Response ID ANON-WK6N-8H51-C

Submitted to **Consultation Paper for the National Preventive Health Strategy**
Submitted on **2020-09-28 12:59:59**

Development of the National Preventive Health Strategy

1 What is your name?

Name:
Matilda Haas (submitting on behalf of organisation)

2 What is your email address?

Email:
matilda.haas@mcri.edu.au

3 What is your organisation?

Organisation:
Australian Genomics

Vision and Aims of the Strategy

4 Are the vision and aims appropriate for the next 10 years? Why or why not?

Vision and aims :
Introduction
The current vision and aims of the proposed strategy cover a broad scope which is important to allow for the staged introduction of new approaches to preventative health over the course of the next ten years. However, it is our view that genomic technologies are, and will continue to play a significant role in preventative healthcare and therefore warrant inclusion in the strategy from the outset. We would urge the Steering Committee to ensure that the National Preventative Health Strategy aligns with Australia's Long Term Primary Health Plan, which states an intention to incorporate genomics in its preventative health pillar. Similarly, there are opportunities to align the preventative health strategy with other existing programs and investments in genomic research and translation.

The application of genomic technologies to prevent, diagnose, manage and monitor disease has already been demonstrated. Our submission will focus on these, and some emerging applications of genomics, to show how valuable knowledge of a person's genomic information can be when incorporated into preventative healthcare and how it aligns with the proposed aims of the strategy.

Australians have the best start to life
Reproductive genetic carrier screening, newborn screening and early diagnosis of genetic disorders (including for future reproductive planning) can all make crucial contributions to delivering on the aim of 'the best start to life'.

Preventive screening for thousands of recessive diseases is now technically possible and its applicability in the Australian context is the subject of the Mackenzie's Mission: Australian Reproductive Genetic Carrier Screening Project. Mackenzie's Mission is a $20M MRFF project aimed at determining the feasibility of providing free carrier screening to every Australian couple that wants it. The project will test 10,000 couples for about 750 recessive and X-linked genetic conditions (conditions passed on to children from parents who are 'carriers' of the condition but who do not have it themselves). The project is currently enrolling couples to evaluate the outcomes of screening, the psychosocial impacts reported by participants, the ethical issues raised by reproductive genetic carrier screening, and the health economic impacts of this approach. It is anticipated, based on initial results, that Mackenzie's Mission will show that nationwide preventive genetics for severe recessive genetic conditions is feasible. Outcomes, including a proposed Medicare item number for expanded carrier screening, are expected to lead to sustained implementation and will be an example of how the use of genomic medicine in preventative health can reach a significant proportion of the population.

An emerging concept is that of "whole of life" genomics; starting with genomic testing in newborns, with serial reinterrogation of the genomic data throughout the life course as new medical questions arise. Newborn screening using whole genome sequencing could eventually replace the current heel prick tests, which only cover a limited number of conditions, with the advantage of the genomic information then being available for emergency situations, to gain pharmacogenomic information, and for interrogation for other conditions relevant to a person's stage-of-life. Newborn screening programs already underway in the US and UK are providing valuable insights into the feasibility and ethical considerations relating to the introduction of such an approach in Australia.

Early and rapid diagnosis of genetic conditions in affected children using whole genome sequencing can change the course of management of the condition for the child, and in some cases can influence the prognosis significantly. In addition, finding out whether the disease-causing variant was inherited from the parents or occurred de novo, is powerful for informing future reproductive decisions for the parents (Stark et al., 2019). The Acute Care Genomics study was established in 2018 to implement and evaluate a comprehensive multi-centre network for ultra-rapid genomic diagnosis in the Australian healthcare system. In its first phase, the study provided ultra-rapid genomic testing to more than 200 critically ill babies and children from across 12 Australian hospitals, with results available to most families in just three days. In May 2020, the study team were granted $5M from the MRFF to build further capacity in all Australian states and territories and deliver ultra-rapid testing to more than 240 critically ill children over the next three years. This expanded study will allow researchers to fully evaluate whole-genome sequencing as a first-tier test for ultra-rapid diagnosis and further prepare the Australian workforce. Investment in the capacity for early detection of genetic disorders will have major effects on the introduction of appropriate surveillance for predictable impacts on health as a consequence of the underlying disorder, on restoring reproductive confidence, and on eventual access to precision/targeted therapies.

