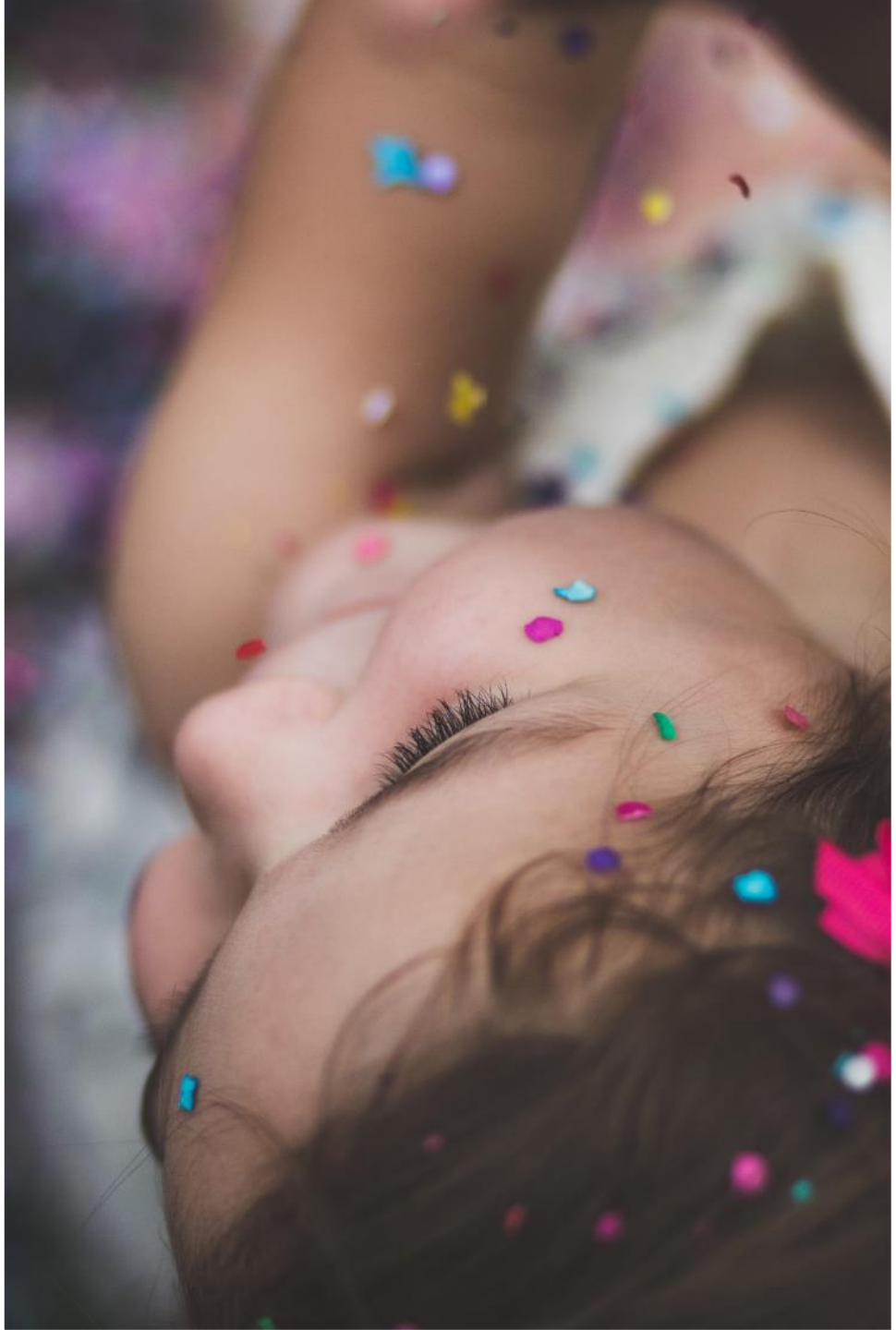
Australian Genomics

National Health & Medical Research Council
Preparing for Genomic Medicine
$25M 2016-2020. (Leveraged $120M)

Prof. Andrew Sinclair
Murdoch Children's Research Institute &
University of Melbourne

8 May 2020

Global Genomic Medicine Collaborative



Our Purpose

- **Provide strategies to government** for the equitable and effective delivery of genomic medicine in healthcare.
- Ensure **genomic and medical data** is stored **safely and shared responsibly**
- Build Australia's **research and clinical expertise** in genomic medicine.
- Enhance Australia's **gene discovery**, **functional genomics** and drug discovery research capacity.
- Advance a new era in clinical delivery where the **patient** is **informed**, **involved** and **empowered**.
- Promote **ethical, legal and social responsibility** in the application of genomic knowledge.

