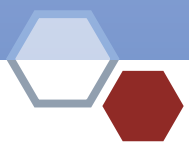
Australian Government
Department of Health

Medical Research Future Fund

Genomics Health Futures Mission

Design, delivery and research priorities: summary of Scientific Strategy Committee recommendations



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1 Design and delivery of the Genomics Health Futures Mission

1.1 Program delivery

Issue

The Genomics Health Futures Mission (GHFM) is building on an established, mature clinical and research genomic landscape, and is thus a large and complex program with many interrelationships. The GHFM's objectives will be undermined if individual GHFM projects are structured as disparate, unconnected programs of work.

Recommendation

The GHFM must be delivered with a unified, coordinated approach and national network, with clarity of vision and transparency in process. It must be overseen and managed with good governance, leveraging core capabilities across funded projects.

Rationale

GHFM coordination and core capabilities will improve efficiency and consistency of delivery across GHFM projects, reduce duplication of investment, and support interproject collaboration.

These activities include:

- a research governance framework providing operational oversight, project and risk management, and strategic and community guidance
- a national coordination network of research managers, genetic counsellors and project officers in each state and territory to facilitate local research implementation and investigator support
- media and communication services to promote awareness and public interest in GHFM projects
- human research ethics and governance management and expertise

- a suite of established participant materials and resources for consent, education and information
- a portfolio of patient survey and evaluation tools for study-specific refinement
- a participant portal and dynamic consent platform to support informed consent and engagement with research participants
- established gene lists, minimum clinical datasets and data management tools to facilitate genomic research and project establishment
- expertise in implementation science, health economics, policy, health equity, social science, ethics and law
- collaboration with patients, support groups and advocates
- engagement with Australian Government and state and territory government departments of health and other government agencies
- engagement with global genomic initiatives to build on our established international reputation in genomics in health
- coordinated data management across GHFM projects to drive data consistency, completeness, and quality — making these datasets available for secondary research will be a key legacy of the GHFM

1.2 Incubator projects

Issue

A funding mechanism is needed for health genomic research priority areas considered strategically important for the GHFM, but that are either too immature for large-scale funding, or risk a fragmented collection of submissions to a competitive call.

Recommendation

- The areas for incubator funding will be recommended by the Scientific Strategy Committee. Incubator project leads will be identified/sought by nomination from the research community, and they will be tasked with forming a national working group of experts in the area.
- Incubator projects will be time limited and will receive funding for international landscape analyses; review of local/national expertise and activity; coordination; convening meetings of leaders in the field; and piloting research approaches.

Rationale

The aim of the GHFM incubator project funding scheme is to fund emerging research priorities with potential for future genomics in health: to build Australian research capacity, establish national networks of leaders to drive advancement of the field, and inform larger-scale funding plans.

Over the term of funding, incubator projects will be expected to report on their findings; pilot potential approaches; recommend structures for further investment; and identify mechanisms for enhancing, maturing and advancing Australian genomic research in the area, including opportunities to leverage additional funding from partnership with industry, state government, philanthropy and other research funding sources.

1.3 Involve Australia

Issue

There is a demonstrable and urgent need to establish effective public involvement in Australian research endeavours. The advances in genomic technology in research and clinical practice, and the associated ethical, legal and social implications (ELSI) of this, need to be managed with the public in a systemic and sustainable way if the outcomes of the GHFM are to be transformative and embedded into Australian health care.

Recommendation

- Development and evaluation of a successful public involvement strategy in the GHFM would be an important and lasting legacy of the program.
- Based on the National Institute for Health Research UK's INVOLVE initiative, Involve Australia will develop and implement policies for patient, public and consumer involvement to guide and enrich GHFM funded projects.
- Involve Australia should be supported with dedicated personnel as part of the core capabilities and coordination of the GHFM. It should be resourced to convene meetings of national and international experts, develop resources and conduct training.

Rationale

The importance of the consumer voice in the strategy, design and conduct of research has become increasingly reported internationally, and is recognised as adding significant value to research outcomes. The shift of cultural norms to increased autonomy in health care, accessibility of information and choice requires research to move from enlisting human subjects to involving research participants. Engaging, involving and informing the public — all health care consumers, including patients, carers and future patients — supports the development of social licence and mitigates the risk of public backlash. Effective public engagement enriches research by improving participant retention and experience, refining research questions and application, and allowing research to be informed by the end users: health care consumers.

1.4 Industry engagement

Issue

While at the forefront of genomics research, Australia remains a maturing and evolving market, and industry players across the genomics value chain are left facing a number of barriers that hinder the maturation of genomic research.

