

HEALTH

How people like you are contributing to the cure for cancer

A revolutionary medical study is attempting to crack the secrets of serious diseases. Those recruited for it tell Julia Llewellyn Smith why they volunteered



Being aware of what your body looks like inside is a real motivator
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In 2010 Dr Peter Craig received a letter sent by the Scottish chief medical officer to randomly selected middle-aged people, asking if he was interested in participating in UK Biobank, a revolutionary new research programme aiming to help scientists to understand why some people but not others succumb to diseases such as dementia, heart disease, arthritis and cancer. The aim was to eventually stamp them out.

Craig signed up. Soon afterwards he spent a couple of hours at a nearby centre answering various health questionnaires and submitting urine, blood and saliva samples to join the 15 million that UK Biobank has collected to date — enough to fill 91 bath

tubs. Over subsequent years he filled in various online questionnaires about diet and lifestyle.

This year Craig was invited to be one of Biobank's second wave. Volunteers were asked to be scanned, with Craig making a six-hour round trip to Newcastle from his home town of Glasgow for five hours of imaging assessments including a detailed brain MRI scan, a heart and abdomen MRI that measured how his heart pumped blood and how fat was distributed around his organs, an ultrasound of the carotid arteries, and a DEXA scan measuring bone density. Craig became the 50,000th person to be scanned by the world's biggest human

imaging project. He also had his height, weight and blood pressure measured, a blood sample taken and completed a lifestyle questionnaire and cognitive function and hearing tests. For a couple of weeks afterwards he had to wear a heart monitor.

It is quite a sacrifice to devote so much time, unpaid, to undergo procedures many regard as unpleasant and invasive but as a university researcher, Craig, 61, understands the importance of doing one's bit for science. "I thought it was a nice way of contributing to health research," he says. "Within the UK, but internationally as well, Biobank is unique because of its massive number of participants and its very extensive range of assessments."

Certainly, since it was founded 17 years ago, the participation of Biobank's 500,000 volunteers — recruited when aged between 40 and 69, when middle-aged health niggles first manifest, and now mainly in their late sixties — has led to some vital inroads into understanding our ageing population's health. Since the study began more than 44,000 participants have died, with the main cause of death being heart disease.

Tens of thousands of others have suffered from strokes, depression and hip fractures. But the range of data available about each individual helps researchers to grasp patterns of who was most susceptible to such illnesses and why.

"The amazing thing about Biobank is that it provides lots of images of people, which show their organs and how they're functioning in the context of a huge amount of information on their genetics, their lifestyle, their environment and their clinical history," says Professor Paul Matthews, head of the department of brain sciences and the UK Dementia Research Institute Centre at Imperial College London and chairman of the UK Biobank Imaging Working Group.

"It means what one can do is relate across these data sets to ask questions. For example, to what extent does genetics predict the size and shape and function of the brain? What factors are associated with increased environment risk and lifestyle risk?" he says.

Dr Naomi Allen, UK Biobank's chief scientist and professor of epidemiology at the Nuffield Department for Population Health, University of Oxford, says that its discoveries are already "having a real impact on the public". She gives the example of patients being able to take simple blood tests showing their risk of heart disease, which — if high — could lead them to be put on statins early in life.

"If we could identify women who are at high genetic risk of breast cancer, based on their entire genetic profile, we could bring them into screening programmes earlier. There are so many possibilities," she adds.

UK Biobank's findings are available to any researcher registered with the organisation. So far, this includes 33,000 researchers from 100 countries, who have published more than 6,000 papers on its data, more than half of which are peer-reviewed, and more than 2,200 papers have been published in the past year alone. More than 1,000 researcher registrations are received a month, alongside 100-plus applications for data a month, with both rates growing. "We build the car, but we let the worldwide research community drive it in the direction they want to take it," Allen says.

Allen cites a recent study by the University of Exeter that used Biobank's database to show how type 1 (insulin-dependent) diabetes — previously considered a disease most prevalent in children and teenagers, "actually happens at the same rate right up until your thirties and forties". Now GPs are testing people in that age range who present with diabetes symptoms for type 1 as well as type 2.

In cardiology, Biobank data was able to prove that trabeculae, which resemble skin

tags on the heart — and which until then, Matthews says, "no one had ever thought very much about" — play a key role in the heart's pumping function, meaning people without them were more at risk of cardiomyopathy, or diseases of the heart muscle. Another vital discovery was that the presence of subcutaneous fat, mostly found in women, puts people at much less risk of heart disease and diabetes than visceral (or belly) fat that's more common in men, leading to the development of a risk score for complications of diabetes based on the way that the fat is distributed in the body.

