



DISCIPLINE OF SURGERY
ADELAIDE MEDICAL SCHOOL
FACULTY OF HEALTH & MEDICAL SCIENCES

PROFESSOR GUY J MADDERN
PhD MS MD FRACS FAAHMS

DISCIPLINE LEAD – SURGERY

DIRECTOR OF RESEARCH
BASIL HETZEL INSTITUTE FOR
TRANSLATIONAL HEALTH RESEARCH

THE QUEEN ELIZABETH HOSPITAL
WOODVILLE SA 5011
AUSTRALIA

TELEPHONE +61 8 8222 6756
FACSIMILE +61 8 8222 6028

guy.maddern@adelaide.edu.au

7th May 2020

Dr Matthew Butlin,
Chair and Chief Executive,
South Australian Productivity Commission,
GPO Box 234,
ADELAIDE, S.A. 5001.

Dear Dr Butlin,

The research community at the Basil Hetzel Institute for Translational Health Research (BHI) located at The Queen Elizabeth Hospital is grateful for the opportunity to provide a submission to the South Australian Productivity Commission Inquiry into Health and Medical Research. Our organisation and site saw the first renal transplant in Australia, pioneered reproductive medicine in South Australia, and more recently has been active in pursuit of a COVID-19 vaccine. We are made up of translational research groups with close links to clinical problems that are solved with carefully conducted scientific studies. The BHI is comprised of researchers from the University of Adelaide, University of South Australia, SA Health, with collaborators from around Australia and internationally.

The possibility to further extend the success of the BHI could be facilitated by modernising and reforming outdated bureaucratic processes within South Australia and providing sustained consistent support to research infrastructure, not only capital but also administrative and research support staff.

We look forward to being of help in this enquiry which is long overdue.

Yours sincerely,

Professor Guy Maddern
BHI Director of Research

The Basil Hetzel Institute: a model for Health and Medical Research in SA Health.

The Basil Hetzel Institute for Translational Health Research (BHI) (previously the Clinical Development Research Centre), was established in its current form in 1996 to foster the research programs of The Queen Elizabeth Hospital (TQEH). The BHI comprises the research efforts of staff and students associated with TQEH, and who may be employed or affiliated with the University of Adelaide, the University of South Australia, other higher education providers, SA Health and the Central Adelaide Local Health Network.

Research at the precinct has a long history of pioneering clinical innovations including:

- Discovery of dietary iodine deficiency in pregnancy as a preventable cause of congenital mental and physical impairment – considered the greatest medical discovery in the prevention of mental impairment.
- First successful renal transplantation in Australia
- First lung reduction surgery in Australia
- First in-vitro fertilization program in SA
- First acute stroke unit in SA
- First autologous stem cell transplant in SA
- Characterisation of the Coronary Slow Flow Phenomenon – a coronary microvascular disorder
- First capsular endoscopy in SA
- First nurse practitioner in SA
- Strong leadership in evidence evaluation of new surgical technologies in association with the Royal Australasian College of Surgeons
- NHMRC Centre of Excellence in Frailty & Healthy Aging
- Researchers at the BHI were the second group in South Australia to be awarded an MRFF grant.

BHI research contributes to the academic literature (331 peer-reviewed journal publications in 2019), generates patents (4 patents currently in national phase), leads to the establishment of commercial enterprises, has impact and influence on clinical care and health services in South Australia and supports the research training of the next generation of HMR researchers. For the 2019 Research Report researchers at the BHI identified their most impactful outcome of the year. In that 12 months alone, the listed achievements included research that changed government policy, developed and trialled new treatments for combating disease, provided greater understanding and recognition of human medical problems and contributed to medical practise. We believe the BHI is a model of successful HMR research in South Australia.

In response to the Issues Paper, a group comprising research leaders, researchers and administration staff of the BHI have prepared a submission. The group has drawn on research activity data, collected consistently for over 20 years, and their own experience as South Australian Health and Medical researchers, to explore the success of the BHI and interrogate the barriers that this community experiences. Please find the findings of the group below, and a list of recommendations.

- ***TQEH is the only CALHN hospital that has an integrated research facility.*** The original research facility, the Clinical Research Development Centre, was replaced by SA Health in 2008 by a stand-alone 4,000 m² purpose-built research facility (the BHI) adjacent to the hospital at Woodville. The facility accommodates a mix of laboratory and clinical research.

The Institute's strengths in research are closely linked to the disease burden of the region. The research programs are focussed on community need and enabled by patients and patient samples from the TQEH clinical programs. Many of the researchers working at the Institute are

employees/students of stakeholder organisations. The value of salary and research support attracted to the BHI in 2019 was in excess of \$20million.

The translational health research program is underpinned by a well-established Committee structure. The BHI Policy Committee, chaired by the Director of Research, BHI, TQEH, comprises representatives drawn from the research leadership of the BHI, of the BHI research community and of key stakeholders. The committee was established to provide strategic advice for the operation of the BHI, to support the Director of Research and to optimise the available support for research programs at the Institute. The BHI Policy Committee is supported by a number of sub-committees, with membership drawn from the BHI and with defined areas of expertise: the BHI Strategic Research Directions Group, the Institute Research Management Committee, BHI Scholarship Committee and the organising committee for the annual TQEH Research Expo. Committees provide an opportunity for clinical and scientific research staff and strategic partners to have input into the functions of the BHI.

The 'Requirements of groups occupying the BHI' policy¹, which established the requirements of research groups moving into the new facility in 2008, underpins operational arrangements for research at the hospital. In line with this policy, research activity is reviewed annually by the Director of Research in consultation with the clinical heads of the research units. The data collected covers publications, graduated students, research directions, funding obtained and areas of tension (delayed student completions, for example). This process is incredibly valuable and serves to forge a common identity and purpose within the research community as well as enabling early detection of changing trends within the BHI.

A small administrative hub, funded in the main by external partners, ensures the efficient and effective running of research at the hospital.

- ***The BHI's spectrum of inquiry is broad*** but is united by a mission to improve clinical care in South Australia through clinical research, therapeutic development and clinical translation of research outcomes. As might be expected, many research outcomes have impact and influence beyond the state. The BHI embraces a broad definition of health and medical research that describes its mission of fostering research from discovery through pre-clinical development, clinical trials and implementation (Figure 1).

With a focus on addressing the clinical issues that impact South Australians, the BHI plays an important role in developing clinical practise in the state. This can be seen in, but is not limited to, the response of the Institute to the COVID-19 emergency:

- Prof. Guy Maddern (R. P. Jepson Professor of Surgery, University of Adelaide and Director of Research, BHI,TQEH) and Prof. Peter Hewett (Head of Colorectal Surgical Unit TQEH and Clinical Professor of Surgery, University of Adelaide) have led the development and communication of guidelines for PPE use during surgery and the use of laproscopic vs open surgery during the pandemic.² These guidelines, developed in South Australia, will be adopted nationally.
- A briefing paper on on surgical urgency in COVID-19 for the Chief Medical Officer of Australia, Professor Brendan Murphy.
- Dr. Branka Gubor-Bauk has formed a coalition of scientists and clinicians to answer key scientific questions about Sars-CoV-2 and the patient response to infection.
- Professor Renuka Visvanathan has contributed informally to triage guidelines for COVID-19 under development for the ICU staff in NSW.