Australians live as long as possible in good health

There is also emerging potential for genomics to address the aim of 'Australians live as long as possible in good health' by:

• identifying risks of developing common diseases with genetic and environmental components through Genome Wide Association Studies (GWAS) and Polygenic Risk Scores (PRS)
• genomic-informed screening programs, and
• identification of individuals for whom surveillance would be beneficial

The application of PRS is still under evaluation and more evidence is needed to support the target populations who should receive risk reducing interventions, but Australia could learn from and build upon large-scale international studies already underway (such as the US NHGRI PRS Consortium and UK Biobank). In terms of informing screening programs, genomics has the potential to stratify people with common cancers for surveillance and treatment (e.g. breast, colorectal, prostate). Ideally, incorporating environmental, genetic risk, epigenetic and other phenotypic factors into a stratified risk profile will mitigate any overdiagnosis and over screening, such as has been observed in some breast and prostate cancer programs.

Having access to pharmacogenomic information would also have strong potential to improve health throughout a lifetime. Roughly 1.7 million Australians receive a medication each year for which, if available, pharmacogenomic information would be relevant. Widespread use of such information could significantly decrease emergency and hospital presentations related to adverse events, with up to 3% of all hospitalisations in Australia resulting from adverse drug events at an annual cost of $1.4B. There are up to 15 gene/drug interactions that already have evidence that would impact on prescribing to patients and would have significant health budget cost-savings. These could be implemented initially as part of a preventative health plan.

While there are variations in the burden of disease across the life course (Australian Burden of Disease Study 2015), many of the key burdens have genetic aspects. For example, in children and young adults there is a high burden from mental health conditions such as anxiety and depressive disorders as well as suicide/ self-inflicted injuries. This is an area where research such as the Australian Genetics of Depression Study and the Australian Government's existing investment in pharmacogenomics research to improve mental health could have an impact. In later life, coronary heart disease and stroke feature prominently, alongside lung and breast cancer as burdens of disease. While cancer screening has already been identified in the Strategy, the outcomes of the programs such as the Medical Research Future Fund (MRFF) supported Cardiovascular Genetic Disorders flagship could also make important contributions.

Australians with more needs have greater gains

There are many potential elements to the aim of 'Australians with more needs have greater gains' that can be supported by the inclusion of genomic technologies in a preventative health strategy. Population genomics is a rapidly evolving space which has the potential to improve our multicultural nation's health equity. In Australia, the Garvan Institute of Medical Research and Murdoch Children's Research Institute have recently co-invested to launch the Centre for Population Genomics. The goals of the Centre revolve around the generation and analysis of genomic data sets from thousands of Australians, and their linkage with clinical and biological information. Specific projects include the development of a new genome reference database, spanning diverse Australian communities, that improves our ability to interpret genetic changes found in Australians affected by genetic disease and linking of genomic data to information on health and disease across the human lifespan. Economic analysis has shown the cost effectiveness of targeting diseases where utility has been shown, such as cancer screening (breast cancer and Lynch syndrome variants) and preconception carrier screening (for example cystic fibrosis, spinal muscular atrophy (SMA) and fragile X syndrome) (Zhang et al., 2019). After proof of principle research, other conditions could be added including rarer conditions and those of decreased penetrance (eg Tay-Sachs, sickle cell anaemia, long QT syndrome, cardiomyopathies) (Zhang et al., 2019).

Greater gains should also be achieved for Indigenous people, who should be engaged as early as possible in strategies for using genomics for preventative health. NHMRC funding to the National Centre for Indigenous Genomics to develop Indigenous genomic representation has enrolled ~ 500 community members to date. Once complete, it is expected to greatly enhance research capability in genetic diseases which commonly affect Indigenous communities. Australian Genomics is collaborating on an Indigenous Precision Medicine Project with a consortium led by the Poche Centre, University of Sydney, focussing on co-design on genomic representation projects with Aboriginal communities in NSW. Indigenous genomics will only progress with the involvement of the communities involved. While genomics initiatives including Queensland Genomics have made inroads in this area with development of Indigenous Genomics Research Guidelines, further investment, intersection and collaboration with the Indigenous Health Research Fund could facilitate further progress.