Such revelations are possible owing to UK Biobank's unprecedented scale. So far, it says, the study has collected 30 petabytes of data, more than would fill 15,000 laptops and which, at average household internet speeds, would take about 50 years to download. Matthews recalls when he was first approached in 2007 about Biobank in relation to research into dementia, the prospect of such a vast collation of data "seemed ridiculous. We were working hard to do those kind of experiments on 20 to 25 people so it seemed an absolutely impossible idea."

UK Biobank's centres in Newcastle upon Tyne, Stockport, Reading and Bristol, where scans take place, are designed to be run as slickly as possible so as not to abuse participants' good will. "People have to remain very still when they're having their images taken, even movements by a millimetre or so make a difference. So helping people feel comfortable enough to maintain that level of stability was a real feat," Matthews says.

Jeff Searle, 74, a former educational researcher from Gateshead, Tyneside, who was scanned in Newcastle in 2018 and then again in March recalls the process being very well organised. "I was expected at 2.30pm, immediately did a questionnaire about what medicines I was on, then was on the computers doing the various assessments and answering more questions and then it's the machines. It's a big deal, you have to strip right off, be in a surgical gown just as in hospital, but again there was very little waiting time and in the waiting areas, there were a lot of posters with information on what Biobank are doing and who they're working with across the world, with very interesting videos running."

Like all volunteers, Searle was not given any feedback about his health from the scans, although concerns flagged are passed on to the volunteer's GP. "I was happy to do it because I understand the importance of good data," he says.

The average UK Biobank volunteer tends to come from a certain demographic and is more likely to be female and to live in less socioeconomically deprived areas than nonparticipants. They are also less likely to be obese, smoke and drink alcohol on a daily basis.

"With all health studies participants are likely to be a little bit healthier and a little bit wealthier but because Biobank is so large, we still have around 88,000 participants who live in the most deprived areas of the country," Allen says. "[And] as long as you have

enough individuals across all levels of the factors that you're interested in — whether it's social deprivation, education, or ethnicity — the associations that you find between an exposure and an outcome are a lot more likely to be generalisable."

And how does UK Biobank persuade participants to be truthful about how much they really exercise and what they eat and drink — something that's notoriously hard to monitor? "Because Biobank is a prospective, longitudinal study, it tries as much as possible to get serial, multiple measures on each person, asking them the same questions on different occasions. That helps to achieve greater understanding of what the ground truth really is," Matthews says. "It's not perfect. But Biobank approaches this in what is currently probably a state-of-the-art of fashion."

Has he altered his lifestyle as a result of UK Biobank's findings?

"I have! I led one of the alcohol studies, and it was really frightening to learn there was no safe limit for alcohol. It affects our organs at any level, so I certainly decreased my alcohol consumption. It's also made me much more aware of the need to keep physically active and watch my diet, because fat distribution and muscle strength are really strong resilience factors. Being aware of what your body looks like inside is a real motivator."

Initially UK Biobank was funded by bodies such as the Medical Research Council and Wellcome, as well as the British Heart Foundation, Cancer Research UK, but more recent studies have been funded by huge pharmaceutical companies such as GlaxoSmithKline and Pfizer. Conspiracy theorists mutter that big pharma is harvesting patients' data (which is stored anonymously). "Biobank's data is available to everyone without regard to whether they're working for big pharma or in an academic community, in the UK or in Africa," Matthews says. "At this point, pharmaceutical companies have put in far more money than the government, with the full knowledge they will not have long-term proprietary access to the data. They're doing so so that it can be shared with the entire community. It's totally democratised science that was before only available to groups that had massive amounts of money."

As volunteers grow older and start to develop diseases such as Alzheimer's and Parkinson's, Matthews is anticipating UK Biobank's third phase. "We're moving — from my standpoint — into the most exciting period, which is being able to see what the determinants of those diseases are." Already, studies have begun on blood proteins to spot potential markers that he hopes can lead to "very low-cost tests to predict late-life diseases".

None of it would be possible without the volunteers' altruism.

"Being involved is a bit of a commitment but most people commit far larger chunks of time to voluntary work with charities and so forth," Craig says. "You do it in the same spirit, for the public good."