¹ <https://www.basilhetzelinstitute.com.au/about/prospective-groups/#terms-of%20occupancy>

² <https://umbraco.surgeons.org/media/5214/2020-04-15-recommendations-on-safe-surgery-laparoscopic-vs-open.pdf>

- ***The research at the BHI can be summarised into seven themes***, representing the traditional and ongoing research strengths of the precinct (Figure 2). An update on research activity can be found in the 2019 BHI Research Report.³
- ***The strategic nexus between clinical need and research priorities*** that characterises the BHI research agenda is unique in South Australia and made possible by the close interface of research and teaching with the hospital's clinical activity. The research programs at the BHI are seamlessly integrated with the clinical programs of the hospital. This is ensured by:
 - A document containing the terms under which research group can occupy the research facility including a term that states 'only health and medical research relevant to Departments and Units of The Queen Elizabeth Hospital will be undertaken within The Institute.'
 - A prerequisite of BHI membership is a demonstrated relationship with the clinical programs within TQEH.⁴
 - Research happens within the clinical spaces of the TQEH wards and the purpose-built research facility on Woodville road, and with collaborators not only located within South Australia but nationally and internationally.
 - The Institute hosts a complex workforce, with a mix of clinical academics, clinician researchers, healthcare workers, health and medical researchers, clinicians in training, emeritus staff and research students. In 2019 the precinct hosted 182 full-time equivalent researchers (Figure 3) and identified a research workforce of approximately 250 staff and 100 students (higher degree by research (HDR) and honours). Research teams are multidisciplinary and complex, capable of bringing to a clinical problem state-of-the-art research and clinical approaches.
- ***Clinical academics and clinician researchers*** are fundamental to the research translation mission of the BHI. These thinking clinicians provide a 'two-way street' in research translation; on occasions identifying a clinical problem and turning to laboratory researchers for answers but equally providing insights into the clinical translation of a laboratory discovery. These unique individuals require dedicated research time amongst their busy clinical activities and thus are often co-funded by the University and Hospital (Clinical Academics). These clinicians play critical roles in the research training of the next generation of MD/Ph.D.s and biomedical researchers in South Australia.

Unfortunately, with diminishing hospital funds and the focus away from clinical research in the hospital there has been a decline in clinical academic appointments in recent years. This trend can be seen in data collected at the BHI (Figure 4). Most concerning, this trend was identified in the McKeon report in 2013⁵, with recommendations that declining participation of healthcare professionals in research be reversed, yet the data from BHI shows that remediation of the situation has yet to have impact. With the anticipated reinvigoration of clinical research within hospitals, it is hoped that this will improve.

- ***The model of research at the BHI has provided basic and clinical research training*** for honours and Higher Degree by Research (HDR) students for more than 30 years through its teaching and research affiliation with the University of Adelaide and University of South Australia.

The McKeon report noted that "Research capacity among health professionals is critical for conducting research, promoting research translation and improving the health system." And recommended that there needed to be support for "...dual research-practitioner education

³ https://www.basilhetzelinstitute.com.au/wp-content/uploads/2020/03/BHI_Research_Report_2019.pdf

⁴ <https://www.basilhetzelinstitute.com.au/about/prospective-groups/#terms-of%20occupancy>

⁵ McKeon, S, (2013), Strategic Review of Health and Medical Research: Better Health Through Research, Final Report, p. 28. http://mckeonreview.org.au/downloads/Strategic_Review_of_Health_and_Medical_Research_Feb_2013-Final_Report.pdf

pathways.”⁶ The need to train clinicians in research practices was considered pivotal to the future strength of the health systems in Australia.

An analysis of our 2019 student body (in total nearly 90 students) showed that 52% our HDR students are graduates of medical programs, with the balance attracted from biomedical and science training degrees. Supervision is shared by the research leaders of the Institute. Most notably, clinical researchers at the BHI take an active role in student supervision (with primary supervisory roles of 44 students in total, 43 located on the TQEH precinct, and 46 co-supervisory roles, of which 39 are of students located on the TQEH precinct). Clinical researchers are involved in the supervision of clinicians (70% of the identified supervisory roles), training the MD/Ph.D. workforce of tomorrow, and biomedical science/science scientists, providing valuable insights into practise-based research need. Through our student training we provide real-life opportunities to make a difference through research to health and medical outcomes that inspires and drives our student researchers.

Students are supported by a range of scholarship support systems, including the Research Training Program, University scholarships, NHMRC scholarships, international scholarship schemes and philanthropically funded scholarships. THRF has a long-standing commitment to support research students at the BHI, providing over \$2,000,000 to support undergraduate and postgraduate research training. These monies are awarded competitively to students keen to join the research programs of the Institute.

- ***Research at the BHI is supported by competitive research funding*** sourced from local, national and international funding bodies. The breakdown of HMR grant funding received to support research activity at the BHI in 2019 is shown in Figure 5. A little over a third of the funding support was received as grants from the federal government funding agencies (ARC, NHMRC, MRFF). The remainder is sourced from a plurality of sources, primarily philanthropic organisations (64%) and non-federal government funding (26%). Over the last five years, the quanta of research funding remained steady, around \$14,500,000, but the contribution of NHMRC funding dropped from just under 60% of total funding in 2015 to 34% in 2019 (Figure 6). This is in line with the noted fall in federal HMR funding attracted by South Australia. The shortfall in federal funding has been made up with competitively awarded philanthropic grants.

In total, BHI researchers were investigators on 21 NHMRC grants in 2019, with an average value of just under \$230,000/annum, and 72 grants from non-government sources, with an average value of \$91,500/annum. Increasing the research funding contribution from philanthropic sources has enabled research activity to continue but does increase the time research leaders spend applying for competitive funding and reduces research staff security, as philanthropic grants are smaller and often of limited duration.

- ***The BHI fosters the translation of health and medical research*** into health reforms, policy development, treatments, clinical and therapeutic regulation, public health implementation and companies. The institute has acted as an incubator for many translational discoveries and continues to do so. Examples of these include:
 - Renal transplant unit (now at the RAH)
 - The Robinson Research Institute (now at University of Adelaide)
 - The Coronary Angiogram Database of South Australia (CADOSA) (now a statewide clinical quality register)
 - BiomeBank (now in the Thebarton Innovation Precinct)
 - Chitogel Ltd. (Wellington, NZ)
 - Zeroscar Ltd (Adelaide, Australia)

⁶ McKeon, p. 75 and Recommendation 4.b.

- Australian Safety and Efficacy Register of New Interventional Procedures–Surgical, collaboratively run with the Royal Australasian College of Surgeons to assess innovative health care technology
- The Australian and New Zealand Audit of Surgical Mortality (ANZASM), which collects all surgical deaths within Australia in association with the Royal Australasian College of Surgeons and has provided research opportunities for many young surgeons undertaking higher degrees.
- AmbiGen falls prevention technology

Case studies discussing the role of BHI in incubating current translational projects can be found in Figure 7. Key to these narratives is the importance of the collocation of broad range of skills and infrastructure so discovery can be tested in pre-clinical models (including animal facilities) and clinical trials within the one organisation.

- **Researchers at the BHI are highly collaborative** and this activity serves the BHI through access to infrastructure, expertise, fund-raising and publications. All research groups at the BHI in 2019 reported active research collaborations.⁷ The BHI is well connected, claiming:
 - 128 SA-based collaborators with researchers located in the key HMR organisations of the State (excluding collaborations within the BHI, TQEH precinct) (Figure 8),
 - 54 national collaborators;
 - Internationally based collaborators in 23 countries (Figure 9).

