



# Health 2020

NEWSLETTER | SEPTEMBER 2020



## Health 2020 in 2020

When we first started this study in 1990, we named it Health 2000 to highlight its future-facing aspect. Then 2000 went by, and so we renamed it Health 2020. Now that this once-futuristic date is our present, and the study is still going strong, we thought we'd take the opportunity to celebrate this milestone by telling the story of Health 2020's evolution through its first 30 years.

**HEALTH 2020**

A study of lifestyle and health

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## How it started

Health 2020 was planned to be the flagship research platform for the newly formed Cancer Epidemiology Centre at Cancer Council Victoria in 1986. Dr Nigel Gray was keen that the research took advantage of the organisation's long-term stewardship of the Victorian Cancer Registry.

When Health 2020 was conceived, its design was shaped by research that showed that post-world war 2 migrants from Southern Europe were less likely to be affected by certain cancers. We wanted to see whether this might be due to aspects of their diet and lifestyle, which were notably different to those of Australians of British descent. Health 2020 actively recruited migrants from Southern European migrant communities; nearly a quarter of Health 2020 participants were born in Italy or Greece.

Thus, Health 2020 was designed to investigate prospectively the roles of diet and lifestyle in causing cancer and other non-communicable diseases. It was developed in parallel with the *European Prospective Investigation into Cancer and Nutrition* (EPIC) cohort at a time when diet and nutrition were considered important to cancer causation but there was little detailed information that would be adequate to inform prevention.

Our original research proposal encompassed a broad range of questions, with a strong focus on the influence of individual foods and food groups, macronutrients and micronutrients on the risk of cancer. To this end we also stored blood samples collected at baseline, to permit the analysis of dietary markers detectable in the blood, rather than relying on dietary questionnaire responses alone.

To enable research on heart disease and diabetes as well as cancer, we also took direct physical and clinical measurements of all participants.

## How it changed

As we addressed our research questions over time, we adapted our data collection at each follow-up to refine our approach and better answer remaining questions. We also repeated blood sampling and

physical measurements to be able to assess any effect of changes over time.

What we did not anticipate at the start of the study was the rapid growth in genomic technology and knowledge. Health 2020 blood samples, which we collected originally solely to measure dietary and other markers, became a highly valuable source of DNA to examine genetic risk factors for disease. This field of research has been our principal focus for the past 15 years.

## What we found

Health 2020 has produced over 900 scientific publications (and counting!). The most influential papers have come from pooling data with other cohorts in international consortia. Examples include the finding that overweight and obesity are associated with increased risk of many cancers as well as death from any cause; and the identification of common genetic variants associated with risk of breast, bowel and prostate cancer.

## Moving forward

Health 2020 continues to be a valuable resource, both for our own research as well as for collaborative studies with Australian and international research groups. Ongoing work led by Cancer Council Victoria researchers focusses on alcohol and other risk factors for stomach cancer (led by Dr Harindra Jayasekara – see also our 2017 newsletter), biological mechanisms underlying the effect of obesity on post-menopausal breast cancer (led by Professor Dallas English), and developing better prediction models for breast cancer risk (led by Associate Professor Robert MacInnis).

Looking ahead, Health 2020 has been joined by Cancer Council Victoria's next large cohort study, the Australian Breakthrough Cancer (ABC) Study. The ABC Study started in 2014 as a comprehensive, high-quality resource for national and international research into how to prevent cancer and other diseases.

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### Reference:

Milne RL *et al.* Cohort Profile: The Melbourne Collaborative Cohort Study (Health 2020). *Int J Epidemiol.* 2017 Dec 1;46(6):1757-1757i.

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## New Research

### Epigenetics

In our 2018 newsletter, we told you about our study concerning DNA methylation, a common natural process whereby methyl groups (each made up of one carbon atom and three hydrogen atoms) attach to sites in a gene's DNA and alter the gene's function. A methylated gene is 'switched off' and will not be active. Methylation is called an **epigenetic** rather than **genetic** mechanism because it regulates the function of genes in the body's cells without changing their DNA sequence.

The relationship between DNA methylation and cancer is now a very active research topic. Two recent studies are good examples. In these studies, our researchers analysed DNA from Health 2020 participants' blood samples, taken both at baseline and at the second round of follow-up (approximately 11 years later).