Australian Genomics Health Alliance

Australian Genomics

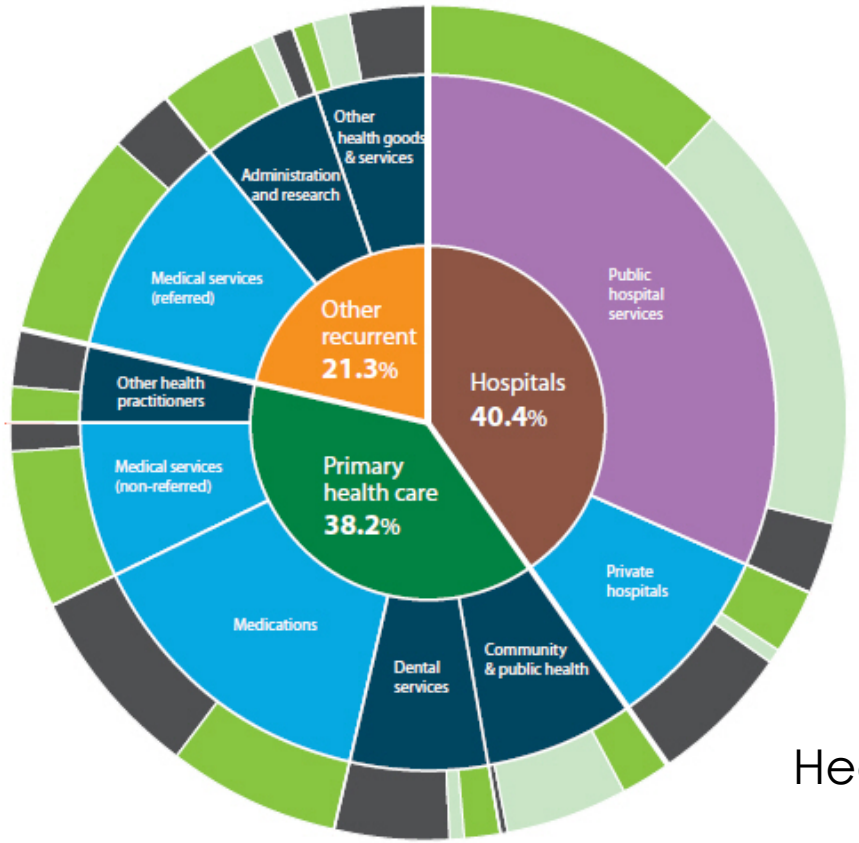
FOUNDATIONS, DESIGN

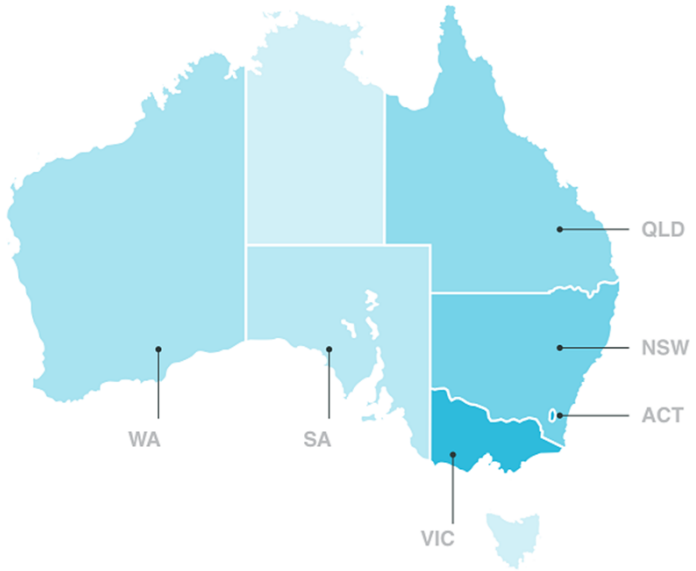
VISION / DESIGN

- Shared leadership around the country
- Recognition that whole of system change will be needed
- Leveraging established centres of excellence in different jurisdictions
- Agnostic of technology
- Initially targeting genomic applications in rare disease and cancer

Australian Genomics Health Alliance

The Australian Health Care System





Health service funding and responsibilities

Australia's Health 2014, AIHW

Australian Genomics Health Alliance

Australian Genomics

National Partners

Australian Genome Research Facility
BioGrid Australia
Bioplatforms Australia
CSIRO
Mito Foundation
National Computational Infrastructure
Rare Cancers Australia
Rare Voices Australia

International Partners

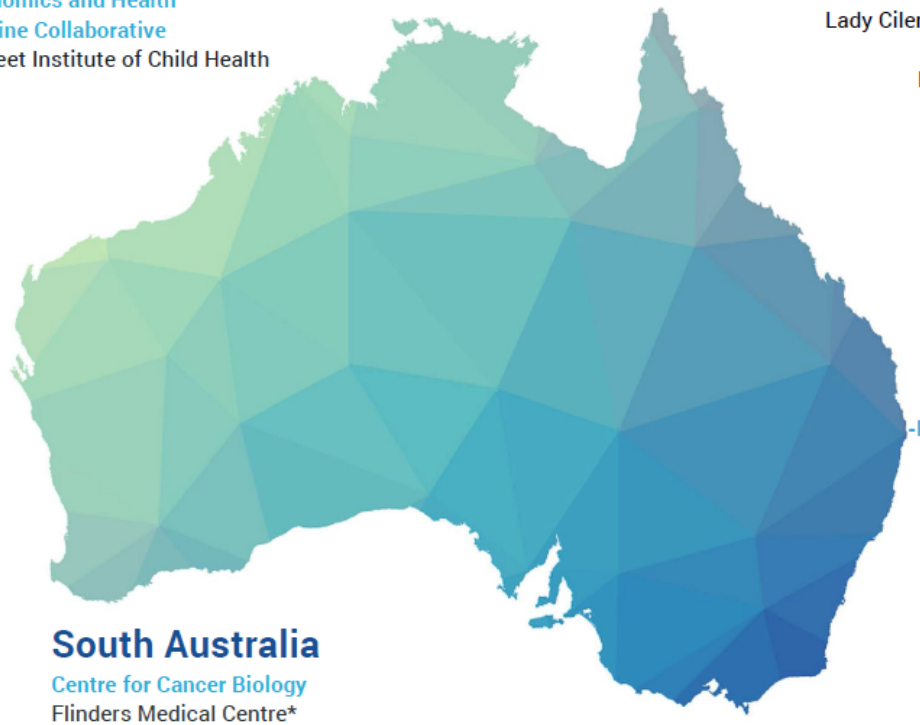
Baylor College of Medicine
Broad Institute of MIT and Harvard
Genomics England
Global Alliance for Genomics and Health
Global Genomic Medicine Collaborative
UCL Great Ormond Street Institute of Child Health

Peak Professional Bodies

Human Genetics Society of Australasia
The Royal College of Pathologists of Australasia

Northern Territory

Royal Darwin Hospital



Queensland

Diamantina Institute
Genetic Health Queensland
Gold Coast Hospital*
Institute for Molecular Bioscience
Lady Cilento Children's Hospital
Nambour General*
Pathology Queensland
Princess Alexandra Hospital
QIMR Berghofer Medical Research Institute
Queensland Genomics Health Alliance
Queensland University of Technology
Royal Brisbane and Women's Hospital
The University of Queensland
The Wesley Hospital

New South Wales

Blacktown Hospital*
Border Medical Oncology*
Centre for Genetics Education
Children's Cancer Institute Australia
Children's Medical Research Institute
Garvan Institute of Medical Research
-Kinghorn Cancer Centre
-Kinghorn Centre for Clinical Genomics
Genome.One
Hunter Genetics
John Hunter Children's Hospital
Liverpool Hospital
Macquarie University & AIHI
Nepean Hospital
NSW Health Pathology
Prince of Wales Hospital
Royal Hospital for Women
Royal Prince Alfred
Sydney Children's Hospitals Network
The University of Sydney
University of New South Wales
Westmead Hospital

Western Australia

Fiona Stanley Hospital
Genetic Services of Western Australia
Harry Perkins Institute of Medical Research
King Edward Memorial Hospital
Path West
Princess Alexandra Hospital
Princess Margaret Hospital
Royal Perth Hospital
Sir Charles Gairdner Hospital
Telethon Kids Institute
The University of Western Australia

Australian Capital Territory

Canberra Hospital
The Australian National University

South Australia

Centre for Cancer Biology
Flinders Medical Centre*
Royal Adelaide Hospital
SA Pathology
SAHMRI
The University of Adelaide
University of South Australia
Women's and Children's Hospital

Tasmania

Royal Hobart Hospital

Victoria

Austin Health
Bendigo Hospital*
Florey Institute
Geelong Hospital*
Melbourne Bioinformatics
Melbourne Genomics Health Alliance
Monash Health
Monash University
Murdoch Children's Research Institute
Peter MacCallum Cancer Centre
Royal Melbourne Hospital
South West Health Care Warrnambool*
The Alfred
The Royal Children's Hospital
The Royal Women's Hospital
The University of Melbourne
Victorian Clinical Genetics Services
Victorian Comprehensive Cancer Centre
Walter and Eliza Hall Institute

Australian Genomics Health Alliance

*Flagship specific site SUPER WGS: Cancers of Unknown Primary

Key activity hubs

Australian Genomics
OUR APPROACH

Australian Genomics Health Alliance

National diagnostic & research network

National data federation & analysis

Evaluation, policy & ethics

Workforce & Education

RARE DISEASE FLAGSHIPS

CANCER FLAGSHIPS

REPRODUCTIVE CARRIER SCREENING (MACKENZIE'S MISSION)

CLINICAL OUTCOMES

PREVENTION

EARLY DIAGNOSIS

EARLY INTERVENTION

MONITORING

PRECISION THERAPY

REPRODUCTIVE CONFIDENCE

ANALYSIS To provide a strong, ethically informed evidence base for applying genomics to clinical practice

POLICY Practical strategies to inform Australian health system planners and policy makers

PROGRAMS, PROJECTS & FLAGSHIPS

RARE DISEASE FLAGSHIPS

- Neuromuscular Disorders
- Neurodevelopmental Disability
- Genetic Immunology
- Acute Care Genomics
- Cardiovascular Genetic Disorders
- Mitochondrial Diseases
- KidGen Renal Genetics
- chILDRANZ Interstitial Lung Disease
- HIDDEN Renal Genetics