Several BHI researchers hold adjunct positions within other HMR organisations to facilitate access to infrastructure and technology.

Collaboration is integral to how researchers at the BHI approach research, as these two example show:

- *In response to the recent COVID-19 pandemic, BHI researcher Dr Branka Gubor-Bauk, pulled together a team of South Australian researchers to undertake a program of COVID-19 research (COVID-SA). Branka's approach started with her reaching out to 2 South Australian researchers working in relevant fields to gauge interest; only one of these researchers was listed as an active, existing collaborator.⁸ This small group consulted more widely (14 potential collaborators via Zoom) before forming a new collaboration between 5 researchers/clinicians in 5 HMR organisations. The group have appointed a steering committee, adding 4 researchers and 2 HMR organisations to the coalition. This process took between 3 and 4 weeks to achieve.*
- *The CRE in Frailty and Healthy Aging, led by Prof. Renuka Visvanathan (TQEH), brings together a team of CIs from the University of Adelaide, Flinders University, University of South Australia and Torrens University. Through Prof. Visvanathan the CRE is linked to ROSA at SAHMRI and the CRE in Translating Nutritional Science to Good Health based at the Royal Adelaide Hospital and the University of Adelaide. The centre embraces a multidisciplinary approach to clinical research, with collaborations in Computer Science, Architecture and Mathematics.⁹*

There is a willingness from South Australian HMR researchers and clinicians to work together and form teams, as exemplified by this experience of the BHI.

⁷ 2019 BHI Research Report, https://www.basilhetzelinstitute.com.au/wp-content/uploads/2020/03/BHI_Research_Report_2019.pdf

⁸ Ibid.

⁹ <https://www.basilhetzelinstitute.com.au/research/research-theme/ageing/centre-research-excellence-frailty-healthy-ageing/>

Dynamic response to health challenges often requires collaboration between organisations. This can be made difficult by bureaucratic obstructions, despite the research staff's willingness to participate or the importance of the problem. The difficulty in gaining multiple approvals (including ethics, governance, contracts and funding agreements for multicentred projects) can be frustrating and slow. Surely, a single ethics and governance assessment should be all that is required for a program of research to be undertaken within SA. Like others, researchers at the BHI have experienced issues when collaboration between organisations is required. The following narratives illustrate the impact of such issues.

- *Associate Professor Joanne Young is the principal investigator of a statewide clinical research project to explore the reasons for the alarming increase in young-onset bowel cancer in our community, as well as to seek genetic mutations which families may unknowingly carry. To undertake interviews of patients and examination of clinical and family histories, ethics and governance approvals must be obtained from multiple jurisdictions across the state and funding must be transferred between institutions. When two local jurisdictions did not agree on the wording of a funding agreement delays of over 12 months were incurred and resolution included third-party arbitration.*
- *When adopting a broader definition of HMR, there is recognition that many researchers of the BHI need to seek ethics approval for the use of animals experimentally. This has, in some instances, proved difficult. The BHI has access to the animal facility at TQEH; these facilities coupled with ease of access to the facility by staff from the BHI represent a major advantage to researchers at the precinct. As reported by Prof. Eric Gowans, many of these advantages can be eroded by the weight of regulatory issues associated with approval by the animal ethics committee (AEC) of the relevant institutes to enable the work to commence. Throughout the period that the Virology laboratory has been established at the BHI (10 years) it has been necessary to gain ethics approval from the University of Adelaide AEC (as staff in the laboratory have University appointments) and from SA Pathology (since the animal facility is owned by SA Health). This unnecessary duplication, which may now be resolved, resulted in many hours of extra work for investigators and often in differences in conditions and animal numbers that could be used in an experiment. Few if any of our national and international competitors have to undergo such rigorous evaluation which are, simply put, the result of a power struggle. Even now, although there are reciprocal arrangements in place, there is not a whole of sector approach to animal ethics and multiple ethics may still need to be sought. Delays in animal ethics for one project, of some 3 years, have resulted in the Virology laboratory organising experiments to examine the efficacy of an HCV vaccine in the animal facilities of our collaborator in China. While there is general agreement that the University AEC is an integral component in the process, perhaps some consideration of risk versus benefit might be considered in future, and some consideration given to the catastrophic effect on staff moral and motivation that results from the intransigence of the AEC. Moreover, the delays have meant that research funds were expended unnecessarily to ensure that staff members were retained. We and others have found the processes leading to approval by the relevant AEC are often cumbersome and streamlining of these processes would lead to increased productivity.*
- *Data collected by health services and governments in the course of healthcare provision is an invaluable resource and has been used by Prof. Renuka Visvanathan in the course of her research into frailty and healthy aging.¹⁰ Prof. Visvanathan's research has informed policy – it*

¹⁰ For example: Visvanathan R et. al. Prolonged wait time prior to entry to home care packages increases the risk of mortality and transition to permanent residential aged care services; findings from the registry of older south Australians (ROSA). *J Nutr Health and Aging* 2019; 23: 271-280 (This research was cited in the Royal Aged Care Commission Interim Report released 31st of October 2019 where one of the key recommendations was “ to provide more Home Care Packages to reduce the waiting list for higher level care at home”. The Commonwealth has also responded by releasing additional

*was cited in the Royal Aged Care Commission Interim Report and has responded to the need for evidence identified by the 2018 report of the General Practise and Primary Care Clinical Committee: Phase 2 of the Medicare Benefits Schedule review taskforce. From this example it is clear that **access to medical records can be a powerful driver of research.***

The electronic health record system (Sunrise Medical Records system) rolled out in the Central Adelaide Local Health Network/SA Health, is a rich source of clinical data that could be used by South Australia researchers to achieve outcomes like those reported by Prof. Visvanathan, outcomes that influence patient care, health service delivery and government policy. The records, however, remain a largely untapped resource. Whilst it is hard for SA Health researchers to tap into this resource, it is even harder for non-SA Health employed researchers, such as those employed by the universities and located at the BHI. South Australian researchers could benefit significantly from being able to draw out information for linkage analysis and real time analytics. It remains a challenge for researchers to identify pathways to gain access to information with the system, yet the benefits of appropriate access would seem to be obvious. There are companies that promote products that capitalize on Fast Healthcare Interoperability Resources (FHIR) and support the exchange of electronic health records. The records represent unexplored opportunities that, if ethical access for research is facilitated, could value add to the investment in the Sunrise Medical Records system and provide South Australia with a research advantage. We would argue that access should be facilitated.

Delays and barriers of these types are not uncommon, they critically affect the flow of the project, occupy large swathes of investigator time, and as such, are counterproductive. These barriers do not just cause unnecessary delays, but they can have more significant impacts on research staffing and the HMR mission of the state. Building productive and sustainable collaborative relationships between stakeholders is challenging but the rewards can be extraordinary. Many nascent collaborations, or even experiments, don't make it past the start line because of the seemingly insurmountable nature of bureaucratic barriers, losing the state a quanta of research wins that it can ill-afford to lose. Given the size of the HMR sector in South Australia we would welcome the development of a whole of sector approach to research governance

South Australian Governments and Government Departments have been successful in creating capital works (eg SAHMRI, new Royal Adelaide Hospital, Lot 14) but have been less successful in establishing agile, dynamic and relevant structures that encourage a culture of collaboration and translation within the HMR community, or acted to minimise the duplication and bureaucracy to facilitate collaboration. There is no whole of government approach to HMR industries, as pointed out in the Issues paper, with at least 3 Departments (DHW, DIS, DTI) claiming some role in the sector. Thus, initiatives within one sector of Government are often difficult to link together with another, for reasons of timing or staff appointments. An approach that is more outcome focussed rather than process driven may help, as would approaches that prioritise well-articulated pathways for discovery to translation research.

