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# IMPACT Research Showcase 2023 Digital Abstract Booklet

## CENTRE FOR INNOVATION IN INFECTIOUS DISEASE AND IMMUNOLOGY RESEARCH

# A novel health service model to optimise antimicrobial stewardship in Australian primary care

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## Background

The estimate suggests that 30-50% of antibiotic prescriptions are inappropriate either in choice, dose or duration in primary care. We aim to design a general practitioner-pharmacist antimicrobial stewardship (GPPAS) health service model to optimise antibiotic use in Australian primary care by addressing diagnostic uncertainty, patient demand for antibiotics and gaps in GP-pharmacist collaboration.

## Methods

Since 2017-2023, a systematic review, a scoping review, a rapid review, nationwide surveys and qualitative studies of GPs and pharmacists in Australia and a pilot study were conducted to inform the GPPAS model. Systems Engineering Initiative for Patient Safety framework guided the theoretical structure of the GPPAS model.

## Results

A novel GPPAS health service model has been successfully designed to guide implementation of i) antimicrobial stewardship education program, ii) antimicrobial audits, iii) point-of-care diagnostic testing, iv) delayed antibiotic prescribing and v) routine review of antibiotic prescription by fostering GP-pharmacist collaboration. A GPPAS pilot program involving stewardship education demonstrated improvements of appropriateness of antimicrobial prescribing by GPs in Australia; choice of antimicrobial from 73.9% to 92.8% ($p < 0.001$), duration from 53.1% to 87.7% ($p < 0.001$) and guideline compliance from 42.2% to 58.5% ($p < 0.001$) post-intervention. A national clinical governance structure has been built to foster the implementation of the GPPAS model.

## Conclusions

The GPPAS model will impact evidence-based antibiotic use practices and policies in primary care, and guide how future care should be delivered in the community for safe use of antibiotics. Future randomised controlled trial is needed to better understand the model's effectiveness and cost-effectiveness.

# Be Connected: Improving access to hepatitis B care in regional Victoria.

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## Background

Australia is not on track to meet the World Health Organization (WHO) targets for hepatitis B elimination. Access to care is a major barrier for people living in regional Victoria. This study aims to gain insight into the needs of people living with hepatitis B in the Barwon South West region of Victoria. This will involve mapping the distribution and prevalence of the population requiring care and interviewing healthcare workers to understand their experience and gain insight into their perspectives on hepatitis B models of care. Outcomes will inform an improved care model that will support community-based hepatitis B care.

## Methods

Data mapping: at-risk population data was collected from the Australian Bureau of Statistics 2021 census, hepatitis B notifications data collected from the Victorian Department of Health and hepatitis B testing data collected from Australian Clinical Labs. Data mapped using ArcGIS.

Interviews and thematic analysis: Up to 30 interviews with healthcare workers will be conducted. These include general practitioners (GPs), S100 Hepatitis B prescriber GPs, community and refugee health nurses, specialists and nurses from the Liver Clinic and interpreters.

## Results

The Local Government Area (LGA) with the highest notification rate was Greater Geelong 11.2 notifications/100,000 people/year). The at-risk population for postal areas (POA) within this LGA ranged from 1.1% to 15.5%.

Recruitment for the qualitative interviews is currently underway.

## Conclusion

Improving access to care in the Barwon South West Region will require culturally competent and multidisciplinary approaches that overcome the challenges routinely faced by patients living in regional Victoria.

# Comprehensive Case-Control Study of Protective and Risk Factors for Buruli Ulcer, Victoria Australia

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## Background

*Mycobacterium ulcerans* infection (Buruli Ulcer, BU) incidence in Victoria has been increasing and in new geographic locations. Reasons for this remain unclear. This detailed case-control study explored host, environmental and behavioural risk and protective factors associated with BU.

## Methods

Postal questionnaire data for 245 BU cases notified to the Victorian Department of Health between June 2018 and June 2020, and 481 postcode-matched controls were analysed. Age- and sex-adjusted odds ratio (aOR) for factors associated with BU were obtained using conditional logistic regression.