CANCER FLAGSHIPS

- Acute Lymphoblastic Leukaemia
- Cancer Risk In the Young (RISC)
- Lung Cancer Diagnosis
- iPredict Somatic Cancer
- Hereditary Cancer Syndromes
- Super WGS - Cancers of Unknown Primary

National Diagnostic & Research Network	National approach to data federation & analysis	Evaluation, Policy & Ethics	Genomic Workforce & Education
National Clinical Genomic Consent	Clinical Variant Classification & Sharing	Policy Development	Opportunity & GAP Analysis
Clinical Variant Re-classification	Genotype-Phenotype Data Capture & Analysis	Health Implementation Research	Needs Assessment
Functional Genomics	Phenotype Ontologies & eHealth	Health Economics	Evaluation framework for genomic education
Mainstreaming Genomic Pathology Reports	Variant Pipeline Evaluation & Quality Assurance	Ethical Analysis of clinical genomics	Patient Participation Understanding Analysis
MSAC Application Pipeline	Data Governance, Aggregation & Sharing	Evaluation	
Genomics in the Community	Panel APP	Network Analysis	
Unmet Needs for Genomic Testing	CTRL Participation Portal & Dynamic Consent	Ethics, legal & policies of Genomic Data Sharing	

- NATIONAL STEERING COMMITTEE
- INDEPENDENT ADVISORY BOARD
- INTERNATIONAL ADVISORS
- JOINT COMMITTEE FOR DIGITAL HEALTH & GENOMICS
- NATIONAL IMPLEMENTATION COMMITTEE
- COMMUNITY ADVISORY GROUP
- INTERNATIONAL GENOMIC INITIATIVES

Australian Genomics Health Alliance

Australian Genomics

BY NUMBERS 2019

450 Collaborators & Investigators

Recruitment Sites 32

102 Staff

21 Clinical Projects

103 Organisational Partners

115 Ethics & site submissions per annum

$25M Research Funding

23 Program Sub-projects

1000 Meetings per annum

6 Advisory Committees

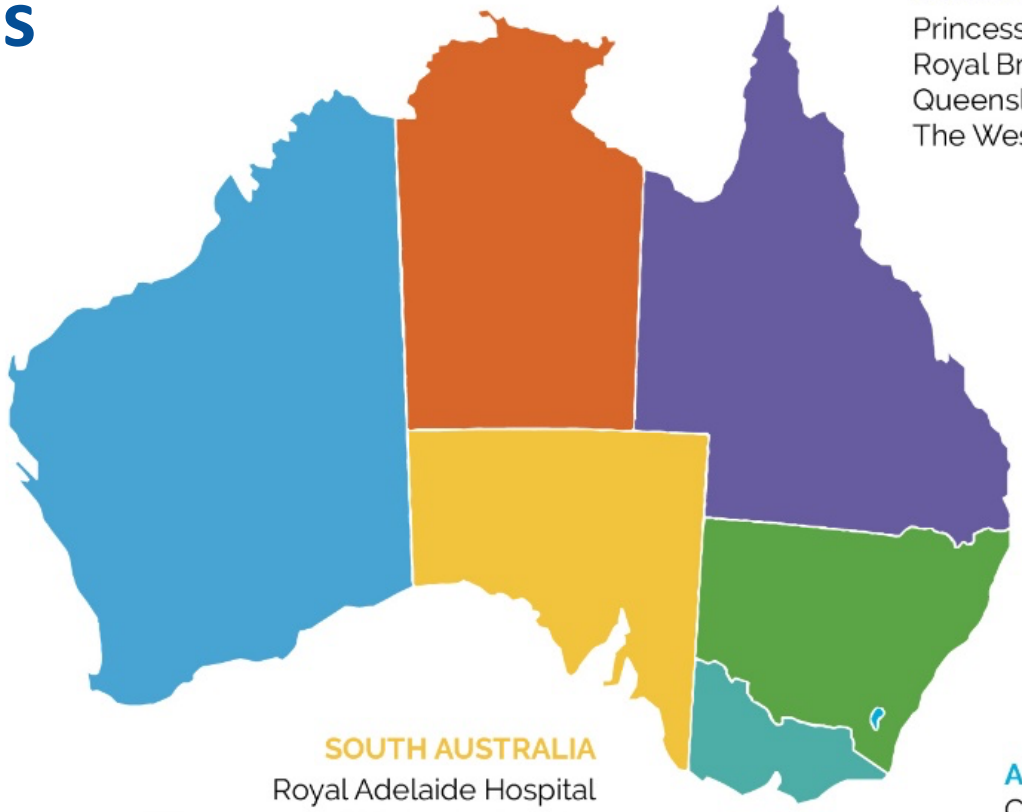
60 Contracts per annum

3000 Participants

Australian Genomics Health Alliance

Clinical Recruitment Sites

A NATIONAL FOOTPRINT



NORTHERN TERRITORY
Royal Darwin Hospital

QUEENSLAND
Princess Alexandra Hospital
Royal Brisbane and Women's Hospital
Queensland Children's Hospital
The Wesley Hospital

WESTERN AUSTRALIA
Fiona Stanley Hospital
King Edward Memorial Hospital
Pathwest QEII Medical Centre
Perth Children's Hospital
Royal Perth Hospital
Sir Charles Gairdner Hospital

NEW SOUTH WALES
Hunter Genetics
John Hunter Children's Hospital
Liverpool Hospital
Nepean Hospital
Prince of Wales Hospital
Royal Prince Alfred Hospital
Sydney Children's Hospital
St Vincent's Hospital
The Children's Hospital at Westmead
The Royal Hospital for Women
Westmead Hospital

SOUTH AUSTRALIA
Royal Adelaide Hospital
Women's and Children's Hospital

AUSTRALIAN CAPITAL TERRITORY
Canberra Hospital

VICTORIA
Austin Health
Monash Health
Monash Medical Centre
Peter MacCallum Cancer Centre
The Alfred
The Royal Children's Hospital
The Royal Melbourne Hospital
The Royal Women's Hospital