From the perspective of this research community, the government is not engaged in a meaningful way with the research agendas of the State, has not invested in developing the leadership, knowledge, expertise or logistics needed to support the HMR industry sector in the state. Furthermore, historically the government has not used its influence to enforce research outcomes and success as a priority for the leaders of the local health networks or SA Health. While it is hoped

Level 3 and 4 packages) and Visvanathan R et. al. Utilisation of general practice health assessments around an aged care assessment is associated with lower mortality risk in older Australians. In Press 2020 Age and Ageing. (This research demonstrated general practice Medical Benefit Schedule claims for a health assessment within six months of an Aged Care Eligibility Assessment (ACAT) in HCP aged 75 years and above was associated with a 5% lower mortality risk.)

this is changing, the damage of ignoring the importance of research within the health system is considerable.

- ***Stakeholders are an important component of the BHI's functions.*** As a precursor to SAHMRI, BHI is an amalgam of researchers from UoA, UniSA and CALHN. Staffs, infrastructure, funding and governance functions are contributed by our stakeholders – in fact, our stakeholders provide a portfolio of support without which the BHI would be unable to undertake its research mission.
 - ***Universities*** represent critical stakeholders in BHI's success. The BHI faculty includes a number of research leaders employed by the universities, as continuing staff, in co-funding arrangements with CALHN (Clinical Academics) or as grant-funded research staff. Universities provide access to student capital – a critical asset that contributes to the research performance and outputs of the Institute. Accordingly, the Universities contribute to the operational activity by providing financial and in-kind support and research governance (for example, the transfer of research support funds through standardised research contracts and MOUs), as well as sharing their expertise in areas such as Occupational Health and Safety. As an example of University support, the University of Adelaide supports two animal technicians in the CALHN animal facility, salary for the BHI Facility Manager, resources for the maintenance of equipment and critical infrastructure, and contributes financially for the space occupied by University researchers through a payment to CALHN (>\$800,000 per annum).
 - ***CALHN*** contributes staff and staff time to the research programs, supports the maintenance of the physical structure of the BHI, provides research governance services and one staff to the administration of the Institute. In addition, access to the clinical programs at the TQEH is a critical enabler of the research undertaken at the Institute.
 - The ***THRF*** is an important supporter of the BHI. The relationship between the BHI and the THRF (previous the research foundation of TQEH) is long and enduring, and the foundation supports research programs, students, infrastructure and staff at the Institute. In 2019 THRF employed a Scientific Director of Research for the BHI to support the Director and the research community in their research activities.

This model of staffing, funding and support would not necessarily be one that would be obvious but it is a model that has endured as a successful, sustainable, collegial and collaborative approach to HMR that has endured for many years.

- ***Surprisingly, the BHI is not running at capacity.*** The barriers to growth can be found in the attrition in the clinical academic workforce, who provide the clinical leadership at the Institute and drive the research agenda, the recognised difficulty in attracting funding, including MRFF funding, to South Australia, and the inconsistent HMR policy directions from the South Australian Government and SA Health.

Recommendations:

In response to the inquiry's issues paper, we would make the following observations and recommendations:

The BHI is an example of excellence in HMR research. It capitalises on the colocation of dedicated research space with clinical services to pursue a program of discovery and translation that benefits South Australia and beyond.

We would propose the BHI as a MODEL for HMR research in the South Australia health and medical system.

The attributes of the BHI that leads us to this recommendation are:

- A research-inclusive culture that is embraced by the clinical staff of the BHI, TQEH precinct.
- BHI has acted as an incubator for the translation of discovery into practise/commercial endeavour. The BHI merges state-of-the-art, laboratory-based basic research motivated by clinical need, pre-clinical research, clinical trials *and* the implementation of evidence-based clinical solutions.
- The program is supported by a complex workforce, comprising researchers from diverse backgrounds who come together to work on clinical problems and areas of need in South Australia.
- The researchers are highly collaborative, with a strong collegial ethic within the BHI, across SA, nationally and internationally.
- The combination of a complex workforce and a highly collaborative approach makes the BHI nimble and able to muster resources in response to emerging health-related issues quickly and effectively (e.g. COVID-19 response at the BHI).
- The BHI is self-governing, with a formal committee structure and supported by regular activity reporting.
- The BHI is supported by a range of stakeholders who provide support, knowledge, expertise and infrastructure to enable to the institute's mission.
- BHI has a can-do culture and a willingness and the perseverance to work proactively to overcome barriers to HMR.
- The colocation of research organisations within the same research precinct fosters cross-disciplinary and cross-organisational approaches to problems.

The BHI is successful and shows that this model can work to promote clinical translation of clinical research in South Australia. The BHI can be grown with minimal additional resourcing – the site is not at capacity – and can be a model for other translational research endeavours in South Australia

Figure 1

The Australian Research Council (ARC Medical Research Policy Version 2017.1) has developed a comprehensive definition of health and medical research, which may be more appropriate for the development of measurement frameworks in South Australia. The following proposed definition of health and medical research is adapted from this document:

Medical and health research is research that aims to understand the causes, treatment and/or prevention of human diseases and/or the maintenance of human health...[and includes];

- a) Research with direct medical and/or human health aims or purpose, including research on the understanding, aetiology, diagnosis, monitoring, management or treatment of physical or mental disease or other medical and/or human health conditions; or*
- b) Research involving the use or development of animal models of medical and/or health conditions, or the use of animals for the development or testing of diagnostic procedures or therapeutic goods (including devices), for the purpose of better understanding human medical and/or health conditions and developing treatments for medical and/or health conditions; or*
- c) Interventional research in humans, particularly clinical or pre-clinical trials of diagnostic procedures and therapeutic goods (including devices), or research aiming to modify the medical and/or human health condition of behaviour of the human participants; or*
- d) The use or development of equipment, facilities, tools, games, devices, smart phone applications or other items to better understand, diagnose, monitor, manage or treat medical and/or human health conditions.*