## Results

The likelihood of BU was higher for individuals with diabetes mellitus, aOR 2.26 (95%CI 1.13, 4.49), but lower among those with a history of BCG vaccination (aOR 0.59 (0.39, 0.90)). Working outside with soil contact had a higher odds of BU than working indoors in endemic areas. A strong dose-response relationship was observed between the number of possums at residential properties and likelihood of BU; aOR 4.52 (1.48, 13.81) in residents with 1-2 possums, 6.06 (1.85, 19.83) with ≥ 5 possums, compared to residents on properties with no possums. BU was associated with ponds and bore water use at the residence. Insect repellent, covering arms and legs during outdoor activity and immediately washing wounds were observed to be protective; undertaking multiple protective behaviours was associated with the lowest odds of BU.

## Conclusion

Our findings suggest that skin hygiene and protection behaviours and previous BCG vaccination may provide protection against BU in endemic areas, especially for those at increased risk due to health, occupational, or environmental risks.

## Factors associated with infant carriage of antimicrobial resistance genes: a systematic review.

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Background

In recent years, carriage of antimicrobial resistance (AMR) genes has increased dramatically among infants. The reasons for this, however, remain poorly understood. Here we aim to identify potential determinants of AMR, the sites in which AMR genes are carried, and the most prevalent resistant infections.

Methods

Following PRISMA guidelines, we performed a systematic review using PubMed and Web of Science databases covering the years 2000 to 2021. We included studies which investigated AMR genes in infants using next-generation sequencing. Our search yielded 1840 articles, of which 32 were included in the final sample.

Results

The most common identified determinants of AMR were delivery in neonatal intensive care units (n=4), antibiotic exposure in infants' gut microbiome (n=7), caesarean section as mode of delivery (n=3), and mother-to-child bacterial transmission (n=3). 9 of the 32 studies identified two main biological reservoirs of AMR including gut and the nasopharyngeal microbiota. The most common antibiotic resistance classes identified were aminoglycoside, β-lactams, macrolide, and tetracycline. Last-resort antibiotic resistance genes were also detected in infants' guts. Finally, we found the bacteria from order Enterobacterales and Bacteroidetes are commonly identified as carrying AMR genes.

Conclusion

Neonatal intensive care unit, antibiotic use, caesarean section, and maturity of the infant's gut are each independently associated with increased AMR carriage. More comprehensive studies regarding healthy infants and factors such as antibiotic use, mode of delivery and other factors are required. Furthermore, uniformity of AMR databases and bioinformatics pipelines should be addressed to promote inter-study comparisons.

## Hospitalisation – missing an opportunity to link to hepatitis C care: a retrospective study at a regional Australian health service

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### Background

Key to achieving micro-elimination of hepatitis C in Western Victoria is developing targeted, data-driven strategies to increase testing and linkage to care. This study aimed to assess the proportion of patients who are at risk of, or living with, hepatitis C infection, and the number who were tested and linked to care, whilst attending University Hospital Geelong.

### Methods

A retrospective study of adults admitted as hospital inpatients or Emergency Department patients from November 2018 to November 2021. Data were collected from the hospital admissions, Australian Clinical Labs, hospital pharmacy, and hospital outpatient Liver Clinic databases. Separations were selected if they had an ICD-10 code indicating intravenous drug use (IDU) or hepatitis C infection.

### Results

There were 1345 patients with IDU-coded separations and 628 patients with hepatitis C-coded separations (total n=1892. Overall, 323 (17.1%) of patients had hepatitis C virus (HCV) antibody testing (253/323 positive, 70/323 negative), 165 (8.7%) had HCV RNA testing (101/165 detected, 64/165 not detected) and 43 (3.1%) received treatment.

The Emergency Department had increased odds of not providing hepatitis C care (OR 3.29, 95% CI 2.42-4.48). The Mental Health Unit had the highest odds of HCV antibody testing (OR 2.12, 95% CI 1.24-3.63). Obstetrics and Gynaecology had the highest odds of HCV RNA testing (OR 4.38, 95% CI 1.55-12.37).

### Conclusion

A targeted intervention that increases hepatitis C antibody testing of people with a history of IDU whilst hospital inpatients is likely to improve linkage to hepatitis C care at our health service, and contribute to micro-elimination

## Oral-bait BCG vaccination of possums may address the worsening Victorian epidemic of Buruli ulcer

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### Background

Buruli ulcer (BU), caused by *Mycobacterium ulcerans,* is endemic in Victoria, Australia, with an increasing incidence, severity and spread of the disease. It is a potentially severe disease often leading to serious long-term consequences and resulting in significant community costs and concern. Evidence suggests that possums are a zoonotic reservoir for *M. ulcerans.* Currently there are no proven public health interventions to address this worsening disease.