Collectively the thousands of individually rare conditions also add up to a significant unmet health need. While individual diseases may be rare, approximately eight per cent of Australians live with a rare disease (Elliott and Zurynski, 2015). Extrapolated to an Australian population of over 25 million people, this equates to around two million Australians. And approximately 80 per cent of rare diseases are of genetic origin (EURORDIS Rare Diseases Europe 2019. What is a rare disease?). Collaboration and alignment with the National Strategic Action Plan for Rare Diseases could be valuable here. Genetic screening for recessive disease is a precision medicine preventive health measure, and couples can be helped to have healthy pregnancies following identification of increase chance of genetic disorders through the use of In Vitro Fertilisation (IVF) and Pre-implantation Genetic Diagnosis (PGD), medical technologies that are already in use in Australia. Meeting the needs of those most affected by health inequities would include families who already have a child with a disability, including genetic disease. The effects on the families who have such children are devastating and long lasting, including increased financial hardship and increased likelihood of marital breakup – with consequent long-term effects on health of the family.

Investment in prevention is increased

Investments already being made and planned to support greater use of genomic and precision medicine align well with the proposed aim that 'Investment in prevention is increased'. However, there is more to do. There is currently a huge divide between resources available to those living in urban areas versus those living in rural and remote areas and this is equally true in terms of access to genetic services and testing. Australian Genomics has a project underway that will identify the extent of the metro, rural and remote divide and this could be considered as part of a preventative health strategy.

Another key component of a successful national preventative health strategy would be investment in the development of a federated approach to linking health data, electronic medical records, a wide range of test results (including genomic data) and other data sets such as environmental and socio-economic. Harnessing these datasets and applying machine learning approaches would be needed for generating robust risk prediction scores. Having a federated approach to data sharing would be of immense benefit in facilitating preventative health strategies.

Quantifying health system costs associated with diseases with a genetic basis is difficult, and this may have contributed to genetic disease strategies being left

out of health system planning in the past. However, the potential benefits and savings should not be underestimated. A Western Australian study showed that rare disease represented 2.7% of patient stays in hospital in 2010, but accounted for 10% of the hospital budget for the year (Walker et al., 2017).

Elliott, E. & Zurynski, Y. Rare diseases are a 'common' problem for clinicians. Aust Fam Physician 44, 630-633 (2015).
Stark, Z., et al. Does genomic sequencing early in the diagnostic trajectory make a difference? A follow-up study of clinical outcomes and cost-effectiveness. Genet Med 21, 173-180 (2019).
Walker, C.E., et al. The collective impact of rare diseases in Western Australia: an estimate using a population-based cohort. Genet Med 19, 546-552 (2017).
Zhang, L., et al. Population genomic screening of all young adults in a health-care system: a cost-effectiveness analysis. Genet Med 21, 1958-1968 (2019).

Goals of the Strategy

5 Are these the right goals to achieve the vision and aims of the Strategy. Why or why not? Is anything missing?

Goals :
The goals reflect the necessary involvement and interplay between Government; health systems; the natural and built environment; communities and individuals; and science, medicine and technology in building a preventative health strategy. The goals will only be achieved with commitment to funding in all the different areas that contribute to these goals.

Perhaps missing from this section of the consultation is how the success, or achievement of these goals, will be measured. This in turn raises the question of whether the goals should be defined with tangible and measurable outcomes. One example of how current goals might be reframed is, instead of “Communities across Australia will be engaged in prevention”, “Every community in Australia will be engaged in newly introduced prevention programs. Strategies and approaches for delivery of programs will be modified to meet the needs of different communities”.

Comments relating to specific goals:

1. Different sectors, including across governments at all levels, will work together to address complex prevention challenges
This goal should specifically include the commitment of State, Territory and Federal governments to work together. There is also a significant and growing role for consumers in healthcare generally and preventative healthcare in particular. Therefore, co-design with all interested and invested parties, including consumers, should be a key aspect of the strategy.