Recommendation

- Industry engagement and partnerships to enhance the translation of gene-related therapies into human clinical trials should be considered as an area of focus for funding.
- Establishing an industry advisory board will help inform GHFM strategy and direction with industry engagement, and funded activity will be pursued through competitive, co-funded industry partnership grants.

Rationale

Genomics has immense potential for Australian health care. Industry engagement will be an important element of the translation of GHFM outcomes to benefit Australians, and in the stimulation of an end-to-end genomics industry.

1.5 International engagement

Issue

A number of global initiatives are currently working towards standardisation and tools to support the integration of genomics into health care.

Recommendation

The GHFM should support a coordinated and strategic approach to fostering international partnerships and engaging with global genomics activity, both centrally/across the GHFM, and within each funded project.

Rationale

Australia needs to participate in shaping global genomic health strategy and standards to ensure these are fit for purpose in the local setting. Further, Australia is considered an international leader in nationwide health genomics endeavours. Learning from other national genomics initiatives — and sharing our expertise — will cultivate diplomatic relationships and stimulate commercial opportunities.

1.6 Capacity building

Issue

Common approaches and systems across GHFM-funded research are needed to build necessary capacity and capability to achieve the GHFM's objectives.

Recommendation

- The responsibility and strategic focus of the GHFM is on research capabilities and systems to support GHFM projects, but not the development and investment in broader national clinical infrastructure.
- Funded projects are to be encouraged to adopt common approaches, to develop a legacy dataset for future research use, ensure the application of international best practice to human cohort studies, and to permit delivery of evaluation and outcomes across projects.

Rationale

At least 14 countries have committed substantial government investment towards national research initiatives to drive the implementation of genomic medicine into health care. The overarching priority of these initiatives has been in developing infrastructure, which includes national frameworks, standards, and centres for testing and analysis, as well as platforms for collection, storage and sharing of data. However, the Scientific Strategy Committee notes that the development and investment in broader national clinical infrastructure is not the remit nor a strategic focus of the GHFM.

2 Genomics Health Futures Mission research priorities

2.1 Rare disease

Issue

One in 12 Australians have a rare disease,[1] with an estimated 80% having a monogenic or oligogenic basis, yet only 30–40% of these people currently receive a diagnosis through genomic testing.

Recommendation

- That genomics projects on rare diseases are funded throughout the term of the GHFM.
- The GHFM rare disease program will engage in solving the unsolved rare disease cases, with the aim to increase the genomic diagnostic rate to 60–70% over the next 5 years and up to 90% over the next 10 years, and to provide that diagnosis in a timely way to enable the most appropriate clinical care.
- These diagnostic practices are to be implemented into standard clinical care nationally, with links into a functional genomics pipeline to identify therapeutic targets, develop novel therapies and facilitate clinical trials.
- The GHFM rare disease activity should be delivered through a Centre of Research Excellence (CRE)-like model for the multidisciplinary national networks, cohort development and data capture, supported by a centralised budget allocation to fund extended research on genomic sequencing, and further functional genomic studies.

Rationale

Rare disease genomic research has been a strategic pillar of most international genomic initiatives, supporting improvements in diagnostics, advancing understanding of disease mechanisms, and identifying means of intervention and therapy by enabling links into clinical trials.

1 Rare Voices Australia

2.2 Cancer

Issue

Australian research funding currently has a focus on rare cancers and childhood cancer, but common cancers have the greatest impact on the health system. There is a huge burden of disease not being met in early detection, identification of recurrence and targeting therapy.

Recommendation

- Cancer should remain a core priority of GHFM research activity, with funding throughout the term of the GHFM.
- Investment should be complementary to current cancer research programs in Australia. The GHFM cancer program should target cancers with a high burden of disease, particularly in improving screening, early detection and genetic risk of cancers, and biomarker discovery of therapeutic response and resistance, including longitudinal genomic studies of patients.

Rationale

Targeting common cancers will address the significant associated burden of disease and impact on the health system, and may improve the experiences and outcomes of people living with cancer.

2.3 Functional genomics

Issue

As clinical genomics becomes embedded in the Australian health care system, we are increasingly seeing variants in potentially novel disease genes, as well as large numbers of variants of unknown significance (VUS) in known genes. In both instances, there is an urgent and growing need to understand the ramifications of these variants on gene function and disease pathogenicity.

Recommendation

- The GHFM should support distinct yet interrelated domains of functional genomics, applying these methodologies to increase the efficacy of genomics to diagnostics, and to facilitate the development of experimental therapeutics.
- The Scientific Strategy Committee recommends that the area of functional genomics is supported with funding of a functional genomics network to stimulate national activity in novel and known gene modelling; and a competitive call for preferably disease-agnostic, high-throughput and scalable functional genomics platforms for diagnostic and therapeutic models.