### Methods

We will provide the evidence, rationale and research plan for a novel proposal to vaccinate possums in the wild with oral-bait BCG.

### Results

A *M. ulcerans* infection model of ringtail possums has recently been developed at the CSIRO research facility in Geelong. Next steps include possum vaccination with BCG before *M. ulcerans* challenge to assess the level and durability of protection by comparing vaccine with control groups. This could utilise tools developed previously by a BCG-based oral-bait vaccination scheme for brushtail possums against *M. bovis* in New Zealand. In the proposed study, blood samples would be collected to measure the immune responses to BCG vaccination, which would be correlated with immune protection. If effective, attempts would be made to optimize the palatability and feasibility of oral-bait BCG delivery. Finally, testing the effectiveness of oral-bait BCG vaccine against *M. ulcerans* in ringtail possums would be performed in laboratory and real-life field settings.

### Conclusion

Vaccination of possums in the wild with oral-bait BCG provides hope for an acceptable, safe and feasible intervention benefiting human and possum populations by reducing the transmission of *M. ulcerans*.

## Patient-reported quality of life following peri-prosthetic joint infection: a prospective observational study

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**Category:**

Bacterial diseases and infections

**Introduction:**

Joint replacement improves overall quality of life, but few prospective data describe patient-reported outcome measures (PROMs) in patients with peri-prosthetic joint infection (PJI). Using the Short Form Health Survey version 2 (SF-12v2), we aimed to describe the patient-reported physical (PCS) and mental health scores (MCS) at the time of PJI diagnosis and for 2-years.

**Methods:**

Data from the PIANO cohort study were analysed for PROMS. An SF-12v2 questionnaire was administered at baseline, 3, 12 and 24 months. MCS and PCS were scored against age-adjusted population norms.

**Results:**

Of the 783 participants in PIANO, 522 had complete SF-12v2 data across baseline, 3, 12 and 24 months. There were no significant differences between PCS and MCS for hip, knee and shoulder PJI. At baseline, the median (IQR) PCS was 36.9 (30.1 – 45.6) whilst the MCS was closer to the population norm (47.9 [37.5-57.4]). Chronic PJI had lower baseline median PCS and MCS than late acute PJI (LA-PJI; 34.0 vs. 39.5, P=0.007 and 41.2 vs. 51.2, respectively). By 12 months, both the PCS (median difference 3.1) and MCS (3.4) had improved, but the PCS remained well below population age-adjusted norms. There were no further improvements between 12 and 24 months. Clinical cure at 12 months was associated with higher PCS (43.8 vs. 37.9, P<0.0001) as well as higher MCS (55.4 vs. 50.0, P<0.0001).

**Conclusion:**

At baseline, patients with PJI have impaired QoL and despite limited improvement, this is sustained beyond 12 months. Achieving clinical cure is associated with significant improvements in QoL.

**Disclosure of Interest Statement:**

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## Prevalence And Outcomes Of Secondary Infections Among Hospitalised Patients With COVID-19 Or Post-COVID Conditions In Victoria, 2020-2023

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Category:

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Introduction: Secondary infections complicate COVID-19 management resulting in longer hospital and ICU length of stay (LOS), and increased mortality. There is limited information on the prevalence of secondary infections among Victorian COVID-19 patients and variability in reported prevalence (6.9-24%) globally.

Methods: We performed a retrospective cohort study estimating the prevalence of secondary infections complicating COVID-19 and post-COVID admissions in Victoria from January 2020 to May 2023. Admissions were identified from the Victorian Admitted Episodes Dataset (VAED). All relevant secondary viral, bacterial, and fungal infections were identified using corresponding ICD-10 codes. The impact of secondary infections was determined using outcome measures including hospital/ICU LOS using negative binomial regression models, and mortality using Cox proportional-hazard models.

