Melbourne Genomics
Health Alliance

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Proof-of-concept for providing additional genomic findings to adults

Background

'Additional' or 'secondary' genomic findings are changes in genes that indicate a risk of future disease but are unrelated to the reason the patient is undergoing testing. We use the term Additional Findings (AF) when these changes are deliberately sought, rather than being found unintentionally. This is also the term preferred by patients.

Whether to search for such findings and provide them to patients having genomic testing for clinical care is a topic of debate. There are both resourcing and ethical implications.

The provision of AF for a set list of serious, treatable conditions is recommended by the American College of Medical Genetics when patients undergo diagnostic genomic sequencing. It is now standard in the United States to offer AF at the same time as diagnostic testing. European and Canadian guidelines do not actively promote AF analysis, but nor do they preclude it.

Studies internationally are investigating the impact of AF on health outcomes. However, the way in which AF are offered (the 'model of care') also requires careful consideration, as this will have impact on uptake, costs and possibly also outcomes.

Publications

"A novel approach to offering additional genomic findings – A protocol to test a two-step approach in the healthcare system", Martyn, M., Kanga-Parabia, A., Lynch, E., James, P.A., Macciocca, I., Trainer, H.A., Halliday, J., Keogh, L., Wale, J., Winship, I., Bogwitz, M., Valente, G., Walsh, M., Downie, L., Amor, D., Wallis, M., Cunningham, F., Burgess, M., Brown, N.J., Jarmolowicz, A., Lunke, S., Goranitis, I., Melbourne Genomics Health Alliance, Gaff, C.L., *Journal of Genetic Counselling* (2019). doi:10.1002/jgc4.1102

"Introducing Edna: A trainee chatbot designed to support communication about additional (secondary) genomic findings", David Ireland, DanaKai Bradford, Emma Szepe, Ella Lynch, Melissa Martyn, David Hansen and Clara Gaff, *Patient Education and Counselling* (2020) https://doi.org/10.1016/j.pec.2020.11.007

"Evaluating the resource implications of different service delivery models for offering additional genomic findings", Martin Vu, Koen Degeling, Melissa Martyn, Elly Lynch, Belinda Chong, Clara Gaff and Maarten J. IJzerman, *Genetics in Medicine* (2020) https://doi.org/10.1038/s41436-020-01030-8

Project description

The objective of this project was to undertake a proof-of-concept study to better understand the implications of offering additional findings analysis to Victorian patients.

A model of care was evaluated in which adults were offered additional genomic analysis for disease predisposition ('additional findings') *after* diagnostic genomic testing was complete.

Adult participants who had diagnostic testing (or parents of children who had trio whole exome sequencing) through Melbourne Genomics' clinical projects from 2014 onwards were eligible[1].

The proof-of-concept project was led by Melbourne Genomics' Executive Director, Professor Clara Gaff; Clinical Project Manager, Elly Lynch; and Evaluation Project Manager, Dr Melissa Martyn. The Melbourne Genomics members involved were: The Royal Children's Hospital, The Royal Melbourne Hospital, Monash Health, Murdoch Children's Research Institute (Victorian Clinical Genetics Services), Austin Health and The University of Melbourne.

Expert reference groups were formed from the organisations involved, to drive and advise the project.

Activities

Between November 2017 and November 2018, 20 eligible patients were randomly selected each month until 200 people had been approached.

Those electing to receive further information were offered pre-test genetic counselling, with a decision-support kit forwarded prior to this appointment.

Those who attended genetic counselling and consented to AF analysis had their stored genomic data re-analysed for a list of 58 genes associated with adult-onset conditions with known treatments or intervention publicly funded in Victoria. Results were returned by phone or face-to-face.

The process was then comprehensively evaluated:

- Participants were asked to complete surveys at two time-points (pre- and post-results), to ascertain their understanding, experiences and preferences and were contacted six months following testing, to assess recall of results.
- Genetic counselling consultations were recorded and analysed thematically.
- Genetic counsellors involved in the study were interviewed about their experiences of counselling for AF and their perspectives on service provision and models.
- A focus group was held with laboratory personnel involved in variant interpretation to understand laboratory perspectives.
- Health economic modelling to identify cost-effective service models for AF is underway.