Rationale

A research platform to solve genomic VUS from known disease is applicable to both rare diseases and cancers.

2.4 Pharmacogenomics

Issue

The impact of adverse drug reactions on health care is significant: 1.2 million Australians have experienced an adverse medication event in the past 6 months, and 650,000 of these presented to hospital, at an annual cost of $1.4 billion.

Recommendation

- The GHFM should bring together a network of experts in the field to evaluate the pharmacogenomics landscape nationally and internationally, including potential for international partnership (eg with the UK National Health Service), and inform the optimal approach for Australia's research investment.
- The GHFM should establish a national program where pharmacogenomic testing is used to select the best medicines and the best dose for each individual, to reduce preventable medication harm and improve quality of care for all Australians.

Rationale

While it is still an emerging field, research into pharmacogenomics is recognised as having considerable potential, both clinically and for reducing health system costs by reducing adverse events and drug toxicity. A rigorous implementation science research program is needed to develop a scalable approach to rolling out pharmacogenomics.

2.5 Aboriginal and/or Torres Strait Islander health

Issue

Any investment in Aboriginal and/or Torres Strait Islander health or medical research should be guided by a set of principles that are developed, considered and negotiated with Aboriginal and/or Torres Strait Islander people themselves. It remains the responsibility of the genomics community to preserve and protect Aboriginal and/or Torres Strait Islander interests and define the benefit of their work to people and their communities. No progress in Aboriginal and/or Torres Strait Islander genomics can be made without specific investment in and commitment to ensuring and enabling Aboriginal and/or Torres Strait Islander peoples' control and ownership over genomics research, sample curation, decision making over sample use and sharing, interpretation and Indigenous Data Sovereignty principles and practices.

Recommendation

The area of Aboriginal and/or Torres Strait Islander health should be supported with a funded consultation to ensure the GHFM strategy is implemented in an ethical and culturally appropriate way, in addition to funded competitive research opportunities in areas of strategic importance to Aboriginal and/or Torres Strait Islander health.

Rationale

Internal consultations identified three interconnected themes, which were considered critical to ensuring the utility, oversight and appropriateness of genomics research investment for the betterment of health and wellbeing among Aboriginal and/or Torres Strait Islander communities and families. Primarily, these relate to establishing the appropriate foundations to unlock and oversee genetics/genomics research; a focus on the specific needs and requirements within clinical service delivery (clinical genetics); and particular focus on next-generation genomics research.

2.6 Common and complex disease

Issue

Common and complex diseases place significant burden on the health system. The use of polygenic risk scores (PRS) to identify high-risk subgroups of the population is emerging as a research priority area, and has started to attract funding investment internationally.

Recommendation

- The GHFM should bring together a network of experts in the field to evaluate the PRS landscape; identify large cohorts for analysis; and evaluate the optimal approach for Australia's research investment, in the context of international endeavour and in partnership with other MRFF Missions and the NHMRC-funded Australian Prevention Partnership Centre.
- The Scientific Strategy Committee recommends the area of PRS should be funded as an incubator project involving the jurisdictions, noting the preference to front-load this funding to accelerate support with a larger competitive funding round in the short to medium term.

Rationale

Research into the use of PRS to identify subgroups of the population at high risk of common and complex disease is recognised as having considerable potential, both clinically and for reducing health systems costs. Australia has considerable expertise in this area; however, it is as yet an emerging field. Research needs to include implementation of interventions in high-risk subgroups to demonstrate health benefit.

The application of genomic technologies in health is expanding to the interrogation of complex, polygenic disorders, and the evaluation of risk of developing common diseases (such as cardiovascular disease and diabetes) using PRS. Genomics also has transformative potential to stratify people with common cancers for surveillance and treatment, including breast, colorectal and prostate cancer.

2.7 Gene-related therapies

Issue

There is a growing disparity between our abilities to diagnose and to treat individuals with genetic disease.

Recommendation

- The GHFM should systematically address the challenge of realising the full therapeutic potential of genomics, aiming to drive pre-clinical experimental therapeutics to early-phase clinical trials done at international best-practice standards.
- The area of gene-related therapies should be supported with incubator funding and re-evaluated for substantive competitive funding in later rounds. The committee notes the potential for industry partnership or co-investment in this area, and the potential intersection with the rare disease, functional genomics and ELSI GHFM priorities.

