environmental cleaning strategies to prevent healthcare-associated infections](#)

(K Browne and B Mitchell, August 2023 *Antimicrobial Resistance & Infection Control*)

→ Environmental cleaning is an important strategy to prevent the transmission of infectious pathogens, and it's the key to reducing the risk of healthcare-associated infections. This article provides a framework for a multimodal approach to environmental cleaning for healthcare facilities.



3rd theme: Pandemic Preparedness

[A Randomized Trial of Nafamostat for Covid-19](#)

(SC Morpeth, ..., JS Davis et al., October 2023, *New England Journal in Medicine – Evidence*)

- Nafamostat is an old drug used to treat pancreatitis. One of its actions is to inhibit TMPRSS2, which happens to be a cell-surface receptor that SARS-CoV-2 uses to enter cells
- As part of the ASCOT study (led by Steve Tong and Josh Davis), 160 people hospitalised for COVID (but not in ICU) were randomised to receive intravenous nafamostat or standard care
- The nafamostat group had a 93% Bayesian posterior probability of benefit, BUT also had an increased rate of hyperkalaemia and bleeding
- This is a useful proof-of-concept for TMPRSS2 inhibition, but newer safer drugs in this class would need to be developed before it enters clinical use



[FluTracking: Weekly online community-based surveillance of influenza-like illness in Australia, 2019 Annual Report](#)

(SJ Carlson, ..., M Butler and CB Dalton, March 2023, *Communicable Disease Intelligence*)

- Summary of recruitment and participant engagement in 2019 and since the beginning of FluTracking in 2006
- Comparison of the occurrence of cough and fever in relation to influenza vaccination status
- Overview of the weekly proportion of participants with fever and cough during epidemiological weeks between 2013-2019 by jurisdiction



4th theme: Translational Virus Research

[Upper Respiratory Tract OC43 Infection Model for Investigating Airway Immune-modifying Therapies](#)

(JLN Girkin, NE Bryant, SL Loo, ..., NW Bartlett, August 2023, *American Journal of Respiratory Cell and Molecular Biology*)

- Establishment of a murine upper respiratory tract infection model with coronavirus strain OC43
- Investigation of infection-induced immunity and characterisation of the involved cytokines/genes
- Assessment of host-directed immune-modifying therapies by activation of immunity through TLR2/6 agonists (INNA-X) and immune-suppression by corticosteroids (Fluticasone propionate, FP)
- INNA-X accelerated the expression of anti-viral genes. FP increased the viral load and reduced the expression of anti-viral genes. Prior treatment with INNA-X reduced the immune-suppressive effect of FP.

[Mechanical forces suppress antiviral innate immune responses from asthmatic airway epithelial cells following rhinovirus infection](#)

(PC Veerati, ..., NW Bartlett et al., August 2023, *American Journal of Physiology - Lung Cellular and Molecular Physiology*)





➔ People with asthma experience repeated bronchoconstriction that generates mechanical stress within the airway that may impact host antiviral responses and viral replication. This research article investigates the impact of apical compressive stress (one form of mechanical stress) on airway epithelial antiviral innate immune responses. Two asthma models (poor asthma control model and asthma exacerbation model) were established using differentiated primary bronchial epithelial cells and low MOI rhinovirus infection. Viral RNA, interferons and other inflammatory mediators were measured for 96 hours at 24-hr intervals, post-infection. Compressive stress resulted in a suppression of interferons in both models but did not affect viral replication. This data may explain why people with asthma have impaired antiviral responses.



STAFF & STUDENT UPDATES



Nicolai Kristensen



Rejoy Thomas



Ellie Doubleday



Bismi Khadar

Meet Nicolai, Rejoy, Ellie and Bismi. **Nicolai** is an orthopaedic surgeon from Denmark doing a research fellowship with Prof Josh Davis for 3 months here at HMRI. In Denmark, he is doing a PhD on infections in joint replacements. It's a severe and devastating complication, and it could result in higher mortality—that's what Nicolai is investigating through the Danish registries. Here at HMRI, he is looking at a prediction model for infectious complications following knee surgery.

Stuart Browne has sadly left the team to pursue a PhD. Congratulations on this exciting opportunity! **Rejoy** is our new Project Officer for the Pandemic REspiratory Virus survEillaNce Trial (PREVENT). Welcome to the team! After completing his undergraduate degree in Biomedical Science from University of South Florida, USA, Rejoy has worked as a research assistant under cardio-thoracic physicians in one of the largest Veterans' hospitals in Florida, USA. In the meantime, he has also acquired experience in coordinating clinical trials in respiratory illnesses, sleep medicine and public health studies. By recently moving to Australia, Rejoy believes in expanding his network while also working towards his career goal of being a medical scientist. Currently, Rejoy also fulfills the role of Registry Officer for a study with the Asthma and Breathing Programme at HMRI.

Ellie is a new PhD student working under Nathan Bartlett on a project called "Innate Immune Activating RNA Nanomedicines for Cancer". She will determine the therapeutic potential of a drug that incorporates an immune stimulating molecule within a nanomedicine that uses RNA to increase anti-tumour activity. What an exciting opportunity!

Bismi is a registered nurse who works in an aged care facility in Taree. Bismi, a PhD student of Prof Brett Mitchell, is undertaking a multi-centre randomised control trial. In her trial, she is evaluating whether the use of air purifiers, in the rooms of aged care residents, reduces the risk of acute respiratory tract infection. Bismi recently has a paper published, explaining more about the trial. Click [here](#) for the full article.



MEDIA NEWS

Josh did an interview with ABC Radio Newcastle about the NewRun study. Click [here](#) to access the recording.

NEW AFFILIATES WELCOME

Do you know anyone with a research interest in infections who is not yet affiliated with one of HMRI's programs? The first person referring someone who effectively joins our program will receive a \$50 voucher for the HMRI Seaspray Café. Please send the name of your recommended affiliate to Natalie.Niessen@newcastle.edu.au. They will need to register [here](#) and select the Infection Research Program. Once we have the first new official affiliate, we will contact the winner.



WINNER - EASTER EGG HUNT

As you may remember, we had a little Easter Egg Hunt in our last newsletter. Thanks to those who participated and submitted the number of counted easter eggs.

The winner is Nicole Lachapelle from HMRI's Clinical Trial Unit!

Congratulations!

Enjoy your \$50 Voucher for the HMRI Seaspray Café

That's it from us in 2023. We are wishing you all the best for the remainder of the year and a great start of 2024. Merry Christmas and Happy Holidays!

Natalie, Josh and Brett