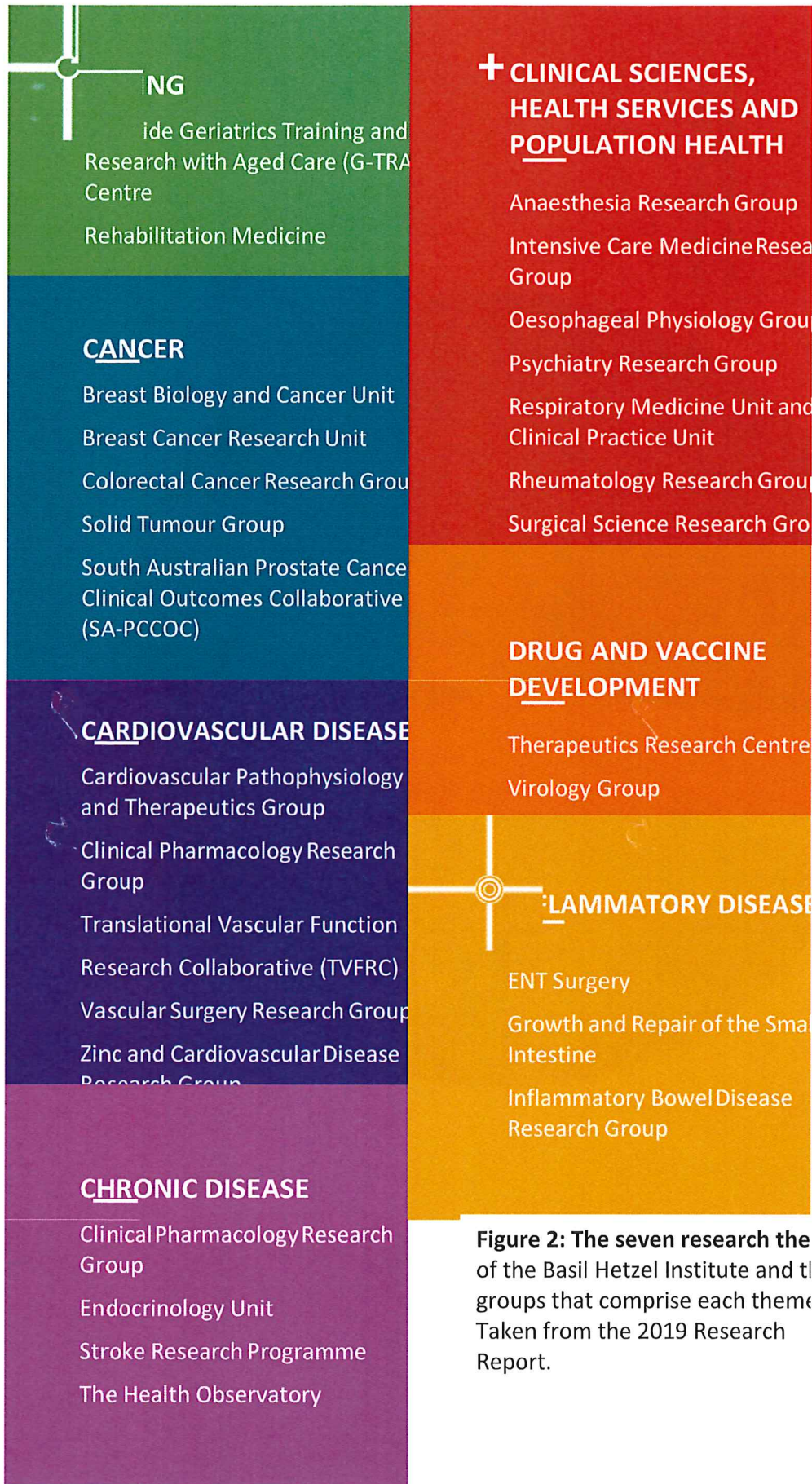


Figure 2: The seven research themes of the Basil Hetzel Institute and the research groups that comprise each theme. Taken from the 2019 Research Report.

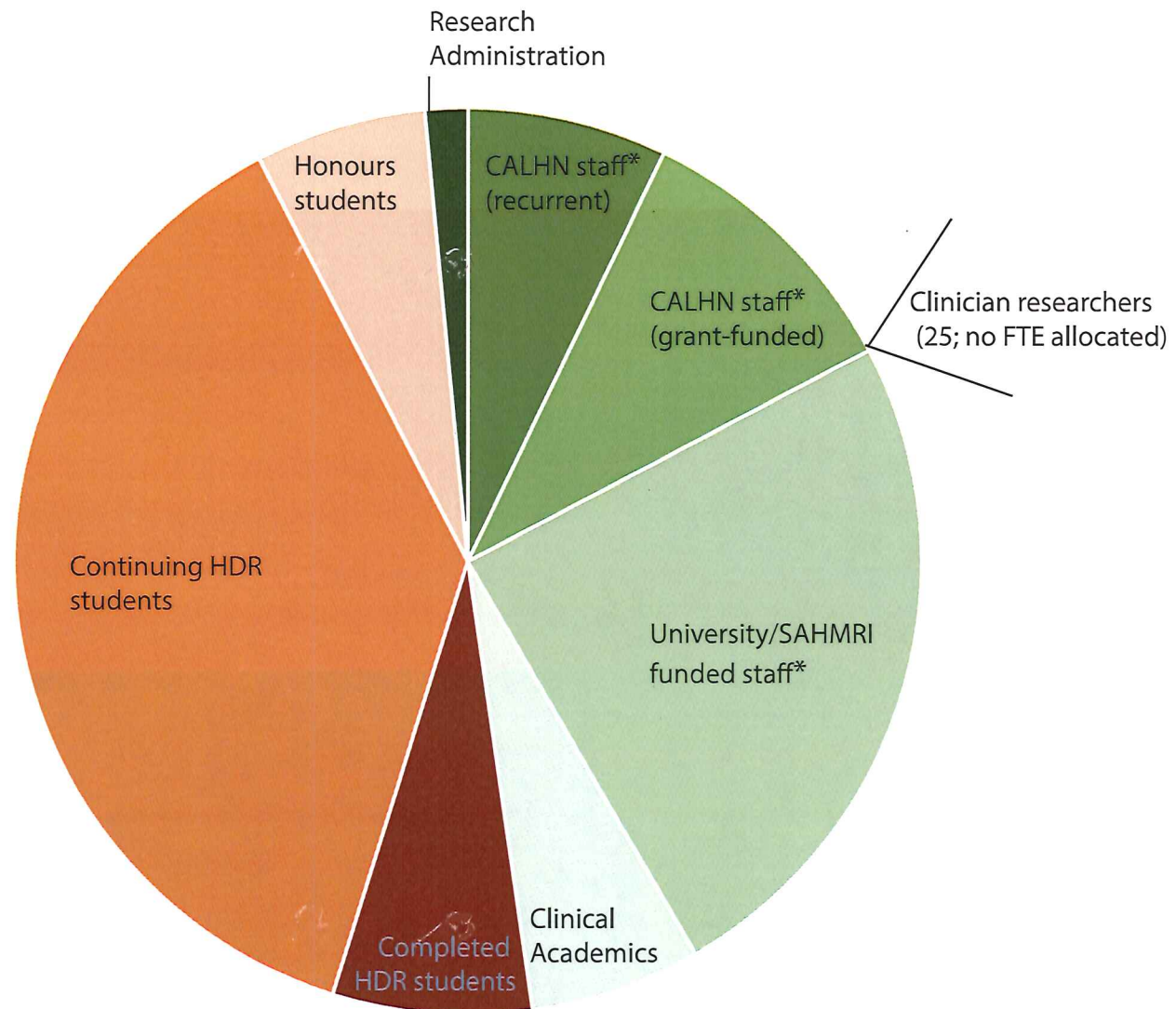


Figure 3: Staff and student profile at the Basil Hetzel Institute for 2018/2019 financial year, in full-time equivalents/enrolments. In the 2019 Research Report groups reported approximately 250 staffs involved in the research effort in some capacity at The Queen Elizabeth Hospital precinct. *non-medical staff.