Rationale

This priority area captures a development pathway from pre-clinical experimental therapeutics to early-phase clinical trials done at international best-practice standards. This optimises the prospect of success and increases the likelihood of transition to the commercial sector, which is a necessity for later-stage trial activity and for bringing therapeutics to the market with resultant health, social and economic benefits. This priority area is heavily technology dependent, and is rich in opportunities for the development of Australian-held intellectual property, bio-manufacturing and for the further development of the Australian biotechnology ecosystem.

2.8 Ethical, legal and social implications

Issue

The ethical, legal and social implications (ELSI) of genomic technologies are many and complex, including (but not limited to):

- the need to foster community trust and confidence
- governance, privacy and participant choice/autonomy
- data management and sharing (analytical capacity, privacy, anonymity, ongoing participation/involvement and control of data sharing)
- consent arrangements for clinical and research settings, including dynamic consent
- industry involvement, including insurance, fairness, competitive and pre-competitive processes, and beneficiaries of industry profits/returns
- clinical and health systems and engagement with health care professionals

Recommendation

ELSI research is a priority for the GHFM, and research into the ELSI of genomics warrants dedicated GHFM funding. This might be allocated in any of three ways: towards sub-projects embedded in larger projects associated with all of the other priority areas; to individual standalone ELSI projects; and towards coordinated, collaborative nationwide ELSI projects.

Rationale

The future delivery of clinical and public health genomics has many intersections with ELSI, so that health care is equitable and ethical, and public resources are used effectively and efficiently. Internationally, the importance of addressing current and emerging ELSI associated with the use of genomic technologies in health care is embedded in large-scale genomic programs.

2.9 Genomic screening

Issue

Genomic screening has considerable promise as a means to identify individuals who are at increased risk for a particular health concern, and who might benefit from clinical interventions. Reproductive carrier screening provides reproductive choices to couples to identify those with an increased chance of having children with severely debilitating and often fatal genetic conditions, including conditions where early treatment can improve a child's health.

Recommendation

The GHFM should consider providing additional funding in future rounds to other areas of genomic screening (eg non-invasive prenatal testing, newborn screening), in addition to funding reproductive carrier screening research with the $20 million Australian Reproductive Carrier Screening project, Mackenzie's Mission.

Rationale

There remains a need for research into other models of screening, including non-invasive prenatal testing and newborn screening.

2.10 Infectious disease

Issue

A recent independent World Health Organization evaluation scored Australia highly in terms of protecting the public from emerging infectious threats, but advised that while Australia is 'leading the research field in the area of complete genome-based laboratory techniques, the use of genome data in disease surveillance could be better harnessed.

Recommendation

- Infectious disease/pathogen genomics priorities for future funding rounds should be informed by the Pathogen Genomics Flagship projects, and ongoing analysis of the research landscape and health priorities nationally and internationally.
- Infectious disease/pathogen genomics was the first GHFM Flagships stream, with a $32 million grant round in 2019. As the outcome of this round is yet to be announced, it is unclear what infectious disease research areas have been addressed.

Rationale

Australia has developed strong foundations in infectious disease genomics for public health. Opportunities lie in achieving more rapid high-resolution testing and predictive measures; the ability to sequence directly from clinical samples; and more cost-effective solutions and better data infrastructure.

In addition to the public health context, infectious disease genomics has the potential to impact on precision medicine through several distinct avenues. Examples include integrating pathogen-specific identifiers with host response, genomically determined biomarkers of prognosis (informing clinical care), pharmacogenomics (informing antimicrobial selection and dosing), antimicrobial resistance (informing antimicrobial selection), and tracking antimicrobial resistance in hospital-acquired infections.

2.11 Australian Genome Reference Database

Issue

There is a lack of diversity in current reference databases (eg gnomAD). This is recognised as a critical barrier to both clinical and research genomic endeavours.

Recommendation

The Scientific Strategy Committee agreed with the importance of substantial expansion of genome reference databases to cover the full range of Australian diversity and ensure that the benefits of genomic medicine can be extended to all Australians.

Rationale

The underrepresentation of Australian diversity in current international variant reference databases (eg gnomAD) poses a significant barrier to genomic advancement in both clinical and research domains. To successfully deliver the vision of the GHFM, and to embed genomics into Australian health care, an Australian genome reference database is required that is representative of Australia's rich cultural makeup, including Aboriginal and/or Torres Strait Islander people, as well as major immigrant populations.

Providing accurate frequencies for rare, potentially pathogenic variation will require at least 1,000 genomes from each of a set of diverse communities, spanning groups that are represented in Australian clinical genetics settings but underrepresented in global reference databases.