The researchers looked at whether, and to what degree, DNA methylation patterns are associated with **smoking** and with **alcohol consumption**. They identified many new associations between these two habits and DNA methylation and also showed that the methylation changes associated with them appeared largely reversible.

These studies add to existing findings of links between established cancer risk factors and DNA methylation and demonstrate that changing habits such as smoking and drinking – even later in life – could help reverse past damage, at least in part.

#### References:

Dugué PA *et al.* Smoking and blood DNA methylation: an epigenome-wide association study and assessment of reversibility. *Epigenetics*. 2020 Apr;15(4):358-368.

Dugué PA *et al.* Alcohol consumption is associated with widespread changes in blood DNA methylation: Analysis of cross-sectional and longitudinal data. *Addict Biol*. 2019 Dec 2:e12855.

### Changes in body weight over life

Another recent study using Health 2020 data analysed the association between obesity (as measured by Body Mass Index, BMI for short), and the risk of death. The researchers compared adults who had a healthy BMI in their early 20s and maintained a healthy BMI, with those who started with a healthy BMI but became overweight or obese as they aged.

The researchers found that the greater the increase in BMI, the higher the risk of obesity-related cancers, so that, relative to those who maintained a healthy weight, those who became overweight by middle-age were 30% more likely to develop one of these cancers, while those who became obese were 50% more likely.

These findings highlight the importance of weight management throughout adult life. The researchers conclude that, since obesity is already a major health issue and will likely increase for future generations, policies and prevention programmes are needed to target weight management starting early in life.

#### Reference:

Yang Y *et al.* Trajectories of body mass index in adulthood and all-cause and cause-specific mortality in the Melbourne Collaborative Cohort Study. *BMJ Open*. 2019 Aug 10;9(8):e030078.

**BMI** is calculated by dividing your weight in kilograms by your height in metres squared. The WHO has adopted BMI as an index of obesity: a BMI less than 18.5 indicates underweight, BMI 18.5-24.9 healthy weight; BMI 25-29.9 overweight and BMI 30 or greater as obese.





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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.

1. Dugué PA, et al. **Overall lack of replication of associations between dietary intake of folate and vitamin B-12 and DNA methylation in peripheral blood.** Am J Clin Nutr. 2020 Jan 1;111(1):228-230. doi: 10.1093/ajcn/nqz253. PubMed PMID: 31907529.
2. Papadimitriou N, et al. **Physical activity and risks of breast and colorectal cancer: a Mendelian randomisation analysis.** Nat Commun. 2020 Jan 30;11(1):597. doi: 10.1038/s41467-020-14389-8. PubMed PMID: 32001714.
3. Escala-Garcia M, et al. **A network analysis to identify mediators of germline-driven differences in breast cancer prognosis.** Nat Commun. 2020 Jan 16;11(1):312. doi: 10.1038/s41467-019-14100-6. PubMed PMID: 31949161.
4. Barrow TM, et al. **Analysis of retrotransposon subfamily DNA methylation reveals novel early epigenetic changes in chronic lymphocytic leukaemia.** Haematologica. 2020 Jan 9. pii: haematol.2019.228478. doi: 10.3324/haematol.2019.228478. [Epub ahead of print] PubMed PMID: 31919093.
5. Zhong J, et al. **A Transcriptome-Wide Association Study (TWAS) Identifies Novel Candidate Susceptibility Genes for Pancreatic Cancer.** J Natl Cancer Inst. 2020 Jan 9. pii: djz246. doi: 10.1093/jnci/djz246. [Epub ahead of print] PubMed PMID: 31917448.
6. Fachal L, et al. **Fine-mapping of 150 breast cancer risk regions identifies 191 likely target genes.** Nat Genet. 2020 Jan;52(1):56-73. doi: 10.1038/s41588-019-0537-1. Epub 2020 Jan 7. PubMed PMID: 31911677.
7. Kapoor PM, et al. **Combined associations of a polygenic risk score and classical risk factors with breast cancer risk.** J Natl Cancer Inst. 2020 May 2. pii: djaa056. doi: 10.1093/jnci/djaa056. [Epub ahead of print] PubMed PMID: 32359158.
8. Zhang H, et al. **Genome-wide association study identifies 32 novel breast cancer susceptibility loci from overall and subtype-specific analyses.** Nat Genet. 2020 Jun;52(6):572-581. doi: 10.1038/s41588-020-0609-2. PMID: 32424353.

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