

NEWSLETTER



Welcome to the Autumn 2021 edition of the INTERVAL Newsletter

Through the 'Blood Donors Studies' BioResource, samples and data from the INTERVAL study are contributing to a variety of research studies – we hope you enjoy reading about a few below. **Thank you for contributing to this valuable research tool!**

Research studies utilising INTERVAL data from the Blood Donors Studies BioResource

Restless legs syndrome (RLS) is a constantly recurring problem affecting the nervous system that can cause mental and physical health problems. RLS creates an overwhelming urge to move during the evening or night. This sensation causes impaired sleep, a reduced quality of life and an increased risk of depression, anxiety disorders, hypertension and, potentially, cardiovascular disease. As RLS is a common side-effect of frequent blood donation, the Blood and Transplant Research Unit (BTRU) in Donor Health and Genomics seeks to better understand the condition, thus improving donor health.

Find out more (lay summary on the BTRU website): <https://tinyurl.com/8j9d3d3h>

Research paper: <https://pubmed.ncbi.nlm.nih.gov/33239738>

Email: donorhealth@medschl.cam.ac.uk if you can't access any of the papers within this newsletter.

Researchers have used data from the INTERVAL study to perform **genome-wide association studies** (GWAS). These studies examine all of the common genetic variation in a population (i.e. "genome-wide") and identify associations between the variation and a disease or quantitative trait. For example, red blood cells (RBCs) play a critical role in oxygen transport and iron metabolism. Genomic analyses have identified thousands of small changes in the genetic code (variation) that correlate with differences in RBC characteristics (e.g. size, iron content, etc). Understanding this genetic variation is important as it contributes to health issues, such as anaemia (a condition in which you lack enough health red blood cells to carry adequate oxygen to your body's tissues) and heart disease.

Once genetic variations have been identified, researchers aim to understand the biological mechanism behind the association, which genes are involved and the function of these genes. One method to accomplish this task is a **recall-by-genotype** study. Individuals from the INTERVAL trial,

who have consented to join the National Institute for Health Research (NIHR) BioResource (<https://bioresource.nihr.ac.uk>), may be contacted to participate in a study, based on their genetic make-up. Volunteers, whom have been identified as having specific genetic variations which correlate to disease, donate blood and researchers then study characteristics of the RBCs within the samples.

Linking INTERVAL data to electronic health records

During the COVID-19 pandemic, the disease caused by the new coronavirus SARS-CoV-2, our researchers have been using the Blood Donors Studies (BDS) BioResource (www.donorhealth-btru.nihr.ac.uk/project/bioresource) to investigate whether genetic and other factors affect the risk of developing COVID-19. This work is possible through the ability to link to data from electronic health records (www.donorhealth-btru.nihr.ac.uk/project/electronic-health-records). We currently receive data about COVID-19 test results, hospital treatment, Intensive Care stay, General Practice (GP) records and information on Deaths and Cancer diagnoses. We will also be receiving Antibody Testing data, Vaccination data and Stroke Audit data for INTERVAL study participants to enable further research into COVID-19.

A very large international collaboration has collected:

- Information about proteins
- Electronic health record data
- Mendelian randomisation (MR) analyses (a statistical method that uses genetics to provide information about the relationship between an exposure and an outcome. A GWAS (see above) first identifies which genetic variants are used in a MR study).
- Information about drugs that might be of relevance to COVID-19

This data—from multiple data sources (including the INTERVAL study)—was used **to identify already existing drugs that can be adapted to manage or treat early stage COVID-19.**

Results suggested that already existing drugs targeting the *IFNAR2* gene and the *ACE2* gene could be used to manage patients hospitalised from COVID-19. The next step is to evaluate the safety and ability of *IFNAR2* and *ACE2* to produce the desired result (efficacy) against COVID-19 through randomised clinical trials.

Find out more (lay summary on the BTRU website): <https://tinyurl.com/h2jz837y>

Research paper: www.nature.com/articles/s41591-021-01310-z

Update on TRACK-COVID study

In May 2020 we began recruiting individuals into our new study, TRACK-COVID (www.trackcovid.org.uk), which aims to: (1) determine the risk factors for infection of the new coronavirus (SARS-CoV-2) and (2) investigate why only some people have symptoms. The primary aim is to understand the frequency and

evolution of symptoms compatible with COVID-19, the disease caused by the coronavirus. The secondary aim is to define and monitor the evolution of antibodies to SARS-CoV-2 infection and vaccines.

~90,000 individuals previously recruited into the INTERVAL, COMPARE and STRIDES studies were invited to participate. As of July 2021, ~20,000 have consented and provided COVID-19-related information using an online questionnaire. Participants answer this questionnaire on a monthly basis and will be invited to participate until December 2021, which will generate useful data for analysing symptoms associated with new COVID-19 variants (i.e. Alpha, Delta, etc). A subset of ~15,000 participants provided six weekly capillary blood samples which will be analysed for COVID-19 antibodies.

In May 2021, participants were notified that TRACK-COVID would be participating in the UK Longitudinal Linkage Collaboration (UK LLC; <https://ukllc.ac.uk>). This involves linking participants' de-identified study data to health and administrative records and storing this information in a Trusted Research Environment (TRE). A TRE is a highly secure space for researchers to access sensitive data. The UK LLC aims to answer pressing COVID-19 questions through accelerating progress in establishing a pioneering health data and research infrastructure. Participants were provided with the opportunity to opt out of their data being used in the UK LLC and all participants can opt out of this at any time by contacting the study helpdesk (helpdesk@trackcovid.org.uk). **We thank our Public Contributors for helping us write the email to TRACK-COVID participants, to inform them of this research.**

Blood and Transplant Research Unit (BTRU) in Donor Health and Genomics

Our 'Blood Donors Studies'—INTERVAL, COMPARE and STRIDES—fit under the umbrella of the BTRU in Donor Health and Genomics. Led by Emanuele Di Angelantonio, Professor of Donor Health, the Unit aims to: (1) address major questions about the health of blood donors, (2) produce strategies to improve blood donor safety and (3) ensure a steady supply of blood to the NHS.

Find out more about the Unit and our studies: www.donorhealth-btru.nihr.ac.uk

Interested in working with us? Email: donorhealth@medschl.cam.ac.uk

Visit our YouTube channel to learn more about our research:
www.youtube.com/channel/UCeS9CPB2_QGcBsnORnNQyjQ

Follow us on Twitter: @DonorHealthBTRU

As an INTERVAL participant we will continue to update you on the study. Published papers will be posted on our website: www.intervalstudy.org.uk/publications and we'll let you know, by email, when they are available. To make sure you receive our emails, please let us know, by emailing: donorhealth@medschl.cam.ac.uk, if you change your contact details.