

Nov 2022

The National Centre for Infections and Cancer. NHMRC CRE App # 1116876, NHMRC Synergy grant#2011100

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NCIC Report

Nov 2022

Preamble:

There is compelling evidence that infection in cancer patients remains a leading cause of death and a significant cost to the healthcare system. No group is systemically addressing this problem in Australia nor is it addressed in national cancer strategies.

This Synergy program aims to:

1. Establish a national infrastructure for cancer specific infection surveillance.

2. Nationally implement life saving and harm minimising clinical care pathways.

3. Introduce innovative technologies to support the detection of and improve care of infections.

4. Build workforce capacity in infections and cancer

Purpose:

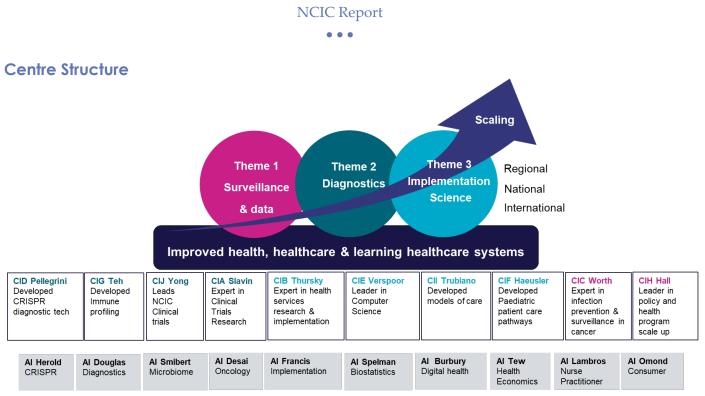
The purpose of this report is to provide feedback on Synergy activities to date and to outline progress towards sustainability.



The National Centre for Infections in Cancer was conceived in response to data on infections in cancer being a leading cause of death and a significant cost to the healthcare system.

To date, no group has systematically addressed this problem in Australia nor is it addressed in national cancer strategies.

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Centre manager: Dr Megan Crane

Clinical trials team: Rachel Woolstencroft, Gwyn Ng, Marcel Stewart, Hayley Page, Jess Demajo, Chhay Lim, Jenny Gallagher, Surekha Tennakoon, Natalie Saunders, Emily Klimevski, Beatrice Sim, Nick Laundy PhD students: Victoria Hall, Gemma Reynolds, Jasmine Teng, Alison Lemoh, Dan Neoh

Funding report

Commonwealth funding for cancer and infection projects

NCIC began in 2017 with \$2.5 million in funding as an NHMRC Centre for research Excellence. In Jan 2022 the NCIC was awarded a further \$5 million NHMRC synergy grant until 2026. Since beginning in 2017 we have secured a total of \$20 million in NHMRC and MRFF grants for projects in infections in cancer.

Table 1 (Lead investigator funding)

| Investigator | Year | Study/Project | Source | Funding |
|---------------|------|----------------------------------|--------|-----------------|
| Monica Slavin | 2017 | NCIC | NHMRC | \$2.5 million |
| | 2019 | Investigator | NHMRC | \$1.6 million |
| | 2020 | CSMART | MRFF | \$2.169 million |
| | 2022 | Synergy | NHMRC | \$5 million |
| Karin Thursky | 2016 | PICNICC | NHMRC | \$600,000 |
| | 2017 | No place like home | BCV | \$445,000 |
| | 2019 | AFS | NHMRC | \$1.6 million |
| | 2022 | Appropriate Antimicrobial Use | MRFF | \$3 million |
| Gab Haeusler | 2019 | No place like home | MRFF | \$1.2 million |

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| Ben Teh | 2021 | Investigator grant | MRFF | \$1.1 million |
|----------------|------|--------------------|------|------------------|
| | 2022 | Foundation grant | PMCC | \$50,000 |
| Jason Trubiano | 2018 | Allergy | BCV | \$400,000 |
| Abby Douglas | 2022 | Foundation grant | PMCC | \$50,000 |
| | | | | \$19.714 million |

In addition NCIC investigators have been named on and receive funding through our network collaborations.