CSIRO has prototyped a 'chatbot' (chat robot) for delivery of information to patients about AF[2], as an adjunct to genetic counselling.

Dubbed 'Edna' (E-DNA), the chatbot is the first of its kind globally developed specifically to support genetic counselling for adults being tested to ascertain future risk of preventable or treatable conditions. Edna is currently undergoing a feasibility trial with patients, genetic counsellors and genetics students, and is slated to undergo a larger-scale patient trial in the near future.

Outcomes and lessons learnt

Findings from this project will be made available following publication of results.

Impact

This was the first study internationally to test such a 'two-step' approach to additional findings as a clinical model of care.

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[1] Other eligibility criteria: patients who consented to be contacted for further research and are English-speaking. Not all eligible patients were approached.

[2] A chat robot ('chatbot') is a computer program that uses artificial intelligence to simulate conversation. This rapidly emerging technology presents an opportunity to make better use of genetic counsellor time. As an adjunct to the AF study, a 'trainee' chatbot was developed and is in refinement (in conjunction with CSIRO) to augment genetic counselling for additional findings.

Project team

Name	Organisation	Role
Clara Gaff	Melbourne Genomics	Executive Director
Melissa Martyn	Melbourne Genomics	Evaluation Project Manager
Elly Lynch	Melbourne Genomics	Clinical Project Manager
Alison Trainer	RMH / PeterMac	Clinical geneticist
Anaita Kanga-Parabia	Melbourne Genomics	Research assistant
Anna Jarmolowicz	Melbourne Genomics	Genetic counsellor
Anna Ritchie	MCRI/VCGS	Medical scientist
Belinda Chong	MCRI/VCGS	Medical scientist
Belinda Creighton	Monash Health	Genetic counsellor
Crystle Lee	MCRI/VCGS	Medical scientist
David Amor	MCRI/VCGS	Clinical geneticist
Dean Phelan	MCRI/VCGS	Medical scientist
Emily Allen	MCRI	Genetic counsellor
Emily Higgs	RMH	Genetic counsellor
Fiona Cunningham	Monash Health	Genetic counsellor
Giulia Valente	Melbourne Genomics	Genetic counsellor
Heather Chalinor	Austin Health	Genetic counsellor
Helen Curd	Monash Health	Genetic counsellor
Ivan Macciocca	MCRI/VCGS	Genetic counsellor
Jane Halliday	MCRI	Epidemiologist
Janney Wale	Melbourne Genomics	Community Advisory Group member
Katherine Rose	Monash Health	Genetic counsellor
Kirsty West	Melbourne Genomics	Genetic counsellor
Kristin Rigbye	MCRI/VCGS	Medical scientist
Lilian Downie	MCRI/VCGS	Genetics fellow
Ling Lee	Melbourne Genomics	Evaluation officer
Louise Keogh	UoM	Health sociologist
Lucinda Salmon	Austin Health	Genetic counsellor
Maie Walsh	MCRI/VCGS	Genetics fellow

Maira Kentwell	RMH / PeterMac	Genetic counsellor
Matthew Burgess	Austin Health	Genetic counsellor
Megan Cotter	Austin Health	Genetic counsellor
Michael Bogwitz	RMH	Genetic counsellor
Michelle Torres	MCRI/VCGS	Medical scientist
Naomi Baker	MCRI/VCGS	Medical scientist
Natalie Thorne	Melbourne Genomics	Head of Innovation and Technology
Natasha Brown	MCRI/VCGS	Clinical geneticist
Paul James	RMH / PeterMac	Clinical geneticist
Rigan Tytherleigh	Melbourne Genomics	Research assistant
Robyn McNeil	Melbourne Genomics	Evaluation officer
Rona Weerasuriya	Melbourne Genomics	Evaluation officer
Sebastian Lunke	MCRI/VCGS	Medical scientist
Sze Chern Lim	MCRI/VCGS	Medical scientist
Vanessa Kumar	MCRI/VCGS	Medical scientist
Yael Prawer	Melbourne Genomics	Genetic counsellor