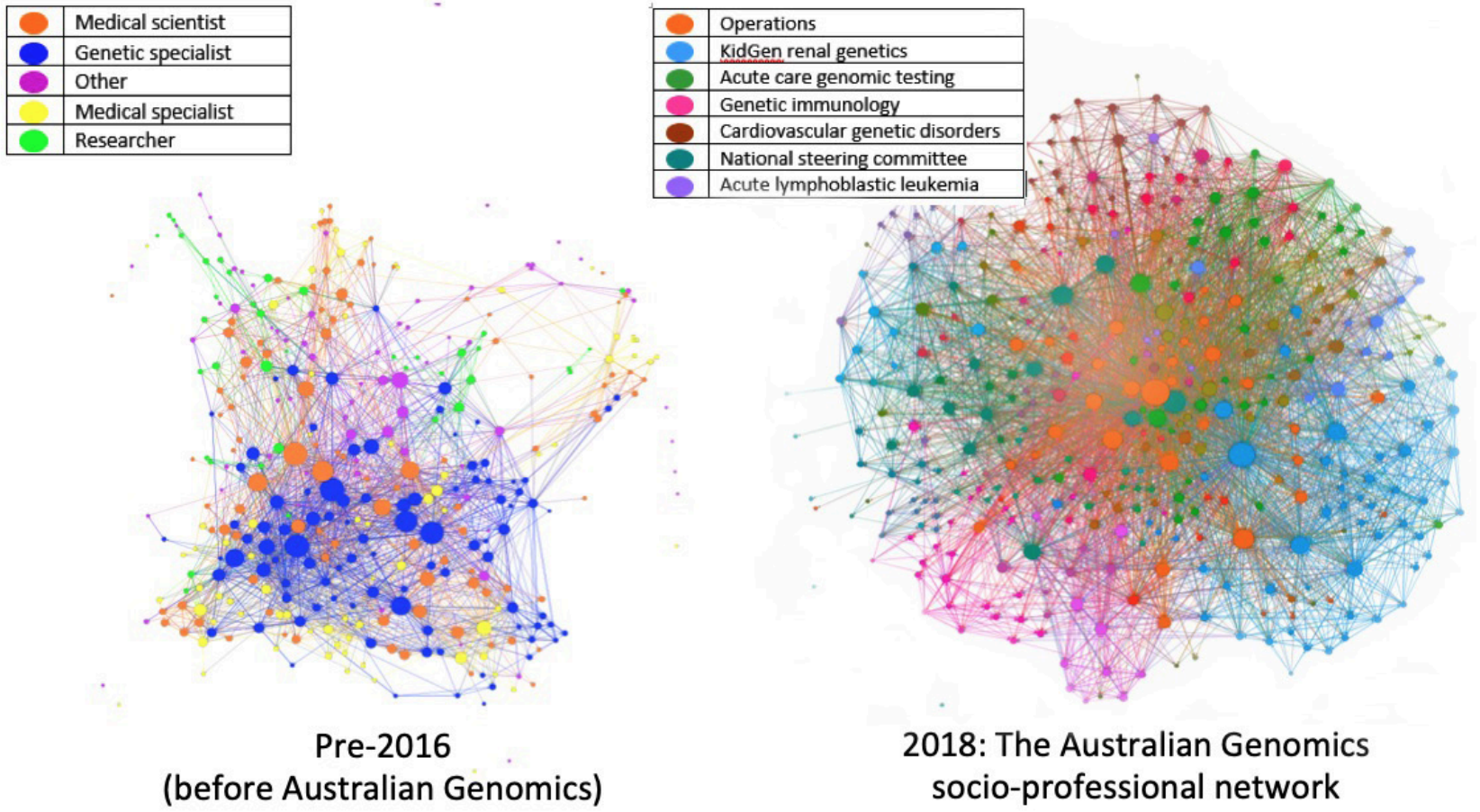
TASMANIA
Royal Hobart Hospital

Potential for a single cohort of 25M people...

Australian Genomics Health Alliance

Building a learning community of clinical genomics

A SOCIAL NETWORK STUDY



Long JC, Pomare C, Best S, Boughtwood T, North K, Ellis LA, Churruca K, Braithwaite J. ***Building a learning community of Australian clinical genomics: a social network study of the Australian Genomic Health Alliance****. BMC Medicine. 2019. 17 (1) : 44.*

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Clinical Flagships:
PROGRESS TO DATE

FLAGSHIP	TARGET	TOTAL RECRUITED	STATUS
Neuromuscular Disorders	105	123	CLOSED
Mitochondrial Disorders	150	161	CLOSED
Epileptic Encephalopathy	105	105	CLOSED
Brain Malformations	110	102	CLOSED
Leukodystrophies	50	41	EXTENDED
Intellectual Disabilities	100 (trios)	58	EXTENDED
Renal Genetics	360	379	EXTENDED
Genetic Immunology	100 (trios)	149	EXTENDED
ChILDRANZ Interstitial Lung Disease	50 (trios)	24	OPEN
Acute Care	250 (trios)	143	OPEN
Cardiovascular Genetic Disorders	600	79	OPEN
Genomic Autopsy	300	119	OPEN
HIDDEN Renal Genetic Disorders	200	16	OPEN
	2480	**1499**	
Acute Lymphoblastic Leukaemia	300	234	OPEN
Somatic Cancer	400	372	CLOSED
Germline Cancer - Paed / AYA	1400	750	OPEN
Hereditary Cancer Syndromes	190	107	OPEN
Lung Cancer Diagnosis	150	45	OPEN
SUPER WGS	100	10	OPEN
	2540	**1518**	
Mackenzie's Mission	10,000 (couples)	0	PENDING
TOTAL	**5020**	**3017**	**60%**

Average diagnostic rate, Rare Disease Flagships: 40% (28-69%)

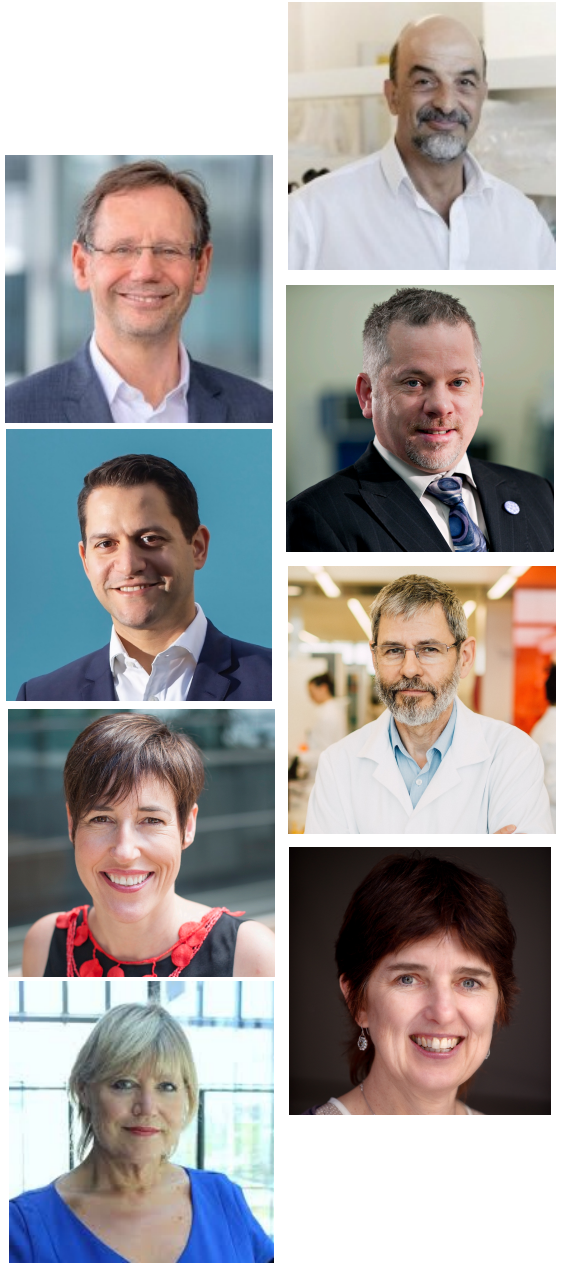
Several Flagships extended to capitalize on established network

Actionable findings, Cancer Flagships: 45%

Outcomes and Impacts

PROGRAMS

- **National clinical genomic consent** materials finalised
- **Childhood Syndromes and Intellectual Disability** –Govt subsidise genomic tests
- Patient and public education: **genomicsinfo.org.au** launched
- **Australian Functional Genomics Network** established
- Genomics **policy web resource** live
- **Health economic and implementation science** evaluations of flagships, participants, clinical delivery systems and the public
- Assessment of the **genomic knowledge of health workforce**, and availability of training and education being reported
- **Data management infrastructure** live



Australian Genomics Health Alliance

Data Management Work Flow and Capabilities

'Shariant' Platform
Classified variants and curation evidence shared across laboratories

