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MEDIA RELEASE

"MEDICALLY ACTIONABLE" GENETIC RESULTS: ETHICAL CHALLENGES FOR RESEARCHERS

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AUSTRALIAN medical research studies now generate genetic information on thousands of participants, but not all participants are receiving genetic results, even when they are medically actionable, due to a range of ethical and practical challenges, according to the authors of an Ethics and Law article published online by the *Medical Journal of Australia* today.

"Some genetic results, present in a small portion of participants (< 5%), are considered medically actionable, meaning they are associated with increased risk of adult-onset diseases, where effective risk management, prevention or treatment exists," wrote the authors, led by Jane Tiller, an Ethical, Legal and Social Advisor in Public Health Genomics at Monash University.

"Returning genetic research results can be life-saving, alerting participants to preventive steps that they would not otherwise have taken."

Internationally there is a growing consensus that medically actionable genetic research results should be made available to participants, however, even where participant consent has been obtained, not all Australian studies are returning medically actionable results, due to varying ethical and practical challenges.

"For example, research participants may provide samples for altruistic reasons, before research analysis, without expectation of re-contact. Should results be returned to these individuals, especially those unaffected by indicated disease? Is there a legal or ethical requirement to make results available or liability for withholding them," asked Tiller and colleagues.

"Risk estimates for many genes are still uncertain, complicating decisions around medical actionability and the time frame for returning results.

"Some participants may experience surprise or distress on learning about genetic risks.

"Returning results may also raise the possibility of out-of-pocket medical costs or increased insurance liabilities for younger participants."

Tiller and colleagues presented two research cohort case studies:

Lifepool: a large community-based study of women in the general population

"To date, Lifepool has contacted 73 women previously unaware of their high [breast cancer] risk variants," wrote Tiller and colleagues.

"None of the women identified with a cancer-causing variant would have been eligible for publicly funded testing through the Australian clinical system. Most women took proactive steps to mitigate risk after receiving genetic results. Of the 73 women, 23 so far have undergone risk-reducing surgery (bilateral oophorectomy), mitigating their cancer risk.

"The shared nature of DNA means genetic results are also relevant to participants' blood relatives. Beyond participants who directly received results, 63 relatives were also tested through cascade testing, 32 of whom were also found to have a high-risk variant. These relatives were, on average, substantially younger than the original participants, making this information even more valuable for prevention."

ASPREE: a large cohort study of healthy older people

"Participants consented to re-contact regarding genetic results relevant to personal or family health … However, there is ongoing debate about the most appropriate strategy, given the age of the cohort (average, 75 years)," wrote Tiller and colleagues.

"A small number of (<5%) of ASPREE participants were found to carry medically actionable variants. Many older ASPREE participants with these variants have seemingly outlived their increased risk, displaying no signs of indicated disease at 75 years of age and older.

"Is the information still medically actionable? Do participants still want to know? Should results be returned for the benefit of younger, potentially high-risk family members? What about ASPREE participants who are in cognitive decline or deceased? Is ASPREE obliged to contact these individuals, or their relatives, to provide genetic results?

“Despite having detected genetic information through research analysis that is clinically valid and of clear relevance to personal or family members’ health, ASPREE has not yet commenced returning genetic results, seeking to achieve an appropriate harm–benefit balance.”

Tiller and colleagues concluded that despite growing consensus on the ethical imperative to offer research participants medically actionable genetic results “questions remain regarding the legal obligations and disclosure methods, particularly when research participants lack the capacity to make decisions about receiving genetic information”.

“As genetic information becomes more pervasive and valuable to preventive medicine, the return of medically actionable genetic results will become increasingly important from ethical, legal and medical perspectives.”

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