Results: 194660 COVID-19 and post-COVID admissions were identified with 13467 (6.9%) having a secondary infection; 11,651 (6.0%) bacterial, 1,691 (0.9%) viral, and 385 (0.2%) fungal. The odds of secondary infection increased with age (odds ratio (OR), 3.76 (95%CI 3.43, 4.14) amongst those ≥70 years and were higher amongst individuals with chronic conditions (OR: 3.15; 95%CI: 2.88). Patients with a secondary infection had 2.43 (95%CI 2.39, 2.48) times longer hospital LOS, and 9.60 times (95%CI 8.62, 10.73) longer ICU LOS compared to those without. The mortality risk was higher (hazard ratio 2.17; 95%CI: 2.06, 2.27) in those with secondary infections. Admissions of those aged ≥70 years, those with chronic disease, the unvaccinated, those from the most socio-economically disadvantaged areas were associated with increased risk of secondary infections and poor outcomes.

Conclusion:

Secondary infection occurred in 6.9% of COVID-19 associated hospital admissions in Victoria from 2020 to 2023 and were associated with increasing hospital length of stay, ICU admission and length of stay, and mortality, with bacterial secondary infections being the most prevalent (6.0%).

## Programmatic synergies for co-surveillance of malaria and COVID-19 infections among vulnerable communities in Ghana.

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### Abstract

Malaria control and surveillance in sub-Sahara Africa has stalled in the past three years, partly due to reallocation of resources for COVID-19 interventions. In Ghana where malaria transmission is high and COVID-19 is widespread, *Plasmodium falciparum* and SARS-CoV-2 co-infection rates remain unknown; Subsequently, clinical misdiagnosis poses a threat to control efforts. Therefore, this study aimed to evaluate the epidemiological, clinical, and diagnostic factors to inform malaria and COVID-19 co-surveillance.

Between October-December 2022, 1,065 participants were recruited through multi-site prospective cross-sectional surveys in 12 communities within Greater Accra (metropolitan) and Central (semi-urban) regions of Ghana. Others were recruited through community health programs in the study communities. Each participant provided nasal/throat swabs for COVID-19 PCR-testing, with optional finger-prick blood for malaria RDT-testing; Their data including malaria infection and antimalarial treatment in the past two weeks were recorded in REDCap.

The majority of the study population comprised of adults (18-59 years) and females, 73.6 and 61.1%, respectively, with COVID-19 positivity and vaccination rate being 22.8% and 54.6%, respectively. Overall, 18.1% of participants self-reported having malaria, and this was associated (adjusted odds ratio ≥ 1.55, P-value ≤ 0.022) with study community, COVID-19 clinical disease and positivity. All malaria cases were reportedly self-medicated or clinically treated with antimalarials. Malaria testing (N=136) resulted in *P. falciparum* prevalence of 6.0%, with 2.0% being co-infected with SARS-CoV-2, without overt symptoms.

In communities with active malaria and COVID-19 transmissions, co-surveillance for both infections will provide programmatic synergies, which will be crucial to inform national control and elimination efforts.

## The Impact of Seasonal Malaria Chemoprevention (SMC) on P. falciparum Population diversity

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### Abstract

Seasonal Malaria Chemoprevention (SMC)has been proven to be effective in high-transmission areas of seasonal malaria in sub- Saharan regions. Although studies have shown the potential effectiveness of this intervention, no studies have been done to elucidate the impact of this intervention in the changes of parasite population. We conducted a pilot study as part of the International Centre of Excellence in Malaria Research (ICEMR) programme to evaluate the impact of SMC intervention on parasite genetics by hypothesizing that SMC would lead to a reduction in parasite genetic diversity.
We examined samples from cross-sectional surveys collected before and during the implementation of SMC from the Dangassa, Mali in 2015. Genotyping was done using SNP barcoding of 81 samples collected between 2013 – 2019. The barcodes included 175 biallelic SNP markers and further used for downstream population genetic analyses. We obtained 69 high quality genotypes and identified 80 polymorphic SNPs to measure patterns of population diversity and structure (minor allele frequency > 0.10). We then compared parasite populations before and during SMC using nucleotide diversity statistics, Principal Co-ordinate Analysis and pairwise Identity-by-decent to observe population diversity and structure and parasite relatedness. Preliminary analyses revealed no clear genetic differentiation, reduced diversity or increased clustering patterns comparing the parasite populations collected before and during treatment. The study demonstrated a limited impact of the SMC intervention on the parasite population suggesting that further sustained control efforts will be needed to interrupt transmission. The study also demonstrates the utility of this SNP barcode for parasite genomic surveillance in West Africa.