Matchmaker Exchange

Data Quality Assessment
Quality reports on BAM + VCF data produced by *qprofiler* software

Data Access Agreements
Data Governance Policies
Data Access Committee

Data Access and Approvals System
Approvals issued automatically (low-sensitivity) or via data access review (high-sensitivity)

Clinical Consultation

Clinical Sequencing Laboratories
PathWest
NSW Health Pathology
VCGS
SA Pathology
GENOME ONE

Classified Variants
Reported & Unreported
Curation Evidence

Genomic Data
VCF
BAM
FASTQ

Metadata
laboratory, sequencer, library preparation etc

Upload Genomic Data + Associated Metadata

Genomic Data Repository
Phase 1 genomic data store
amazon web services S3
Phase 2 comprehensive genomic data catalogue
Arvados

Access to individual-level data

Access to summary-level data

Genotypes

Gen-Phen Database
'Variant Atlas'
Genotypes and Phenotypes available for interactive summary-level queries and visualisations

Biospecimen

Accredited
Pathology Reports

Minimal Clinical Datasets

CTRL Consent Portal

REDCap
Research Electronic Data Capture
Australian Genomics Study Database

Flagship Clinical Phenotypes
Patient phenotype data

Standardised Clinical Phenotypes
Patient phenotype data coded in SNOMED / HPO terms and represented in FHIR format
SNOMED CT
FHIR

Phenotypes

Beacon Network



Shariant: share variants

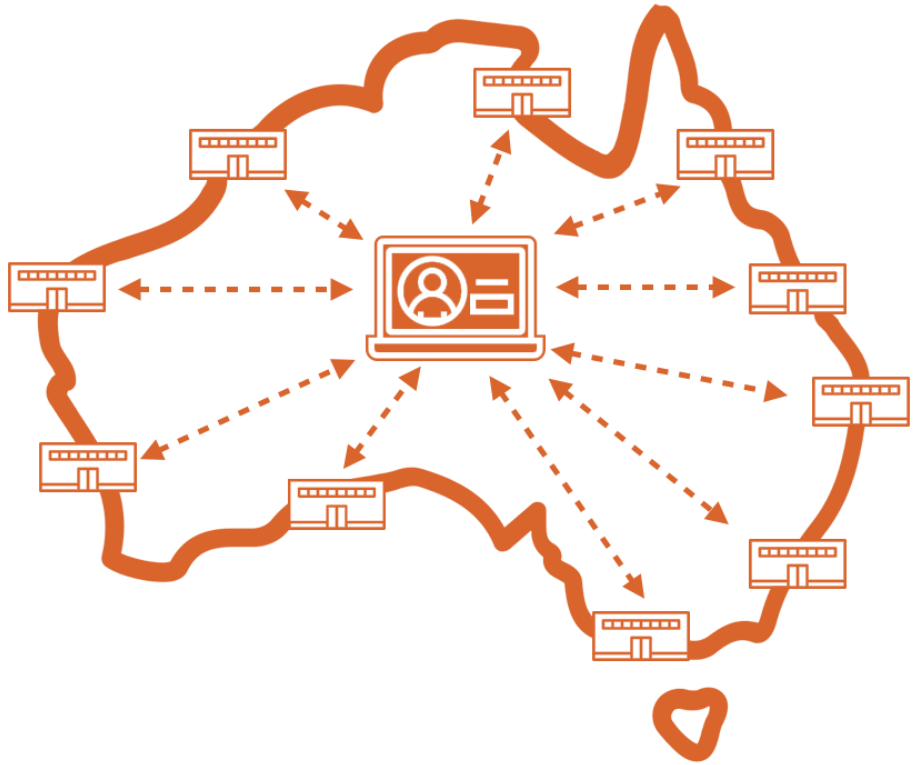
AUSTRALIAN GENOMICS VARIANT CLASSIFICATION SHARING PLATFORM

Share clinically curated variants with structured supporting evidence and phenotypes between Australian labs

Allow collaborative monitoring & review of curated variants

Act as a central administrative node for submission to international databases such as ClinVar

Sharing of Expertise



Submission to International Databases

Discrepancy Resolution

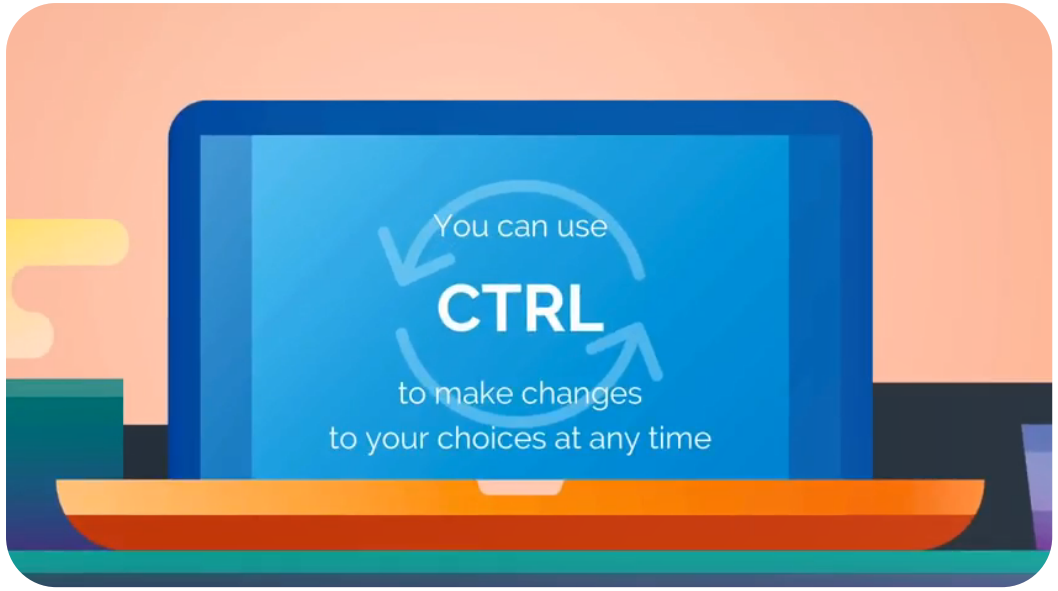
via email notifications and in-built communication platform