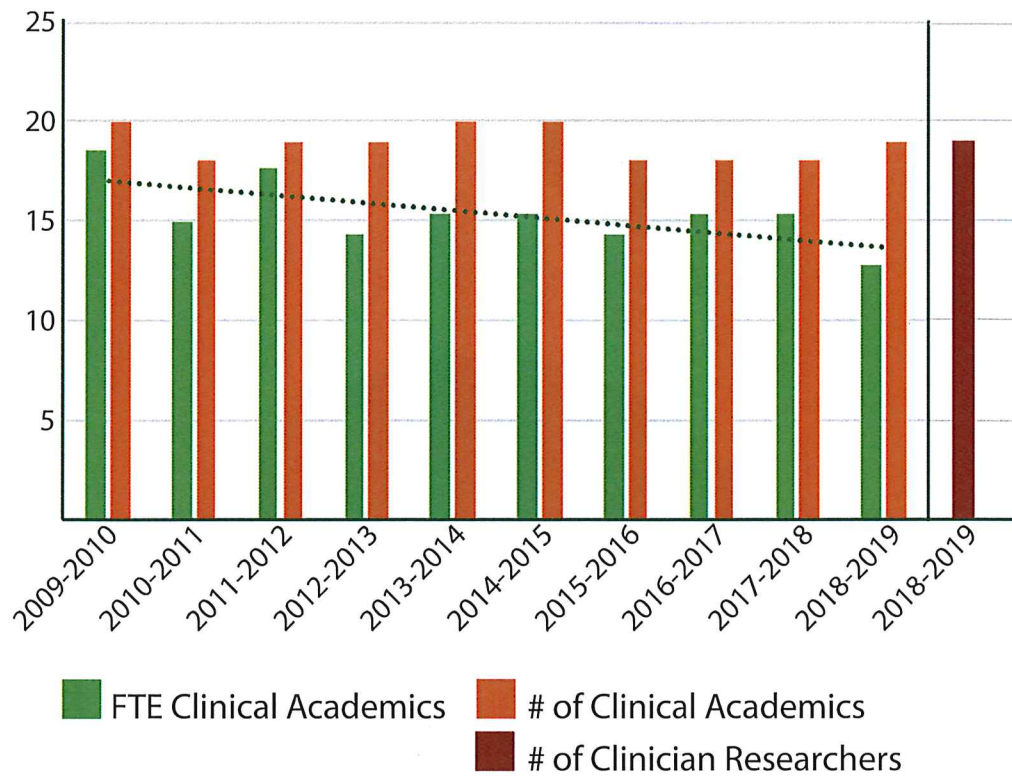


Figure 4. The clinical Academic workforce working at The Queen Elizabeth Hospital between 2009-2010 and now, shown as full-time equivalents and number of staff. The trendline tracks the FTE at the site over time. Numbers have been compiled from the Departments of Medicine, Surgery and Psychiatry. Source: the BHI Annual Audit. Also shown is the number of clinicians active in the research programs at the BHI. In total, the BHI hosted 38 active clinician researchers in The Queen Elizabeth Hospital precinct in the 2018-2019 financial year.

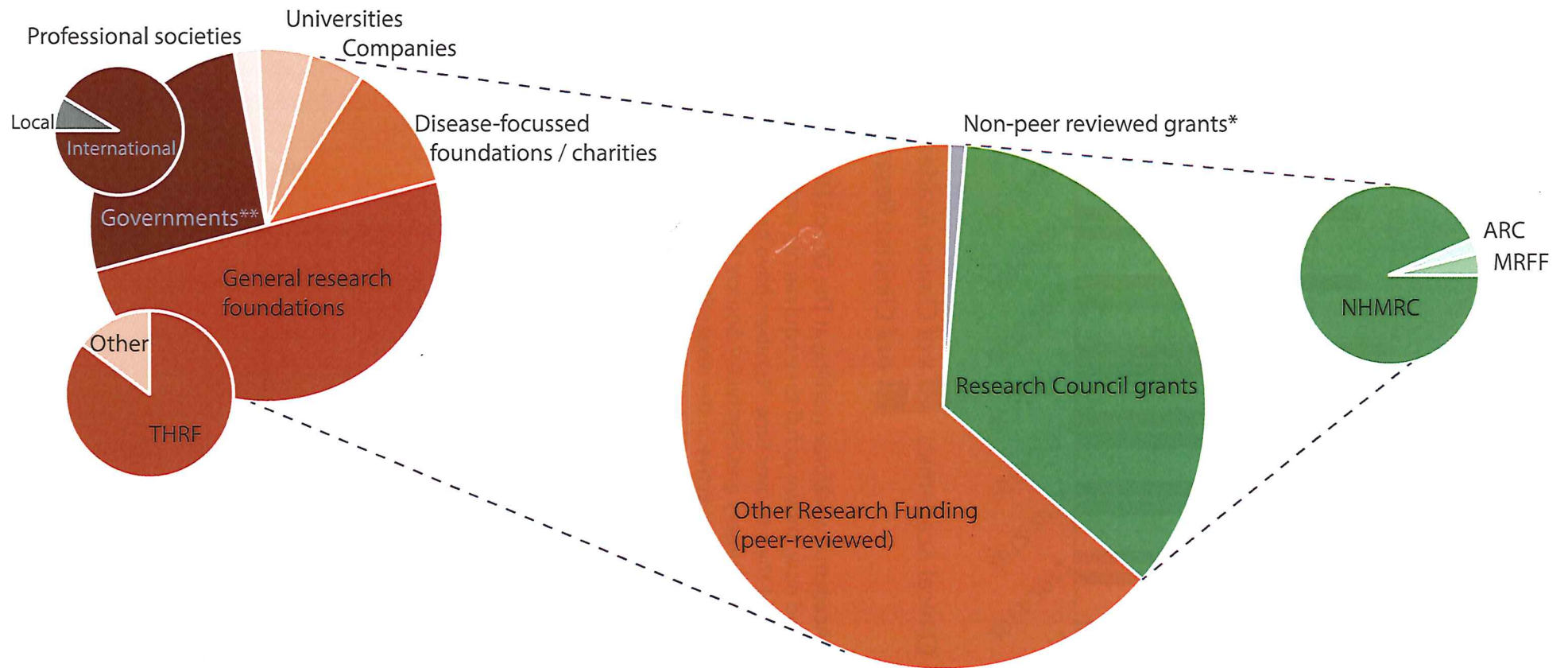


Figure 5: A breakdown of funding support for research conducted at the Basil Hetzel Institute in 2019 (Source: The Research Report, 2019). The total pool of funding support was \$14,336,186. (THRF: The Hospital Research Foundation). * Excludes externally funded clinical trials. **Non-federal Government funding sourced from local government and international governments.