4. Communities across Australia will be engaged in prevention, and
5. Individuals will be enabled to make the best possible decisions about their health
Engaging communities in prevention and individuals in making decisions about their health will require investment in targeted, relevant and well-designed public education and engagement programs. This will be particularly important where new and emerging technologies like genomics are to be introduced, since most of the Australian public will have had limited exposure to date.

As an example, in terms of making reproductive decisions, currently the vast majority of Australian couples have no knowledge about what recessive diseases they are both carrying and therefore may pass on to any children they might have. Reproductive genetic carrier screening informs couples about their carrier status and therefore enables them to make the best possible decisions about their health, according to their values.

6. Prevention efforts will be adapted to emerging issues and new science
We believe this goal should be re-envisioned so that prevention efforts should embrace, apply or incorporate new, cutting-edge science and technologies, rather than simply “adapt” to new science.

Genetic disease has not traditionally been a large part of preventive population health programs. Newborn screening is made available but only for a very limited set of diseases through the newborn heel prick test. Non-invasive prenatal testing for chromosomal anomalies is now being carried out for most pregnancies in Australia and a small amount of carrier screening is done in Australia on a user pays basis. This is most commonly for cystic fibrosis, fragile X and spinal muscular atrophy, though other commercial entities provide a service for a broader panel of genes. Both RANZCOG and RACGP have recommended that couples should be informed about carrier screening.

Mobilising a Prevention System

6 Are these the right actions to mobilise a prevention system?

Enablers :
The strategy notes that “Consultations indicated a need to reorientate the health system to promote health, which includes embedding prevention as part of routine health service delivery including in primary health care, hospitals, and community health services.” One of the key factors here will be ensuring preventative healthcare services are funded adequately alongside the current approaches which are more focussed on treating episodes of ill health. To give an indication of the size of the shift that is needed, the Western Australia Sustainable Health Review reported that only 1.6% of the State health budget is spent on prevention.

The concept of each individual’s genome being a risk factor is, perhaps, a relatively new concept. It is only recently that access to genomic sequencing has become sufficiently affordable to allow its use at a population health level. Each person’s genome is an amazing resource for preventive health – for preventing chronic disease, for preventing adverse drug reactions, for allowing couples to have healthy children. Preventive precision medicine is something for Australia to grasp early and reap the benefits.

To introduce genomics at scale for a preventative health program, there will need to be adequate funding and development of infrastructure around testing technology and data infrastructure. Increased investments in these areas should be targeted and well-informed by the evidence coming from health-services research like that being done by the various Genomics Health Alliances around Australia.

Comments relating to specific actions:

Information and literacy skills
All Australians should be enabled to have access to high quality, evidence-based information about how to stay healthy. In relation to reproductive carrier screening, currently too small a percentage of health care professionals or members of the Australian public have sufficient knowledge of reproductive carrier screening. The same conclusion could be drawn about the application of genomic testing for diagnosis of rare disease, common disease and cancer.

Partnerships; Preparedness, Research and Evaluation
Actions around partnerships, research, evaluation and preparedness provide an opportunity for the preventative health strategy to align with other existing and future programs such as the MRFF missions (Health Genomics, Brain Cancer, Million Minds Mental Health, Dementia, Ageing and Aged Care, Indigenous Health, Stem Cell Therapies, Cardiovascular Traumatic Brain Injury) and programs such as the National Plan to Reduce Violence against Women and their Children.

An example of the importance of research and continued evaluation is the BreastScreen program. Despite sustained funding, there seems to be no improvement in breast screening uptake rates. When BreastScreen Australia was introduced in 1996 uptake was 52% and in 2017 it was 55%. The program is consistently falling behind the target of 70% uptake. Monitoring and developing an understanding why some programs don't work at the population level as expected should be an important part of implementing this Strategy, and should help to identify priority areas for investment where the greatest gains can be achieved.

There is also a need for stronger partnerships between researchers and policy makers to improve the translation of evidence.

Monitoring and surveillance
There is still much to be done in the development of robust and reliable risk prediction scores for major health burdens. To achieve this will require the development of a comprehensive health informatics infrastructure which can aggregate, analyse and interpret data from a wide range of sources including health, environmental, socio-economic, lifestyle and hospitals.