Controlled Access

Australian Genomics Health Alliance

The community

CTRL PARTICIPANT PORTAL



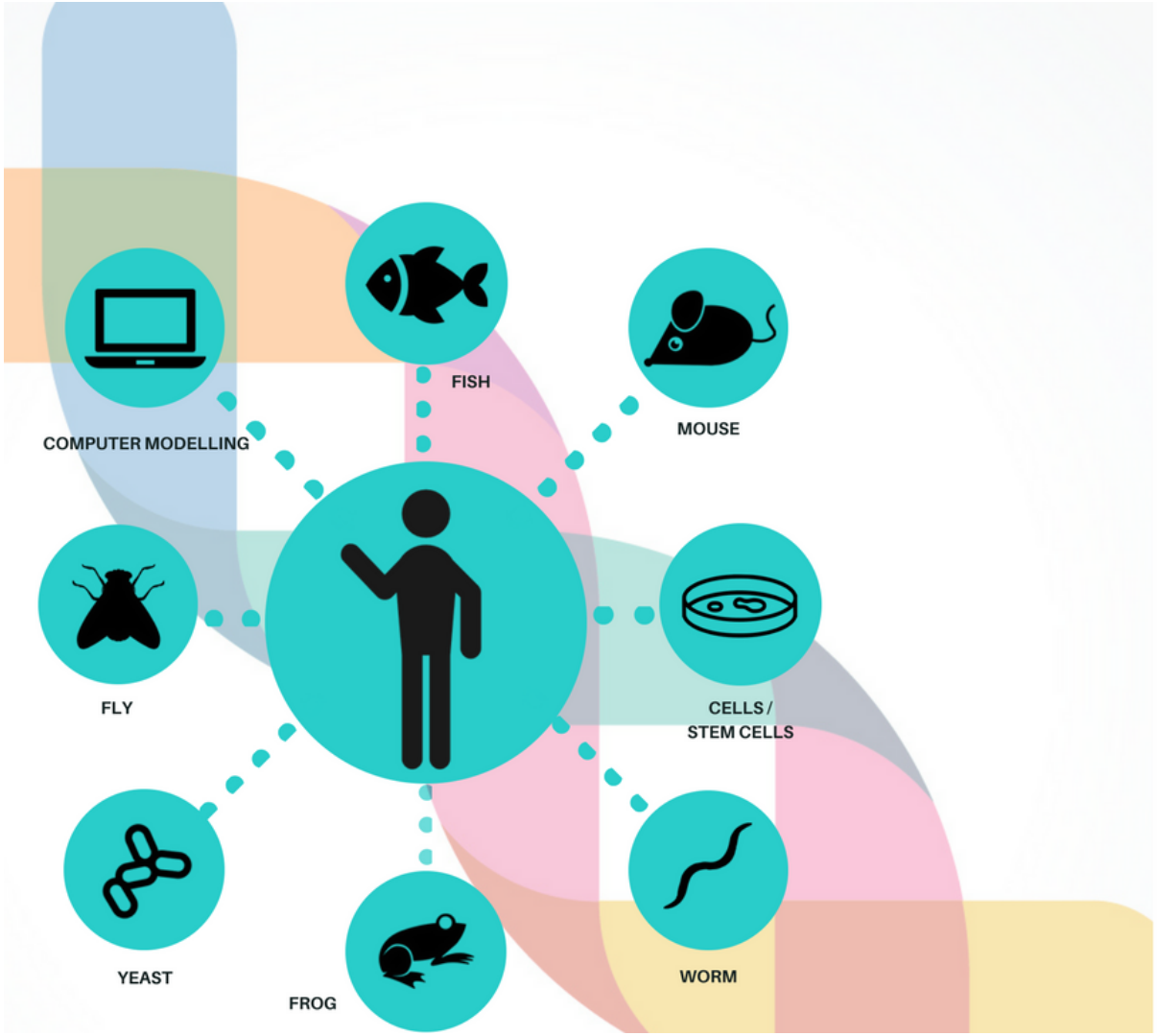
We understand that participants want to have more control over their involvement in research.

This is why we have developed a new online research consent and engagement platform for our participants called **CTRL** (control)

CTRL gives granular, dynamic consent options, access to information, surveys and reports, and a means to communicate with study investigators.

Australian Genomics Health Alliance

Australian Functional Genomics



Australian Functional Genomics Network is a group of over 250 researchers and clinicians from across Australia with the aim **of integrating functional genomics into the diagnostic paradigm** for managing rare diseases and cancer in Australian patients.

- **Connecting clinicians with researchers** to investigate function of newly discovered genes and variants of unknown significance.
- Enriched cohorts for **Gene Discovery**. Disease Mechanism. **Therapeutic Targets.**
- **Based upon the successful Canadian RDMM network**
- 2nd National Conference, Sydney November 22, 2019

functionalgenomics.org.au

Australian Genomics Health Alliance

COMMENTARY

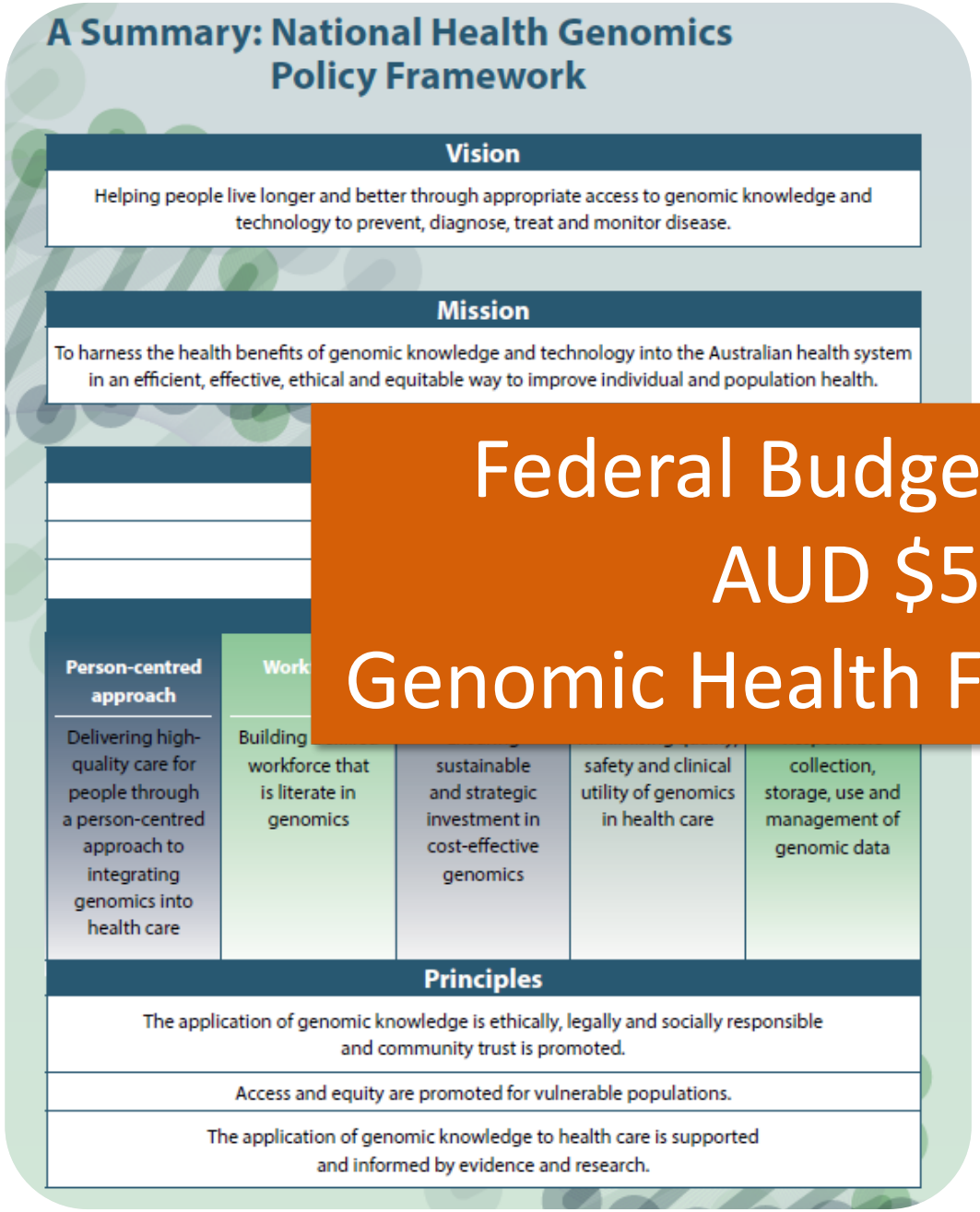
Australian Genomics: A Federated Model for Integrating Genomics into Healthcare

Zornitza Stark,[1,2,3] Tiffany Boughtwood,[1,2] Peta Phillips,[1,2] John Christodoulou,[1,2,3] David P. Hansen,[1,4] Jeffrey Braithwaite,[1,5] Ainsley J. Newson,[1,6] Clara L. Gaff,[1,3,7,8] Andrew H. Sinclair,[1,2,3] and Kathryn N. North[1,2,3,*]

Australian Genomics is a national collaborative research partnership of more than 80 organizations piloting a whole-of-system approach to integrating genomics into healthcare that is based on federation principles. The aim of Australian Genomics is to assess the application of genomic testing in healthcare at the translational interface between research and clinical delivery, with an emphasis on robust evaluation of outcomes. It encompasses two bodies of work: a research program prospectively providing genomic testing through exemplar clinical projects in rare diseases, cancers, and reproductive carrier screening and interdependent programs for advancing the diagnostic, health informatics, regulatory, ethical, policy, and workforce infrastructure necessary for the integration of genomics into the Australian health system.