Table 2 (Non lead funding)

| Year | Study/Project | Lead Investigator | Source | Funding total |
|------|---------------------------|------------------------------------|--------|---------------|
| 2022 | Immune responses to COVID | Katherine Kedierska (UoM) | MRFF | \$3 million |
| 2021 | META-GP | Deborah Williamson (RMH) | NHMRC | \$7 million |
| 2021 | Super bugs II | Lindsay Grayson (Austin health) | NHMRC | \$2 million |
| 2021 | CRE-Respond | Jason Roberts (UQ) | NHMRC | \$2.5 million |
| 2021 | C-FIND | Marc Pellegrini (WEHI) | MRFF | \$870,000 |

Industry funding for cancer and infection projects

Since establishing the NCIC clinical trials team in 2017 we have worked on a number of investigator initiated and pharma initiated clinical trials. The Clinical trials team of 4 research nurses (Gwyn Ng, Haley Page, Marcelle Stewart and Jess Demajo) a data manager (Belinda De Poi), 2 clinical trials assistants (Chhay Lim and Jenny Gallagher) and 3 laboratory assistants (Surekha Tennakoon, Natalie Saunders and Emily Klimevski) is led by nurse manager Rachel Woolstencroft and medical lead Dr Michelle Yong.

Table 3 (Investigator initiated and pharma initiated clinical trials)

| Investigator | Year | Study/Project | Source | Funding |
|---------------|------|---------------|---------|------------------|
| Monica Slavin | 2018 | F2G | F2G | \$70,000/patient |
| | 2019 | Paraflu | Ansun | \$45,000/patient |
| | 2018 | Restore | Cidara | \$70,000/patient |
| | 2020 | APX001 | Medpace | \$50,000/patient |
| | 2020 | SYNERGIA | Syneos | \$50,000/patient |
| | 2019 | Posa | MSD | \$120,000 |
| | 2020 | RSV | Janssen | \$50,000/patient |

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| Ben Teh | 2019 | Flu vax I | MSD | \$60,000 |
|----------------------|------|------------------------|--------|--------------|
| | 2022 | Flu vax II | Sanofi | \$50,000 |
| | 2021 | PROSECCO | Merck | \$100,000 |
| Michelle Yong | 2018 | Cresct | MSD | \$270,000 |
| | 2020 | Cresct expansion | MSD | \$250,000 |
| | 2022 | Paxlovid | Pfizer | \$123,000/pt |
| Abby Douglas | 2019 | PIPPIN | Gilead | \$60,000 |
| Shio Yen | 2020 | CrispBAL | Gilead | \$60,000 |
| Zoe Neoh | 2020 | Auslopro | F2G | \$300,000 |
| | 2022 | Fungal surveillance | Gilead | \$60,000 |

Track record

Publications Time period: Jan 2017- Jun 2022

- Total 1219 papers, 1547 citations
- Average 12.3 citations per paper
- 41.5% are due to an international collaboration, 56.8% are a national collaboration
- Average Field weighted citation impact factor 1.94
- 36.2% in top 10% journals
- 69.1% are in the field of Medicine, also publish in fields of Immunology, Biochemistry and Pharmacology

Public engagement

Table 4

| Туре | Analytics |
|---------------------------|--|
| Website | 2017: 737 unique visitors, 2,165 page views |
| | 2019: 2384 unique visitors, 4498 page views |
| | 2020: 6900 unique visitors, 12000 page views |
| Twitter (28 day snapshot) | 2017: 13.1K impressions |
| | 2019: 14.1K impressions |
| | 2020:15.5K impressions |
| Features | 4x MJA articles on microbiome |
| | 1x Conversation article on Candida Auris |

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| ABC news interview Candid Auris 1X conversation article on Mucor Mycosis and COVID |
|---|
| BBC World news interview Mucor Mycosis and COVID |

Seminars, conferences and education programs Table 5

| Туре | Year | Торіс |
|--|---------|---|
| Conference | 2021 | International Conference of the Immunocompromised Host Society (ICHS) |
| Symposium | 2017 | NCIC Launch |
| | 2018 | What's new in cancer |
| | 2019 | New Frontiers in cancer infection management |
| | 2020 | Fungal infections in focus |
| | 2022 | COVID in ICH |
| Forum | 2019 | Your gut Health: consumer engagement |
| | 2022 | Synergy IM |
| | 2022 | PROSECCO IM |
| Invited speakers | 2017 | Peter Pappas: C.Diff, Paul Verweij: antifungals |
| | 2018 | Josh Hill: ICIs and HSV, Jason Roberts: PK/PD |
| | 2019 | Bob Finberg: Flu, Burton Dickie: novel antivirals, Dena Lyras: FMTs |
| Medical and nursing in- service education | Ongoing | Sepsis pathway in service |
| | Ongoing | ID for Haem- registrar training |

Progress towards sustainability

Infection surveillance

- The NCIC has demonstrated the significant burden of infections using manual surveillance methods [1].
- We have successfully piloted the use of large linked datasets to reduce resource demands of reporting [2].
- We have led the concept of enhanced surveillance for cancer-related infections (sepsis, invasive fungal infections, blood stream infections, and *Clostridiodes difficile*) using gold-standard data linked to administrative data [3-5]

