THIS WEEK

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Family connections

A high-profile arrest in California shows how the long arm of the law can now extend into DNA databases to check for relatives of suspected criminals.

Last week's arrest of a suspect in the Golden State Killer case in California has highlighted how DNA samples that have been volunteered for one purpose — in this case, genealogy — can be used for other reasons, often without the donor's explicit consent. Several ethicists have expressed concern about US detectives using a genealogy website in this way. Coming so soon after the reuse of Facebook data in political campaigns in the Cambridge Analytica scandal, it's another example of how new technology and techniques lead to unexpected conundrums, and how ethical and societal debate must catch up.

The case of the Golden State Killer, linked to at least 50 rapes and 12 murders between 1976 and 1986, had gone cold — although investigators believed they had a reliable sequence of the perpetrator's DNA. Next they needed a match. So, according to reports, they uploaded the data to a popular website that compares people's genetic information to trace their relatives — in effect, creating a profile for him. They got lucky: a match with family members led them to identify and arrest Joseph James DeAngelo.

Just like the Cambridge Analytica case, this one raises the question of how much control people have over information they give to public or commercial databases. DeAngelo's relatives submitted their DNA for the specific purpose of genealogy, which by definition requires the information to be shared and compared. Then they saw it used for something else without their consent. In discussions of the case, users of genealogy services are divided between those who say the police were justified, given the seriousness of the crimes, and those who were shocked by the move.

Such users have received other surprises. Thousands of people have discovered through genetic analyses that their parents were not who they thought they were. Others have found and been reunited with siblings they never knew existed. Such discoveries have implications for users' wider family members, most of whom won't have put their DNA in such a database.

In the California case, the involvement of the police adds an extra dimension. People who choose to upload their DNA could unknowingly be helping police to trace a relative — now and in the future.

Investigators have long coveted the genetic information held in others' databases. After the Swedish politician Anna Lindh was assassinated in 2003, Swedish police asked for access to a suspect's DNA stored in a biobank, so that they could compare it with DNA found at the crime scene. Their access was granted. But other requests have been turned down by courts. In 2006, the Norwegian Supreme Court said that police investigating a suspected armed robber, who had died six months after the crime, could not access his genetic information held by a hospital. The dead can't be libelled, but they can have their privacy invaded. And scientists in Belgium wrestled with these issues in 2016, when they confirmed the location of the 1934 death of King Albert I from blood samples collected there. They decided not to publish sequence details because of possible implications (including paternity and health) for his surviving descendants, including members of the current Belgian and British royal families.

To what extent can scientists and companies who collect such information anticipate future uses and make them clear to participants and customers? There are no easy answers, because many of those uses cannot be anticipated at the time. Still, a 2016 survey showed that online firms that collate and compare DNA for consumers are too vague about how it might be used (E. Niemiec and H. C. Howard *Appl. Transl. Genom.* **8**, 23–30; 2016). On the basis of what they do know, many organizations should take steps to inform people better. (In the California case, users of the site, GEDmatch, were told that "other uses" were possible and that they should remove their data if this was unacceptable.)

"Ethics should lead the conversation, rather than playing catch-up."

If police can use genetic databases to catch killers — even those who are distant relatives of individuals who have submitted their DNA — then perhaps more people will sign up to share their DNA. But they should be told that this is a possibility, and be given the choice to opt out. Meanwhile, more geneticists, ethicists and lawyers need to debate other potential ways in which genetic information is likely to be used, so that ethics leads the conversation, rather than playing catch-up. ■

All that ails you

To improve health care, researchers need to study diseases as they occur: in combination.

When public-health researcher Tolullah Oni travelled from London to South Africa to study HIV, she soon realized she would have to broaden her focus. Physicians there were grappling with twin epidemics — HIV and tuberculosis. The infections often coincide, and so clinicians were working to integrate their treatment of the two diseases.

But Oni found that many of her patients were dealing with a third problem. "We started seeing people who came in with good adherence to their medicines, but somehow someone had missed the fact that their blood pressure was through the roof," she says. To bring them back to health, she would need to treat non-communicable diseases such as high blood pressure and diabetes as well. "We were treating conditions and not people." Oni went on to study the phenomenon in her patient community (T. Oni *et al. BMC Infect. Dis.* **15**, 20; 2015) and is hoping to take the lessons learnt from integrating care of HIV and tuberculosis and apply them to other combinations of diseases.

People are complicated, and their medical problems rarely come neatly packaged as the single diseases that scientists and doctors study. A report released on 19 April by the UK Academy of Medical Sciences (see go.nature.com/2jhmcvf) details the challenges of studying and treating individuals who have multiple medical conditions, known as multimorbidity. Variations in the definition and frequency of multimorbidity across populations have led to wide estimates of its prevalence, ranging from 13% to 95% of patients globally. The report offers a list of recommendations on what health-care providers can do to address the problem of multimorbidity, and identifies the knowledge gaps that need to be filled.

Researchers should take heed: if their work is to translate to the real world, more scientists — at the clinic and the bench — should shift their focus to look at interactions between disorders.