Am J Hum Genet July 2019

Australian Genomics Health Alliance



Federal Budget May 2018
AUD $500M
Genomic Health Futures Mission

Genomic Health Futures Mission

Vision and Scope

To consolidate Australia's international leadership in genomics,

To invest in research into better testing, diagnosis and treatment,

To deliver genomic testing and targeted therapies as standard of care

The Genomic Health Futures Mission is starting from an established research base – building upon state and national genomic initiatives.

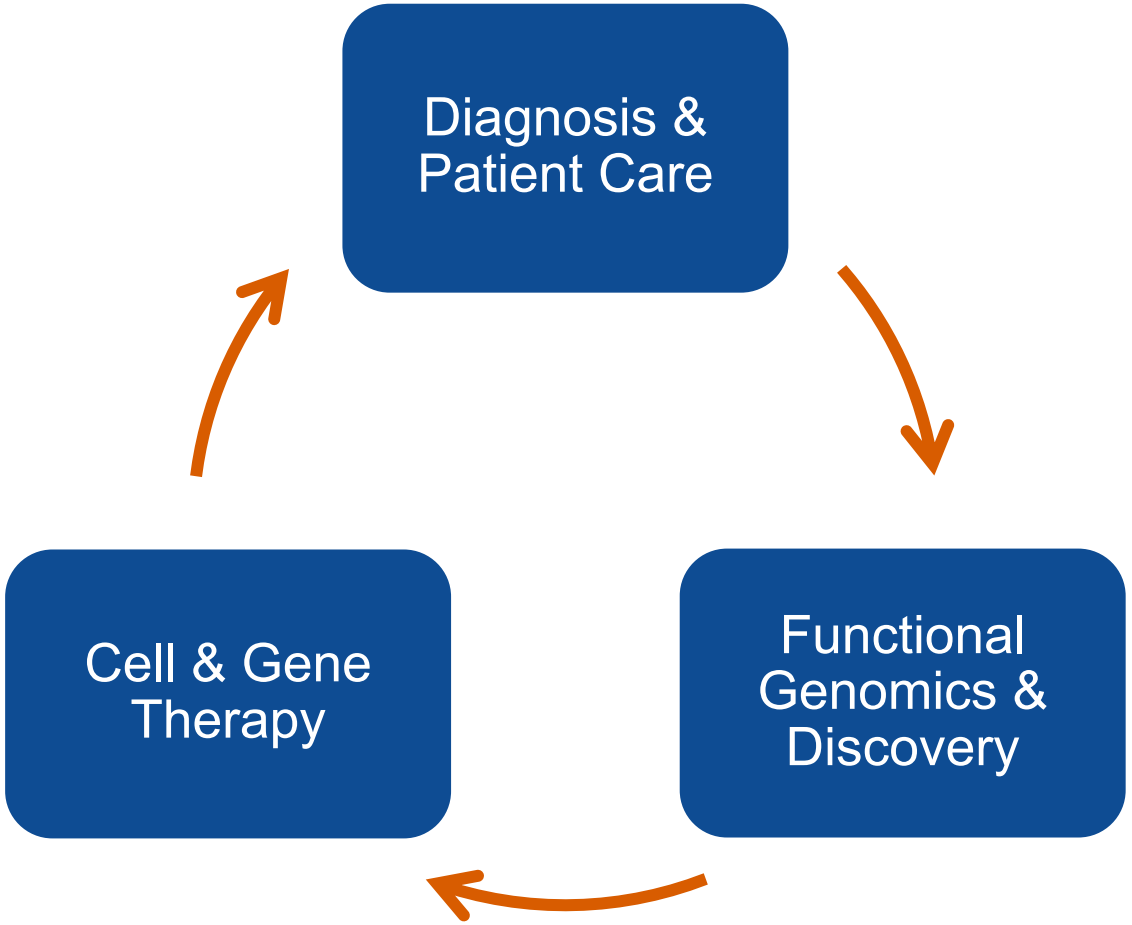
Vision: "Australians live longer and better through Australia's global leadership in research and investment in genomics and related platforms."

Model for delivery of activities

A virtuous cycle improving **diagnosis and patient care** through improved evidence-based access to genomic testing;

Building Australia's **functional genomics and gene discovery** research capacity; and

Helping Australians benefit from advances in **gene technologies and cell therapies**, through expanded research and access to clinical trials.



Priority Areas

New Areas to be developed

Reproductive/prenatal/newborn screening

Infectious diseases

Functional genomics

Common diseases

Gene-related therapy

Indigenous genomics

Industry engagement

Proposed Aim: Pilot for National Reproductive Carrier screening

Pilot to **screen 10,000 couples across Australia for carrier status for more than 700 autosomal and X-linked recessive conditions** pre or early in pregnancy

To **research** the following outcomes:

- Uptake
- Carrier frequencies for genes on the screening panel
- Incidence of high risk carrier couples
- Reproductive decisions made by carrier couples
- Psychosocial outcomes
- Health economics
- Implementation research
- Ethical research