## The role of Staphylococcus aureus colonisation in the severity of disease

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### Background

Approximately 30% of the population are permanently colonised with S*taphylococcus aureus*. *S. aureus* killed over 1 million people globally in 2019 alone. Being colonised gives you a 3x increased odds of having an infection. It has also been seen that colonisation of *S. aureus* can change the immune makeup against *S. aureus*. What is currently unknown is the role it has when combined with other co-morbidities. Does being colonised plus a specific comorbidity make even more at risk of infection. Does being colonised exacerbate a condition not directly linked to *S. aureus.* This preliminary scope of the literature investigated what is currently known in this field

### Methods

Literature from 2000-2022 was sought with the key words of *S. aureus* colonisation and co-morbidity. Articles were included if they were human focused research, interventional,

observational, or systematic studies. Articles not in English, reviews, case studies, animal studies were not included.

### Results

Colonisation of *S. aureus* was observed within the literature to increase the risk of infection in specific co-morbidities such as haemodialysis patients. It was also observed to be associated with increased severity of symptoms in other diseases such as asthma. Not many of these studies were performed in the Australian context.

Conclusion

It is proposed by the authors that *S. aureus* colonisation prevalence needs to be surveyed in the Australian population and further investigation of the impact of these bacteria in disease is warranted. This would be a good collaborative opportunity for multiple disciplinary research across multiple diseases.

## Transmission dynamics and population structure of P. falciparum and P. vivax in Mondulkiri Province, Cambodia

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### Background

A cross-sectional survey conducted in Kaev Seima District, Mondulkiri Province in Cambodia by the Asia Pacific International Centre for Malaria Research (ICEMR) demonstrated that living and working in forested areas is a risk factor for both *P. falciparum* and *P. vivax* malaria. It is not known whether infections outside the forest are driven by infections acquired inside the forest. Population genetic analyses can reveal transmission dynamics and population structure, as well as the origins and flow of infections between villages.

### Methods

This project aimed to apply SNP barcoding to *P. falciparum* and *P. vivax* isolates from the cross-sectional study to allow population genetic analysis.

### Results

This SNP barcoding of 176 informative, validated SNPs in 34 *P. falciparum* isolates resulted in 127 successfully genotyped SNPs, 9 of which were polymorphic in this Cambodia population. For *P. vivax,* SNP barcoding of 178 informative, validated SNPs in 65 isolates resulted in 53 successfully genotyped SNPs, 19 of which were polymorphic. The analysis revealed low population diversity for both species with no evidence of clustering or population structure between village and forest. Further, genotypes originating from different geographical locations were seen to be highly related.

### Conclusion

These results support the hypothesis that parasites originate in forest areas and are the likely source of infections in villages outside the forest as demonstrated by the high gene flow to and between areas. This information may be used by malaria programs to successfully interrupt and monitor impacts of control efforts on malaria transmission.

## Understanding the spread of Buruli ulcer in urban Geelong: the changing distribution of human cases and the prior detections in possum faecal samples.

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### Background

Buruli ulcer (BU), is a necrotising skin condition, caused by the environmental pathogen *Mycobacterium ulcerans*. Case numbers in Victoria, of this potentially severe disease, have increased from 77 BU cases in 2012 to 339 cases in 2022, and BU endemic areas have been expanding. Previously, BU incidence centred in coastal areas of the Mornington and Bellarine Peninsulas. Importantly, new urban, non-coastal areas of inner Geelong and Melbourne are now contributing significantly to the rise in case numbers.

### Methods

In this study, we describe the changing epidemiology, incidence and spatial distribution of BU cases in Geelong. We compare the distribution and timeline of human BU cases to the distribution of *M. ulcerans* DNA-positive possum faeces from surveys in 2020 and 2022.

## Results

A total of 80 BU cases have been notified for people living in central Geelong areas from 2011-2022. Spatiotemporal analysis showed a clear clustering of cases in areas of Belmont (2019-2022) and Highton (2022), with clustering also noted in Newtown (2020-2021). Clusters occurred in highly focal geographic areas and were close to *M.ulcerans*-positive possum faecal samples (median 199m (IQR 88, 393) from case residence) detected within 8-31 months prior to the human case diagnosis.

## Conclusion

Epidemiological analyses and faecal possum surveys has allowed the rapid detection of new BU endemic areas in Geelong. This enabled important public health opportunities for targeted prevention messaging and for community and clinician education towards reducing exposures and improving early detection and treatment of BU disease to improve clinical outcomes.