The Zero Childhood Cancer Program (ZERO) is Australia's first national paediatric cancer precision medicine program, focused on real-time recruitment and analysis of patients with high-risk paediatric cancer. The primary aim is a systematic evaluation of the feasibility and utility of a comprehensive molecular profiling platform consisting of germline and tumour WGS, RNAseq and CNS methylome analysis to identify clinically significant variants relevant to the biology of the tumour, diagnosis, clinical management or prognosis. Programs such as ZERO extend well beyond established gene-drug indications, and explore many novel aspects of cancer biology. One of the significant challenges faced in new models of personalised medicine is distilling which of the millions of molecular changes within a given tumour are pathogenic and relevant to clinicians. Novel variants are frequently identified which likely have pathogenic roles in cancers, but remain unsupported by functional validation studies. The therapeutic 'actionability' of such variants is a particularly fluid designation, being influenced by the availability of preclinical data, drugs and clinical trials.

MACKENZIE'S MISSION

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Mackenzie's Mission, the Australian Reproductive Carrier Screening Project, is a research project funded by the Medical Research Future Fund that aims to screen 10,000 couples for 1300 genes associated with >700 genes. The project is studying uptake, proportion of couples found to be at high risk, reproductive decisions made by those couples and psychosocial,

health economic, ethics and implementation research related to carrier screening. Despite some pandemic-related hitches, the project is progressing well; preliminary data will be presented.

IS AUTOMATED GENOMIC REPORTING READY FOR PRIME TIME?

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The process of reducing the large genomic datasets obtained from sequencing a genome, to a smaller and more manageable filtered set of variants for analysis, is already usually an automated pipelined process. Similarly, many laboratory and bioinformatic workflows are already amenable to basic laboratory automation.

To explore taking genomic reporting to the next stage, it is possible to utilise more powerful bioinformatic tools. These can include linear programming, large-data science, machine learning and deep learning/artificial intelligence. While some of these techniques have sophisticated mathematical underpinnings, once developed, they are surprisingly easy to apply and use.

Examples will be given of the application of these tools to clinical problems. Their diagnostic performance already exceeds the capabilities of human experts, their speed similarly outperforms humans, and the reproducibility and consistency (and ease of use) of this approach strongly contributes to reduction in variability and resultant improvement in quality. Further applications include real-time point-of-care genomic diagnosis, and automated background reanalysis of unsolved cases.