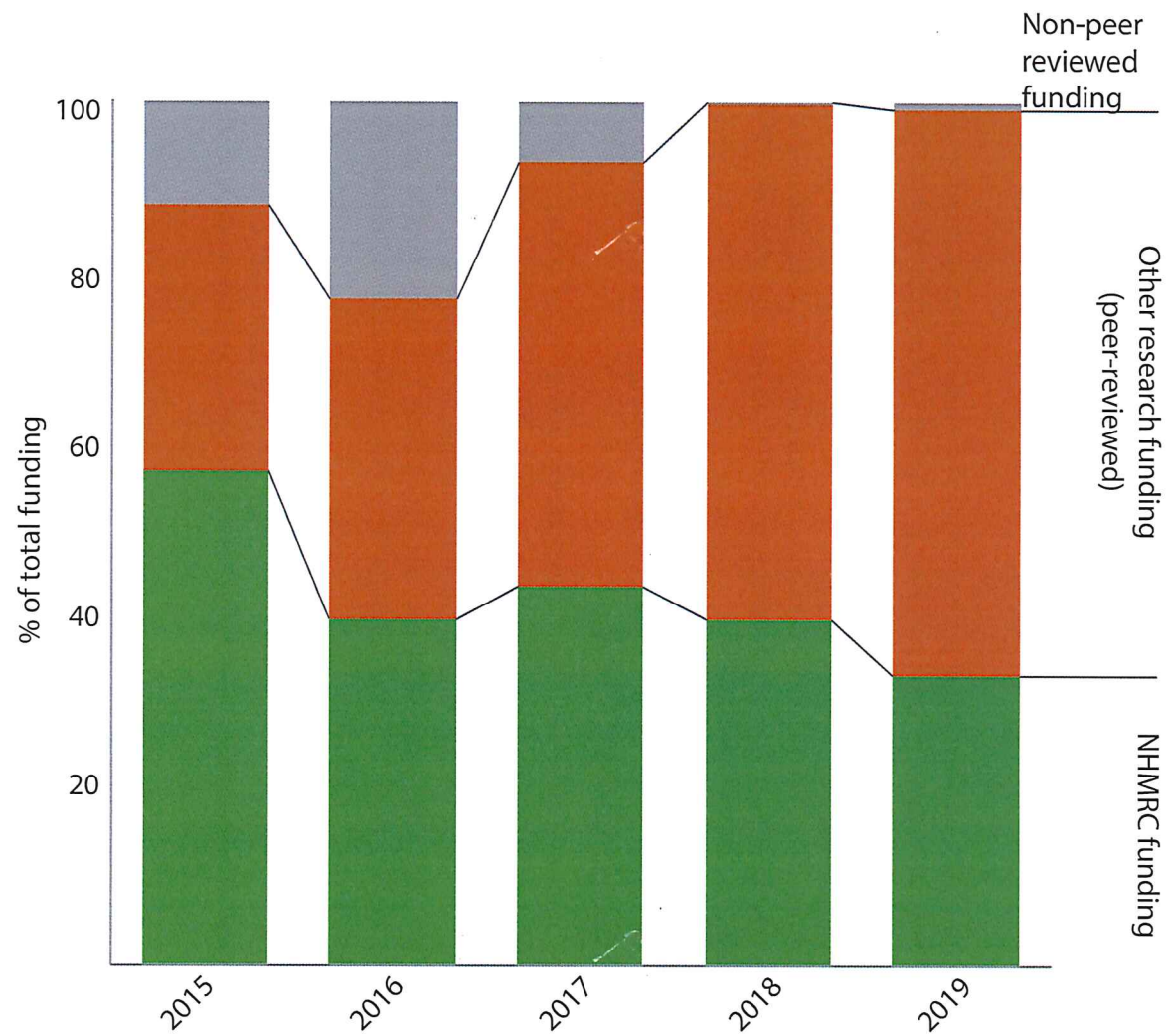


Figure 6: Percentages of funding awarded, by category, over the last 5 years at the Basil Hetzel Institute (Source, 2015-2019 Research Reports). While the quanta of funding has remained relatively stable (\$14,560,000 +/- \$754,000), the institute has become more reliant on non-NHMRC funding.

Figure 7.

Translation at work at TQEH and the BHI – case studies

The Coronary Slow Flow Phenomenon

Chest pain arising from the heart (called angina) is typically due to a narrowing in the large coronary arteries. This is diagnosed by introducing dye into the coronary arteries and taking an x-ray movie (a coronary angiogram). If narrowings are not observed, the patient is usually told that the chest pain is not cardiac and discharged.

TQEH clinicians were intrigued by these angina patients, and detected that although the arteries were not narrow, the movement of the dye through the arteries was slow – ‘the Coronary Slow Flow Phenomenon’.

Whereas most clinicians considered this phenomenon as an ‘angiographic curiosity’, TQEH clinicians began systematically investigating these patients. The resulting clinical and laboratory-based research demonstrated

- a. The clinical features of this disorder,
- b. Abnormalities in the coronary microvessels, which explained the cause of the angina,
- c. An effective treatment for the disabling recurrent angina experienced by these patients – Mibefradil.

Clinicians at the BHI, TQEH embrace research in their clinical practise – in this example this resulted in the discovery of *a new disorder* and *a novel effective therapy*, and a *patent* (in conjunction with TQEH Research Foundation and the Hospital).

This research is ongoing. Mibefradil was subsequently discontinued because of drug interactions leaving these patients without an effective treatment. BHI, TQEH researchers are undertaking another laboratory-based study to identify the properties of Mibefradil that were beneficial to patients with Coronary Slow Flow Phenomenon and to identify alternative therapies. Using human microscopic blood vessels from discarded surgical tissue, they identified key drug targets on the blood vessels where mibefradil was working. This has led to further clinical trials examining potential treatments for the Coronary Slow Flow Phenomenon.

This case study demonstrates how the BHI fosters collaboration, by providing an enabling culture that prioritises research, laboratory facilities to support the investigation of clinical observations and clinical trial structures that can translate clinical research into clinical practise, and all for the benefit of the patient.

Figure 7 cont.

Chitogel

Up to one third of all people who undergo sinus surgery experience blocked nasal passages afterwards due to scarring and this requires further surgery to correct. This statistic underscores a clear clinical need, recognized by the ENT surgeons at the BHI.

Work carried out at the BHI/TQEH precinct has been instrumental in bringing a new surgical hydrogel, with enhanced anti-inflammatory properties, Chitogel, into use. The gel limits scarring and improves wound healing after sinus surgery, reducing the need for revision surgery and thereby lowering associated health care costs. The BHI provided a framework for the ENT surgery team, led by Prof. PJ Wormald, to work on the development of Chitogel from invention, through preclinical and clinical testing into a product formulation. Chitogel has been approved by the FDA and MEDSAFE and has been released onto the US and NZ market. EMA and TGA is approval imminent. The economic impact is enormous with a global reach, the establishment of 2 start-up companies (Chitogel Ltd, located in Wellington (NZ) and Zeroscar Ltd, located in Adelaide (SA), and investment of >\$10 million from venture capital funds to establish an ISO accredited manufacturing plant and securing a distribution agreement with the medical device giant Medtronic.

The BHI's translational research program, which supports and integrates basic, preclinical and clinical research, and teaching activities, and with a focus on addressing urgent clinical needs, was instrumental to the success of this project.

SAYO

SAYO (South Australian Young Onset) colorectal polyp and cancer study is a multidisciplinary registry which seeks to find the reasons for colorectal and appendix cancer occurring in individuals under 55 years in SA. During the course of this study, cancer predisposition mutations have been identified in families who are unknowingly carry these changes as incidental findings. The results are shared with the adult genetics unit of SA at RAH and families are then able to undergo predictive genetic testing and screening for prevention of cancer. In addition, SAYO runs a support group for patients with young-onset bowel and appendix cancer with social events and Q and A sessions with doctors and nurses who specialise in the is field. In this example a research project undertaken at the BHI interacts with, and provides support for, state clinical services and patients in SA

