



How Health 2020 adds to our understanding of genetics and cancer

Health 2020 data collected decades ago is yielding useful results – in ways we couldn't have foreseen



The Human Genome Project was launched in 1990. It took 13 years and US\$3 billion to complete mapping out the billions of DNA bases that make up a full set of a person's genes and everything in between. That is a long time to wait and a huge price to pay for just one genome. But the Human Genome Project led to technological advances that found better, faster and cheaper ways of getting the job done. Today, analysing an entire human genome costs less than \$US 5,000 and only takes a day or two.

Collecting genetic data in HEALTH 2020

HEALTH 2020 was launched in 1990, the same year as the Human Genome Project. The blood samples we collected were originally used to measure blood levels of sugar and cholesterol, and the results were given to participants for their information. In our early studies within Health 2020 we also used the stored blood samples to measure levels of dietary markers, inflammation, lipids, vitamins and hormones.

We had not anticipated being able to ever measure genes, but the fast progress in gene-mapping technology handed us the ability to use these blood samples in a new way, to generate useful knowledge for controlling cancer.

We don't sequence whole genomes of HEALTH 2020 participants; that would be unnecessary and far too expensive. Instead, we perform a genome-wide association study: we extract DNA from the stored blood samples and scan selected locations on the genome (usually around 500,000 out of the ~3 billion DNA bases). These locations host common genetic variants (not rare mutations that put people at high risk of cancer), that make us unique individuals, much like the variants that influence our height or hair colour. These data are used by Cancer Council Victoria researchers to search for new variants associated with cancer risk.

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What can genetic data tell us?

When we compare the DNA scan results for people who have had a certain type of cancer to those from people who don't, we look for patterns: Do any genetic variants crop up more often in people with cancer? That way, we can identify 'suspect' variants that could be influencing the risk of cancer. In the last few years, HEALTH 2020 participants' data have been used to successfully identify genetic markers associated with prostate, breast, bowel, ovary and many other cancers.

Any single genetic variant does not make much of a difference to a person's chance of getting cancer but, collectively, the small risks associated with a large number of these variants can add up to something substantial.

Our researchers usually work in international collaborations, often combining results drawn from hundreds of thousands of participants.

This is because the wider the net we cast – looking at data from as many people as we can, from varied populations – the better our chances of detecting the small risks we search for.

Our ultimate goal is to develop models based on this genetic information that would give a person an indication of whether they were in the low-, mid- or high-risk category for a type of cancer. This information could inform their prevention and screening decisions, and in the future may lead to more effective treatments.

To maintain the privacy of HEALTH 2020 participants, their data is always anonymised, so that collaborating researchers cannot access personally identifying information.

Drinking alcohol and cancer

Dr Harindra Jayasekara has been working on understanding the links between drinking alcohol and the risk of cancer.

When he started his PhD in 2010, Dr Harindra Jayasekara, MD, was handed a treasure trove of data. When HEALTH 2020 was first started, most studies of its kind overwhelmingly asked their participants only about their alcohol drinking in 'the previous 12 months'. What makes the HEALTH 2020 data so valuable is that it was one of the few studies to also gather information about participants' lifetime consumption.

Alcohol is a known carcinogen, acting as a toxin, damaging body tissues and interfering with the body's metabolism. Dr Jayasekara wanted to find whether drinking at younger ages could affect cancer risk in later life. Since then, he and his colleagues have made some interesting – and important – findings.

Breast cancer

Drinking alcohol was already known to be a risk factor for female breast cancer, but the HEALTH 2020 data

identified a critical period that affects the rest of a woman's life: a woman who drinks in the years between her first monthly period and her first full-term pregnancy is at 35% greater risk of breast cancer than a non-drinker. In other words, women who drink before pregnancy have a 1 in 7 chance of being diagnosed with breast cancer, while women who do not drink before pregnancy have a 1 in 9 chance of the disease.

These years are likely important because the breast is more vulnerable to carcinogens during this period of its rapid growth. This process of change is regulated by female reproductive hormones (such as oestrogen) and alcohol has been shown to affect these hormones and disrupt the process.



Harindra Jayasekara

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Colorectal cancer

An analysis of colorectal cancers in HEALTH 2020 participants reinforced the finding that drinking alcohol, even at younger ages, can cause the most common types of colorectal cancer later in life. These findings contributed to the Cancer Council's public health campaign 'Drink Less, Live More' that was launched in 2015.

Future research

More recently, Dr Jayasekara and his collaborators have turned their attention to the link between drinking alcohol

and cancer *survival* as well as cancer *recurrence*.

One of these projects looks at less-common cancers, such as cancers of the pancreas, thyroid, kidney, blood and stomach.

Because these cancers are not common, and it is not good science to reach conclusions based on a small number of cases, HEALTH 2020 researchers are collaborating with other researchers worldwide, making this the largest-ever pooling project for alcohol-related cancer.

Hearts, bones and calcium intake



Previously we reported that Dr Belal Khan was researching calcium intake by HEALTH 2020 participants and whether this has an effect on heart and bone health. Dr Khan's research has also been used by Alexander Rodriguez for his recently completed PhD. Rodriguez examined sarcopaenia, (low skeletal muscle mass), and abdominal aortic calcification (AAC), a hardening of heart blood vessels that is a risk factor for heart disease and stroke.

His results suggest that people with low skeletal muscle mass were more likely to have AAC and more severe AAC than those people with higher muscle mass. These results were most obvious for people who were not considered obese (obesity was defined as a waist/hip circumference ratio of >0.90 for men and >0.85 for women). Maintaining muscle mass, and being physically active, can help reduce AAC and the associated cardiovascular risk.



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How is your data being used?

The information you have generously provided has been invaluable for research into many conditions including cancer, arthritis, cardiovascular disease and eye disease.

Below is a selection of scientific papers that have recently been published using data from Health 2020 participants. Some of this research has involved researchers from across Australia and around the world.

Del Gobbo, L. C., F. Imamura, S. Aslibekyan, et al. ω -3 Polyunsaturated Fatty Acid Biomarkers and Coronary Heart Disease: Pooling Project of 19 Cohort Studies. *JAMA Intern Med.* 2016 176(8): 1155-1166.

Dugue, P. A., A. M. Hodge, M. T. Brinkman, et al. Association between selected dietary scores and the risk of urothelial cell carcinoma: A prospective cohort study. *Int J Cancer.* 2016 139(6): 1251-1260.

Gaudet, M. M., M. Barrdahl, S. Lindstrom, et al. Interactions between breast cancer susceptibility loci and menopausal hormone therapy in relationship to breast cancer in the Breast and Prostate Cancer Cohort Consortium. *Breast Cancer Res Treat.* 2016 155(3): 531-540.

Heath, A. K., E. J. Williamson, D. Kvaskoff, et al. 25-Hydroxyvitamin D concentration and all-cause mortality: the Melbourne Collaborative Cohort Study. *Public Health Nutr.* 2016: 1-10.

Karahalios, A., J. A. Simpson, L. Baglietto, et al. Change in weight and waist circumference and risk of colorectal cancer: results from the Melbourne Collaborative Cohort Study. *BMC Cancer.* 2016 16: 157.

Rodriguez, A. J., D. Scott, B. Khan, et al. Low Relative Lean Mass is Associated with Increased Likelihood of Abdominal Aortic Calcification in Community-Dwelling Older Australians. *Calcif Tissue Int.* 2016 99(4): 340-349.

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