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- We have a proof-of-principal project (Antifungal Stewardship) under development in a current NHMRC project grant (AFS-see table 1)
- We are currently carrying out a national surveillance for fungal infections (AusLoPro- see table 3)

Implementation of clinical care pathways

Table 6

| Pathway | Innovation | Economic savings | Patient outcomes |
|---|--|---|---|
| Cancer Sepsis Pathway [6, 7] | First ever whole of hospital nurse led clinical pathway for recognition and management of sepsis (single site) | Short term ICER of \$8000 per patient on pathway with lives saved. Future costing across cancer types cost effectiveness[8] | Reduction in mortality ~50%, LOS, ICU admission |
| Think Sepsis Act Fast Scaling Collaboration [9] | Cancer sepsis pathway adapted for non cancer hospitals, and implemented in 24 Victorian hospitals | \$11.5 million cost savings for the project Short term ICER cost saving and more effective | Reduction in mortality ~50%, LOS, ICU admission adjusted for sepsis severity |
| Ambulatory pathway of care for low risk neutropenic fever in adults and children | First adult and paediatric low risk FN program. Paed program scaled nationally 8 sites and internationally to 12 sites[10] | Paed: mean cost saving \$12,800 per patient on programAdults: Health economic model projected | Improved QoL, reduction in LOS, increased bed access and no adverse outcomes. |
| Vaccination pathways for high risk patients [11] | Vaccination protocol and counselling service for patients at high risk for vaccine- preventable infections (3 sites) | For evaluation | Near universal vaccination uptake and higher completion rates |
| Point-of-care Antibiotic Allergy delabelling [12] | First ever inpatient and outpatient AMS led delabelling program for antimicrobials. In 2 sites: Peter Mac and Austin hospitals | \$335 per patient cost saving was noted in a cost-effectiveness analysis with an inpatient penicillin delabelling program. | 10-fold increase in narrow spectrum penicillin usage, 2-fold increase in appropriate prescribing |

ICER; incremental cost effectiveness ratio, LOS, length of stay; ICU, intensive care; QoL, quality of life, FN Febrile neutropenia

Innovative technologies

NCIC has established a highly successful Clinical trials group which employs four clinical trials nurses, two clinical trials assistants and two laboratory research assistants. Current pharma and investigator initiated trials (table 3) in cancer patients include:

- Novel antifungals (F2G, Restore, APX001, Synergia),
- Novel antivirals (RSV, paraflu),
- Novel prophylaxis strategies (Flu vax, CSMART {see table 1}, posa)
- Novel diagnostics (Pippin, CrispBAL, Cresct and Cresct expansion)

Workforce capacity

- NCIC employs 31 people on both clinical, trials and research roles (Table 7)
- NCIC has 7 current and 5 completed PhD students (Table 8)

| Ta | b | le | 7 |
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| | | | |

| | Dele |
|----------------------|-----------------------------------|
| Staff member | Role |
| Monica Slavin | Dept head, stream lead, clinician |
| Karin Thursky | Dept head, stream lead, clinician |
| Leon Worth | Dept head, stream lead, clinician |
| Ben Teh | Fellow, clinician |
| Michelle Yong | Fellow, clinician |
| Belinda Lambros | Nurse Practitioner |
| Registrar | Clinician |
| Gab Haeusler | Fellow, clinician |
| Jason Trubiano | Fellow, clinician |
| Abby Douglas | PhD student, clinician |
| Shio Yen Tio | PhD student, clinician |
| Su Ann Ho | PhD student, clinician |
| Olivia Smibert | PhD student, clinician |
| Morgan Rose | PhD student, clinician |
| Megan Crane | Manager |
| Krishna Brannigan | Admin |
| Nick Laundy | International visiting fellow |
| Chhay Lim | Research Assistant |
| Marcelle Stewart | Research nurse |
| Surekha Tennakoon | Research Assistant |
| Natalie Saunders | Research Assistant |
| Rachel Woolstencroft | Research nurse |
| Hayley Page | Research nurse |
| Gwyn Ng | Research nurse |
| Anna Khanina | Fellow |
| Zoe Neoh | Fellow |

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| Jenny Gallagher | Research Assistant |
|-----------------|------------------------|
| Belinda Depoi | Data manager |
| Jess DeMajo | Research nurse |
| Victoria Hall | PhD student, clinician |
| Gemma Reynolds | PhD student, clinician |
| | |