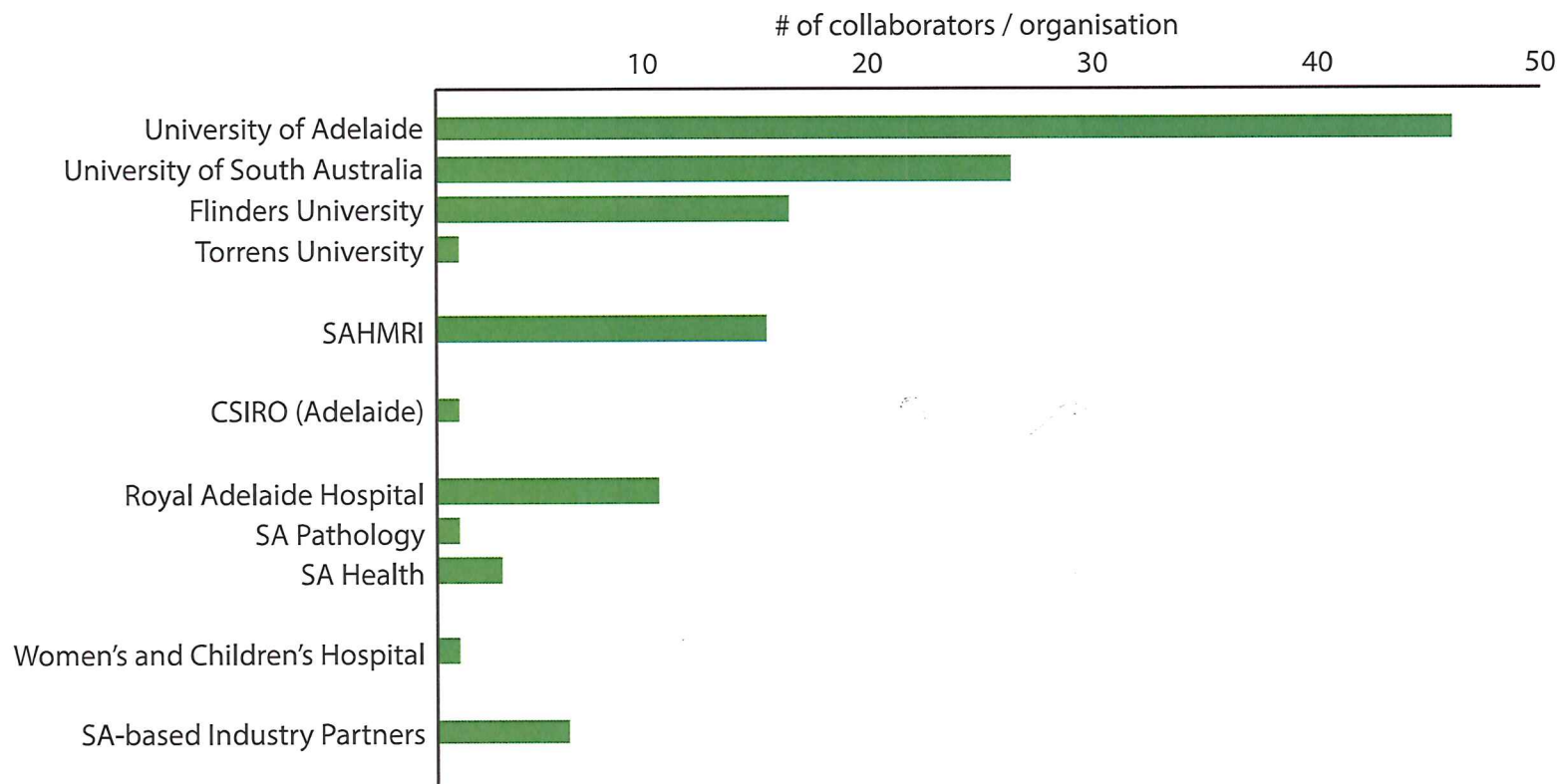
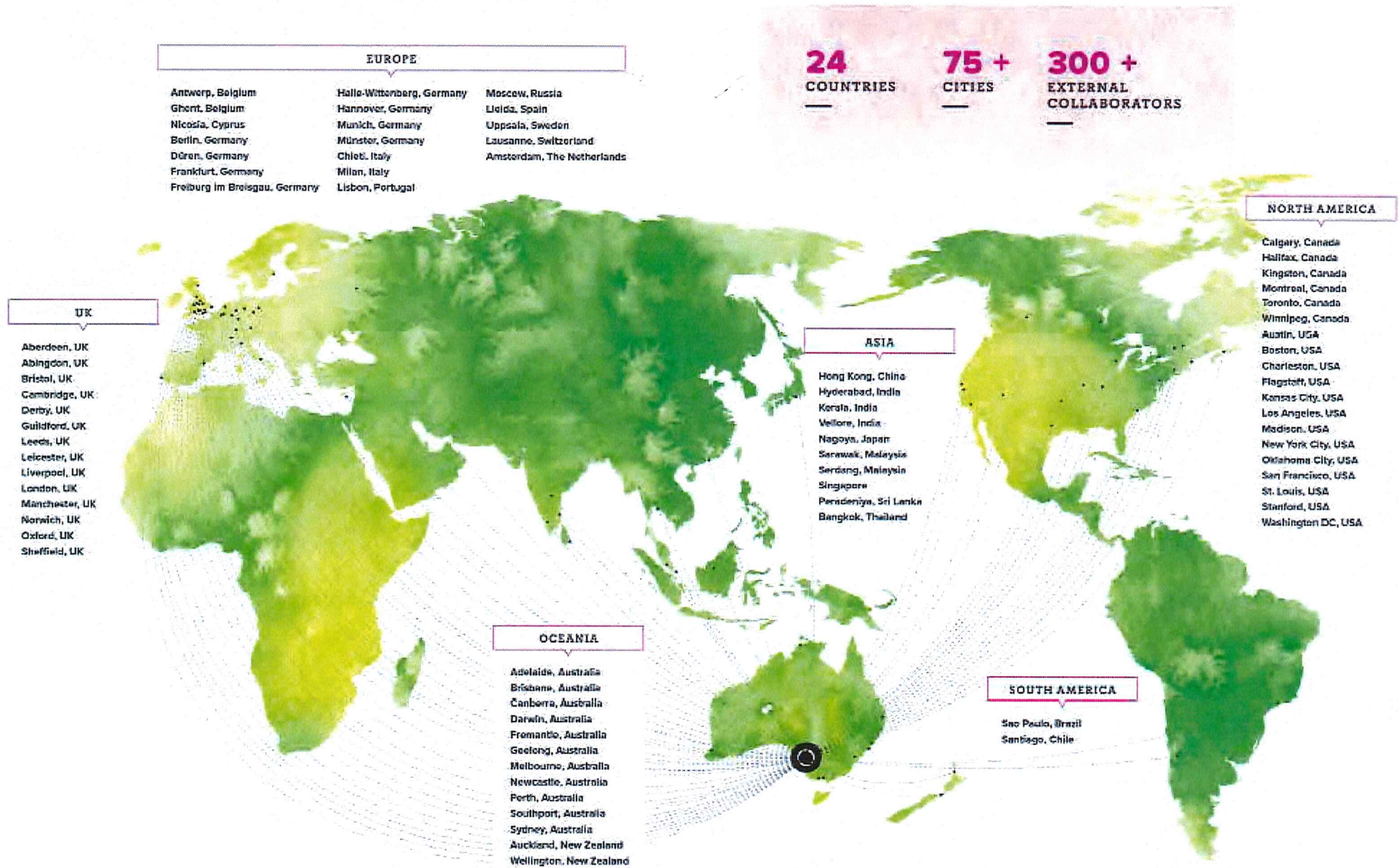


Figure 8. The number of collaborations identified by BHI researchers in the key participants in the Health and Medical Industry of South Australia, grouped as presented in Table 2.1 of the Issues Paper. In all, 128 non-BHI, TQEH, SA-based collaborators were identified.

Figure 9
BHI NATIONAL AND INTERNATIONAL COLLABORATORS 2019



Figure