Editorial: Topical ethical issues in the publication of human genetics research

David Curtis[1,2], Editor-in-Chief and François Balloux[1], Senior Editor

[1]UCL Genetics Institute, UCL, Darwin Building, Gower Street, London WC1E 6BT.
[2]Centre for Psychiatry, Queen Mary University of London, Charterhouse Square, London EC1M 6BQ.

Correspondence:
David Curtis *d.curtis@ucl.ac.uk*
00 44 7973 906 143

The original name of the *Annals of Human Genetics* was the *Annals of Eugenics* and the early contributors to the journal had a historical involvement with what was to become the eugenics movement. In this context, the *Annals* bears a special responsibility to promote the highest ethical standards and to look closely at its own role as a publisher of genetics research. This may extend beyond complying with the general standards of ethical publishing as promoted by organisations such as the Committee on Publication Ethics (COPE) (https://publicationethics.org/about/our-organisation), in particular because there may be issues which are very specific to human genetics. In this editorial we focus on a few which seem to be especially topical and relevant and consider how the *Annals* should respond.

We begin by noting that once scientific findings are published there can be no control over the use to which results are put. Nevertheless, we feel that some findings are more obviously open to abuse than others and that it may be possible to make some value judgements about the relative risks and benefits which might be expected from their publication. For each study there may be a trade-off between a positive scientific value which adds usefully to our knowledge and understanding against a negative value in terms of potential for abuse, which can be considered as the 'societal value' of a study.

The *Annals* has a role in validating and promoting research findings that are technically sound. We further believe the *Annals* should aim to publish studies with an expected globally positive societal value. While we appreciate there may be a considerable degree of subjectivity in the assessment of the societal value of a piece of science, we do not consider that declining a submission on such a basis would amount to censorship. If we declined to consider a submission, it might still be published elsewhere.

In this light, we discuss the following issues which we regard as troubling:

1. Exaggerated claims made for the predictive ability of genetic testing.
2. The use of compulsory DNA collection by repressive regimes.
3. Genetics research which benefits privileged rather than disadvantaged groups.

Genetic research may identify individual variants associated with phenotypes or alternatively multiple variants may be jointly used to construct polygenic scores. In either case, claims may be made that genotypes "predict" the phenotype in question or that they identify subjects who are at "increased risk". This information may be delivered direct to consumers and can be based on

genotype information which the customer themselves provides to interpreting services, making regulation impossible.

With few exceptions, the actual predictive power of the tests is low, with single variants being associated with only modestly increased risk and polygenic scores typically explaining 10% of the variance of a trait or of phenotype liability. Tests are marketed to gain insight into one's own genetic make-up or that of one's children or even, most worryingly, for embryo selection (Kaiser, 2019). However, in our view the gap between the perceived and actual power of these tests means that the risk of consumers misunderstanding the implications of their results is unacceptably high. In terms of disease prediction, polygenic scores tend to yield odds ratios between highest and lowest quantiles of around 5 to 10 whereas health epidemiologists point out that even an odds ratio as high as 100 may not result in a clinically useful test (Wald and Old, 2019). In the light of these considerations, we will be reluctant to consider studies whose main aim seems to be to produce quantitative estimates of risk without yielding insights into underlying biological mechanisms. This will be especially the case for traits without health consequences but which might be seen as socially desirable, such as skin colour, athletic ability or intelligence.

We are aware of credible reports of collection of DNA samples without consent by repressive regimes. We recognise that there is a legitimate role for DNA identification in criminal investigations and that law enforcement agencies may acquire and hold such information in accordance with transparent and ethically acceptable processes. However, we would not regard the collection of DNA samples without consent from large numbers of people as being ethically acceptable, especially if the purpose for this activity is unclear. It has been proposed that DNA-profiling might be used in combination with biometric resources to support "genomic surveillance" but an alternative possibility is that it would allow the identification of individuals for organ donation, which might be carried out on an involuntary basis (Moreau, 2019; Robertson, Hinde and Lavee, 2019). Bearing this in mind, we would not consider submissions whose major aim seems to be to facilitate the identification of individuals or minority groups in order to facilitate repressive measures. Additionally, we will have a high threshold for assurance that DNA samples used for population studies have been freely donated with full informed consent.

There is a belated recognition that genetic studies have tended to focus on subjects with white, European ancestry. The practical benefits arising from this research may be disproportionately valuable for subjects with similar ancestry (Martin *et al.*, 2019). Tests which focus on known pathogenic variants derived from subjects with one ancestry may have a high false negative rate for subjects of other ancestries. In order to address this, we expect submissions which might exacerbate this problem to explicitly address issues around generalisability and potential inequity in the discussion section. Also, we will tend to look favourably on submissions which seek to redress this balance, for example by assessing the frequencies of known pathogenic variants in understudied populations and/or by attempting to identify novel pathogenic variants which are especially relevant to them.

There are doubtless other areas in human genetic research where ethically or societally problematic issues may arise. We will endeavour to be vigilant regarding these and to strive to deal with them appropriately. We welcome further discussion from readers, contributors and other interested parties on these issues.

References

Kaiser, J. (2019) 'Screening embryos for complex genetic traits called premature', *Science (New York, N.Y.)*. NLM (Medline), pp. 405–406. doi: 10.1126/science.366.6464.405.

Martin, A. R. *et al.* (2019) 'Clinical use of current polygenic risk scores may exacerbate health disparities', *Nature Genetics*. Nature Publishing Group, 51(4), pp. 584–591. doi: 10.1038/s41588-019-0379-x.

Moreau, Y. (2019) 'Crack down on genomic surveillance', *Nature*. Nature Research, pp. 36–38. doi: 10.1038/d41586-019-03687-x.

Robertson, M. P., Hinde, R. L. and Lavee, J. (2019) 'Analysis of official deceased organ donation data casts doubt on the credibility of China's organ transplant reform', *BMC Medical Ethics*, 20(1), p. 79. doi: 10.1186/s12910-019-0406-6.

Wald, N. J. and Old, R. (2019) 'The illusion of polygenic disease risk prediction', *Genetics in Medicine*. Nature Publishing Group, pp. 1705–1707. doi: 10.1038/s41436-018-0418-5.