Multimorbidity seems to be growing in countries where the population is ageing and thus more people are living with chronic diseases, and in countries grappling with chronic infectious diseases such as HIV. Health-care providers should look again at how doctors tend to specialize in specific disorders, when it might be better to arm them with the ability to recognize and treat a range of conditions.

Clinical trials have historically focused on single diseases. They often exclude participants with other conditions to boost the chance of getting a cleaner data set (and to reduce risks of unintended harm). But this is beginning to change as part of a push to lower eligibility requirements for many clinical trials. Researchers are also increasingly focusing on supplementing data from carefully controlled clinical trials with 'real-world evidence' — much messier data collected from people who may be taking multiple medications and dealing with multiple conditions. Such studies are a good way to start understanding the effects of multimorbidity. In this issue, a World View describes how to make sure people with anxiety disorder and other complications are integrated into clinical research of pain treatments (see page 7).

There is more to be done. As the report highlights, clinical researchers need to characterize multimorbidity around the world, looking at which conditions are most likely to coincide and in which populations. Already, evidence shows that this varies dramatically by location and wealth. More-deprived individuals in wealthy countries, for example, might be more likely to have multiple chronic diseases; whereas in poorer countries, wealthier individuals might be more likely to have multiple conditions.

"Multimorbidity seems to be growing in countries where the population is ageing."

Such studies could identify the most prevalent and harmful clusters of disease — and so help to focus basic research. Bench scientists also tend to focus on one disease at a time, even if their work sometimes yields insights into a range of conditions. More effort should be put into studying complex combinations of disorders and how they — and their treatments — interact. Studies of ageing, for example, are detailing the causes of inflammation and its impact on multiple organs in the body (M. N. Bouchlaka *et al. J. Exp. Med.* **210**, 2223–2237; 2013).

This requires support from funders, and a wider recognition that the most tractable projects with the cleanest, easiest to interpret results might not be the most worthy of funding. Studying diseases in combination is challenging, but computational and laboratory tools are increasingly available to handle complex data sets and tease out meaning from messy data.

Some funders are already taking steps in this direction: an upcoming workshop held by UK charity the Wellcome Trust, the UK Medical Research Council and other organizations will look at how research can better tackle multimorbidity. This movement needs support in the coming years. Awareness of multimorbidity has been growing steadily: now the question is how best to deal with it. ■

ANNOUNCEMENT

Human embryo and stem-cell research

Research using human embryos and embryonic stem cells draws intense ethical scrutiny and places demands on scientists, funders and journals to follow the relevant regulations. As a publisher of such work, *Nature* and the Nature journals take this responsibility very seriously. For many years, Nature journal editors handling manuscripts on human embryo and stem-cell research have assessed the ethical oversight of the work when deciding whether to publish it. We are now formalizing and amending aspects of this publication policy.

Nature journals encourage stem-cell scientists to embrace guidelines agreed in 2016 by the International Society for Stem Cell Research (ISSCR) as they design, execute and report their research. These 'Guidelines for stem cell research and clinical translation' describe rigorous standards for stem-cell research consistent with international policies that govern biomedical science and clinical trials. To encourage scientists to follow these guidelines, we have identified categories of manuscripts for which we will require authors to send an accompanying ethics statement or will consult an ethicist reviewer.

Under this policy, Nature journals will require an ethics statement from the authors for papers that involve human embryos or gametes, and for clinical studies of cells derived from pluripotent stem cells. This statement must highlight ethical oversight of the work, including the review boards specialized in embryo research that approved it, and details of the consent process for cell donors and recipients.

For manuscripts that we consider especially sensitive, Nature journals will request assessment by an independent ethicist alongside scientific peer review. Such manuscripts will include, but will not be limited to, those reporting genome engineering of human embryos or clinical work with gametes or cells derived from pluripotent stem cells. These ethicist reviewers may provide guidance on formulating the ethics statement to ensure accurate and transparent reporting of approval conditions. Authors may be asked to submit redacted informed-consent documents and review-board documents for evaluation by the ethicist reviewer.

Independent ethics review will also be required for manuscripts reporting work in which intact human embryos or embryo-like structures are kept alive for close to 14 days, a time point that corresponds to the formation of the primitive streak and the acquisition of organismal potential.

At present, many countries — and the ISSCR guidelines — prohibit culture beyond 14 days, a restriction that reflects the conclusions of the 1984 UK Report of the Committee of Inquiry into Human Fertilisation and Embryology (also known as the Warnock report). Whether this rule should be relaxed is currently being debated, triggered in part by technological advances that enable scientists to reconstruct human embryo-like structures from stem cells.

As this and other debates unfold, we anticipate the need to revisit some aspects of our policy in accordance with shifts in best practices for the stem-cell field, driven by advances in science and technology and evolving social norms. *Nature* fully supports an inclusive approach to such discussions, involving broad consultation and dialogue. We hope that our policy complements these efforts by scientists, ethicists, regulators, policymakers and funding agencies. ■