Boosting Action in Focus Areas

7 Where should efforts be prioritised for the focus areas?

Boosting Actions:
Our earlier responses to consultation questions (Q1) provide support for an argument that focus area "4) increasing cancer screening", may be too specific. There are many other diseases where screening can be done, and for which genomic technologies can be the foundation of those screening programs. This includes both rare and common diseases, including cardiovascular and other chronic illnesses, reproductive carrier screening and newborn screening. A broader focus area relating to health screening in general would allow a wider range of screening programs to be considered over the course of the 10-year Preventative Health Strategy.

Continuing Strong Foundations

8 How do we enhance current prevention action?

Continuing Strong Foundations:
The Consultation Paper states the objective for the Strategy to align with, and provide enablers and structure to, existing national strategies and plans in place. The Strategy is in a timely position take advantage of the rich translational research outcomes that will be emerging from the Medical Research Futures Fund (MRFF) Missions, which include the Genomics Health Futures Mission (GHFM). Likewise, there is an opportunity for different sectors to partner together to target future calls of the GHFM to align with aims and goals of the Strategy. Close alignment and leverage between the Preventative Health Strategy and the MRFF Preventative and Public Health Research initiative ($260.4M over 10 years) will be anticipated.

Genomic research projects already well-underway include the Australian Genomic Cancer Medicine Program, Acute Care Genomics, Genomic Autopsy and Mackenzie's Mission – all of which have significant preventative health, early diagnosis and intervention goals. Government should be poised to support the rapid translation of GHFM research outcomes.

Additional feedback/comments

9 Any additional feedback/comments?

Additional feedback:
In order to evaluate the strategy, it will be important to continue to have baseline data on the burden of disease and regular monitoring of changes. According to the AIHW website, Australia's burden of disease estimates are currently being updated to the 2018 reference year, with results expected in late 2021. The regular updating of these estimates must also continue throughout the life of the strategy.

The Consultation Paper does not allude to the associated tools and systems required to make meaningful improvements in preventative health. Big goals need to be fully supported to translate strategy into programs that the public will participate in. For example, if genomics was implemented more broadly as part of preventative health measures, there would be a need for:
• Investment in relevant technology for testing
• Secure systems of genomic data storage
• Consultation on ethical issues raised (two very different examples of ethical issues include the impact of screening on termination of pregnancy, and the over-reliance on cost-saving modelling versus the rights of the individual)
• Creating appropriate scientific and medical advisory groups
• Ensuring approaches include all states, are scalable and equitable

• Addressing current genomic workforce issues (for example, increase workload for genetic services and genetic counsellors)

The public health survey focussed on interventions relating to mental wellbeing, maintaining physical health and independence. This suggests that the consultation did not address the potential for genetic information to provide insights into future health issues, but rather sought respondents to focus their thoughts on behavioural interventions. Additional to that, the Consultation Paper is focussed on phenotype, not genotype or the interplay between genotype and phenotype, or genes and the environment. We urge the steering committee to consider these factors in developing the Strategy.

We are pleased to see the Consultation Paper state that "health is not just the presence or absence of disease or injury - more holistically, it is a state of wellbeing". This aligns with the adjustment of Health Technology Assessment processes to reflect this more holistic approach to evaluating health as ‘wellbeing’. The vast health economic research being published on Australian Genomics clinical cohorts is focussing on the impact of genetic conditions on quality of life for the individual and the family (Wu et al., 2020).

And finally, the COVID-19 pandemic has demonstrated the power of rapid infectious disease genomics for the purposes of both infection tracing and as a first step to developing vaccines. From a public health and preventative health strategy, genomics could not have been of greater importance.

In summary, the aim of our submission has been to demonstrate where genomics can already be applied, or will be ready in the near future, with great impact on preventative health. Preventative health program planners in Australian should keenly follow the progress and outcomes of research in genomic medicine and be poised to translate and imbed research outcomes. “Prevention is better than cure” is a simple, well-known phrase, which highlights the importance of a long-overdue and robust Preventative Health Strategy. The Strategy should focus on achievable goals and accompanying investments in areas where the highest impact can be achieved in the shortest amount of time, and while addressing current health challenges should also predict and plan for the future health challenges Australians will face.

Wu, Y., et al. Parental health spillover effects of paediatric rare genetic conditions. Qual Life Res 29, 2445-2454 (2020).