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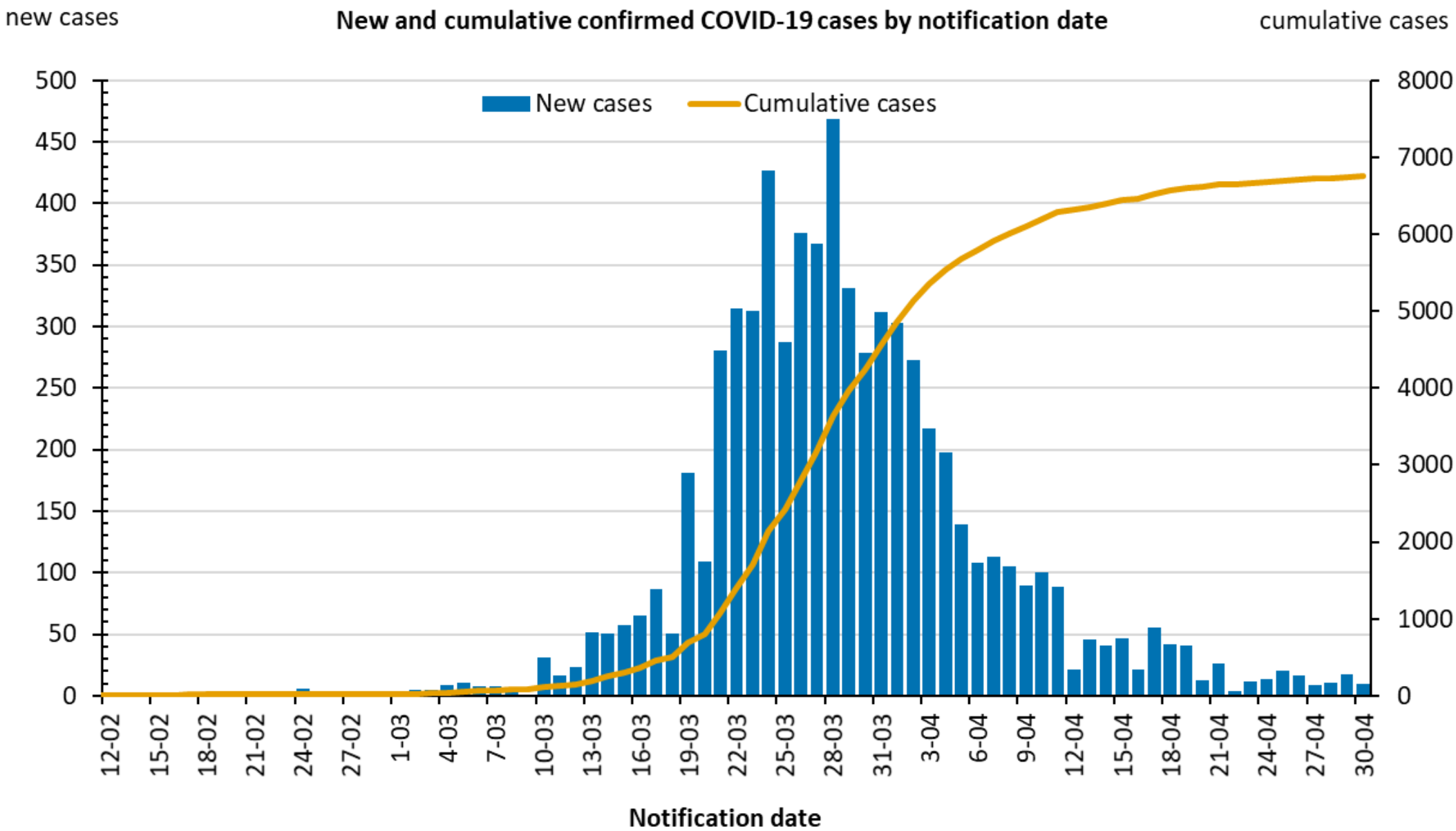
new cases
New and cumulative confirmed COVID-19 cases by notification date
cumulative cases
New cases
Cumulative cases
500
450
400
350
300
250
200
150
100
50
0
8000
7000
6000
5000
4000
3000
2000
1000
0
12-02
15-02
18-02
21-02
24-02
27-02
1-03
4-03
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28-03
31-03
3-04
6-04
9-04
12-04
15-04
18-04
21-04
24-04
27-04
30-04
Notification date

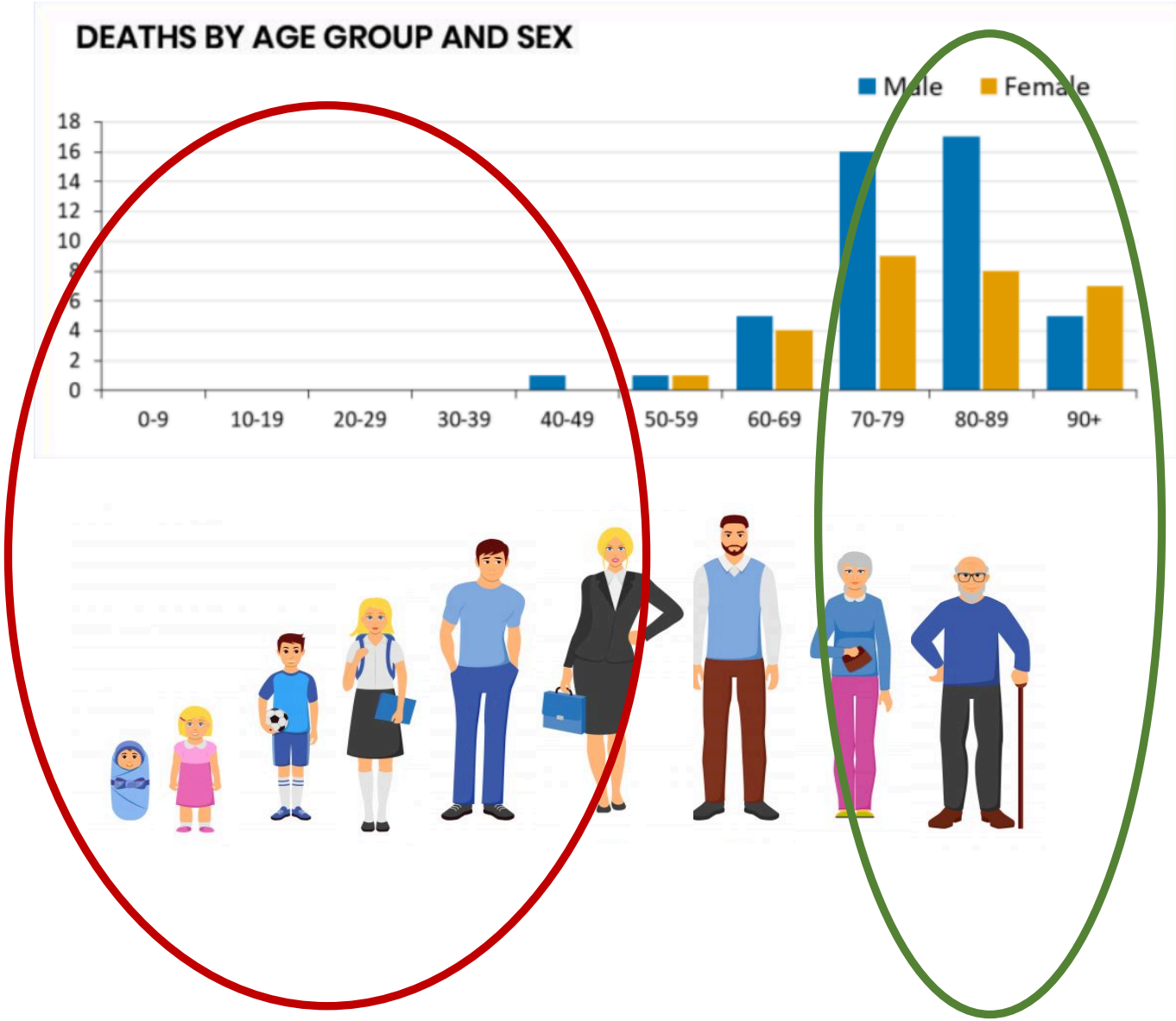
COVID-19 Genomics

We are primarily interested in disease "outliers":

- The young (<50) with no predisposing health issues who appear to have particularly severe disease
- The very elderly (>80?)

or

- Those who are "hyper-exposed" (house companions of infected individuals or ICU workers) who contract COVID-19, but appear to have a particularly mild clinical course



Historically, pandemics have forced humans to break with the past and imagine their world anew. This one is no different. It is a portal, a gateway between one world and the next. We can choose to walk through it, dragging the carcasses of our prejudice and hatred, our avarice, our data banks and dead ideas, our dead rivers and smoky skies behind us. Or we can walk through lightly, with little luggage, ready to imagine another world. And ready to fight for it.

Arundhati Roy: “The pandemic is a portal” Financial Times, 4 April 2020

Thank you!
Questions?

australiangenomics.org.au

Twitter: @AusGenomics