Table 8 PhD students

| Student | Completion year | Scholarship |
|-------------------|-----------------|-------------|
| Abby Douglas* | 2021 | UoM |
| Shio Yen Tio | 2023 | NHMRC |
| Su Ann Ho | 2023 | CRE-REDUCE |
| Michelle Tew* | 2020 | UoM |
| Jake Valentine* | 2021 | UoM |
| Oliva Smibert** | 2023 | NHMRC |
| Victoria Hall | 2024 | NHMRC |
| Gemma Reynolds | 2024 | NHMRC |
| Jasmine Teng | 2024 | NHMRC |
| Julian Lindsay* | 2021 | NCIC |
| Brendan McMullen* | 2020 | UoM |
| Morgan Rose | 2023 | UoM |
| Dan Yeoh | 2022 | UoM |
| *Completed | | |

*Completed

**Recipient of the Gus Nossal NHMRC PhD fellowship and The Rosie Lew PMCC PhD fellowship awards

- In 2020 we appointed an AMS Nurse Practitioner (Belinda Lambros)
- Current research fellows have won numerous awards, are now Head of Department and/or are named as CIA on grants (Table 9)

Table 9 Career Development awards

| Investigator | Year | Award/achievement |
|--------------|------|----------------------------|
| Ben Teh | 2018 | UoM Chancellors Award |
| | 2018 | Vic Premier's award |
| | 2020 | NHMRC Investigator grant |
| | 2021 | Appointed Advisor to ATAGI |
| Gab Haeusler | 2018 | Vic Premier's award |
| | 2019 | UoM Chancellors Award |

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| | 2019 | CIA on MRFF project grant |
|----------------|------|---|
| Jason Trubiano | 2020 | Appointed Acting Head Dept ID Austin Hospital |
| Karin Thursky | 2019 | FAAHMS |
| | 2019 | UoM Kay Campbell Fellowship |
| | 2021 | Assoc, Director HSRIS |
| Monica Slavin | 2019 | FAAHMS |
| | 2021 | UoM Chair ICH |
| Michelle Yong | 2022 | PMCC Women in Science Lea medal |
| Abby Douglas | 2022 | PMCC Significant PhD award |

References

- 1. Valentine, J.C., et al., *Use of a Victorian statewide surveillance program to evaluate the burden of healthcare-associated Staphylococcus aureus bacteraemia and Clostridioides difficile infection in patients with cancer.* Intern Med J, 2021.
- 2. Valentine, J.C., et al., *Classification performance of administrative coding data for detection of invasive fungal infection in paediatric cancer patients.* PLoS One, 2020. **15**(9): p. e0238889.
- Valentine, J.C., et al., Burden and clinical outcomes of hospital-coded infections in patients with cancer: an 11-year longitudinal cohort study at an Australian cancer centre. Support Care Cancer, 2020. 28(12): p. 6023-6034.
- 4. Valentine, J.C., et al., *Sepsis incidence and mortality are underestimated in Australian intensive care unit administrative data*. Med J Aust, 2019. **210**(4): p. 188-188 e1.
- 5. Valentine, J.C., et al., *The current scope of healthcare-associated infection surveillance activities in hospitalized immunocompromised patients: a systematic review.* Int J Epidemiol, 2019. **48**(6): p. 1768-1782.
- 6. Thursky, K., et al., *Implementation of a whole of hospital sepsis clinical pathway in a cancer hospital: impact on sepsis management, outcomes and costs.* BMJ Open Qual, 2018. **7**(3): p. e000355.
- Hiong, A., et al., *Impact of a hospital-wide sepsis pathway on improved quality of care and clinical outcomes in surgical patients at a comprehensive cancer centre*. Eur J Cancer Care (Engl), 2019. 28(3): p. e13018.
- 8. Tew, M., et al., *Incorporating Future Medical Costs: Impact on Cost-Effectiveness Analysis in Cancer Patients.* Pharmacoeconomics, 2019. **37**(7): p. 931-941.
- 9. *Think Sepsis Act Fast Evaluation Report. Safer Care Victoria,* 2019 Available from: <u>https://www.bettersafercare.vic.gov.au/improvement/projects/mtip/think-sepsis-act-fast.</u>
- 10. Phillips, B. *York AC*. Available from: <u>https://www.york.ac.uk/research/coronavirus-</u> research/applied-health/shortening-hospital-stays-child-cancer.
- 11. Teh, B.W., et al., *Impact of a dedicated post-transplant vaccination service at an Australian cancer centre*. Bone Marrow Transplant, 2017. **52**(12): p. 1681-1683.
- 12. Trubiano, J.A., et al., *The impact of antimicrobial allergy labels on antimicrobial usage in cancer patients*. Antimicrob Resist Infect Control, 2015. 4: p. 23.