the tobacco industry are unlikely to become soulmates (a sensible position) but they could be collaborators.

The tobacco industry and its products have to change. Combustible tobacco products are unnecessarily toxic and carcinogenic, as are most oral tobacco products. The future ought to bring reduced toxicity and carcinogenicity and probably a switch from combustible to non-combustible products and to better sources of nicotine replacement therapy. Collaborative research might seem a pipe dream to people, including myself, who have decades of experience of industry duplicity; but if product regulation becomes a reality, as it might be shortly in the USA, trying to work together is timely.

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I declare that I have no conflict of interest.

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Paper of the year 2007

Each year since 2003,[1–4] members of *The Lancet*'s International Advisory Board (IAB) have been asked to nominate the research papers published in the past year that make the greatest potential contribution to clinical research. The request invites incredulity as to how even such seasoned researchers could possibly be both adequately informed about current publications and sufficiently clairvoyant to identify the enduring research landmarks of 2007. The unashamed answer is that the process is not a systematic exercise, but an opportunity to celebrate research and researchers, enriched by the passion of colleagues about the papers that excited them most in the past 12 months. The results are a dozen must-reads (panel) that reflect the importance of public health, the increasing role of genomics, and the recognition of Asia as a major contributor to research.

Despite the many excellent papers from prestigious scientific and medical journals, the choice this year was remarkably straightforward. After ranking the papers, more than half of *The Lancet*'s editors had the same first choice: The Wellcome Trust Case Control Consortium's *Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls*.[5] Indeed, as soon as this study was published, the findings created repercussions in the medical,[6] scientific, and popular press. The American Association for the Advancement of Science cited human genetic variation as *Science*'s breakthrough of the year.[7]

The nomination from *The Lancet*'s IAB member read: "Over the past year there were a few papers that I did enthusiastically mail to friends and acquaintances with an exclamation mark: 'See!' My preference is The Wellcome Trust Case Control Consortium study. First, it showed by example the unique superiority of the case-control design for genetic epidemiology—a point that was already argued in *The Lancet* by Clayton and McKeigue.[8] Second, it demonstrated that for genetic discovery one does not need familial linkage studies, nor familial

***Panel:* Nominations for *The Lancet*'s Paper of the year, 2007**

Barreto ML, Genser B, Strina A, et al. Effect of city-wide sanitation programme on reduction in rate of childhood diarrhoea in northeast Brazil: assessment by two cohort studies. *Lancet* 2007; **370:** 1622–28.

Fraser C, Hollingsworth TD, Chapman R, de Wolf F, Hanage WP. Variation in HIV-1 set-point viral load: epidemiological analysis and an evolutionary hypothesis. *Proc Natl Acad Sci USA* 2007; **104:** 17441–46.

Gray RH, Kigozi G, Serwadda D, et al. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. *Lancet* 2007; **369:** 657–66.

Lartigue C, Glass JI, Alperovich N, et al. Genome transplantation in bacteria: changing one species to another. *Science* 2007; **317:** 632–38.

Ravdin PM, Cronin KA, Howlader N, et al. The decrease in breast-cancer incidence in 2003 in the United States. *N Engl J Med* 2007; **356:** 1670–74.

Stukel TA, Fisher ES, Wennberg DE, Alter DA, Gottlieb DJ, Vermeulen MJ. Analysis of observational studies in the presence of treatment selection bias. *JAMA* 2007; **297:** 278–85.

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Takahashi K, Tanabe K, Ohnuki M, et al. Induction of pluripotent stem cells from adult human fibroblasts by defined factors. *Cell* 2007; **131:** 861–72.

The Wellcome Trust Case Control Consortium. Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls. *Nature* 2007; **447:** 661–78.

Wahlgren N, Ahmed N, Dávalos A, for the SITS-MOST investigators. Thrombolysis with alteplase for acute ischaemic stroke in the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST): an observational study. *Lancet* 2007; **369:** 275–82.

Wolfson LJ, Strebel PM, Gacic-Dobo M, for the Measles Initiative. Has the 2005 measles mortality reduction goal been achieved? A natural history modelling study. *Lancet* 2007; **369:** 191–200.

Yin P, Jiang CQ, Cheng KK, et al. Passive smoking exposure and risk of COPD among adults in China: the Guangzhou Biobank Cohort Study. *Lancet* 2007; **370:** 751–57.

Yu J, Vodyanik MA, Smuga-Otto K, et al. Induced pluripotent stem cell lines derived from human somatic cells. *Science* 2007; **381:** 1917–20.

controls, but that more or less consecutive cases from the general population and a control group representing that population will be efficient and powerful. Third, it showed that genetic admixture in populations need not be a problem, if the study is restricted to persons of reasonably homogeneous ethnicity—a point already made in *The Lancet* by Cardon and Palmer.[9] As such it is a milestone: not just methodologically, but also by its clear explanation of difficult concepts of design and analysis (in boxes). Finally, it also showed that the number of hits is relatively few and that genetic associations are weak."

The study identifies two dozen genetic associations in cohorts of 2000 patients with one of the following disorders: bipolar disorder, coronary artery disease, Crohn's disease, hypertension, rheumatoid arthritis, type 1 diabetes, or type 2 diabetes. All are multifactorial diseases for which both nature and nurture have an aetiological role. Whilst the associations are casual, rather than causal, the genes identified will help to elucidate the molecular pathways that underpin current understanding of disease models. The design will also inform future research, not only by indicating candidate genes but also by demonstrating the economic and technical feasibility of large-scale genome-wide association studies.

In addition, the editors were impressed by the ethos of this study. Over 50 UK centres have collaborated. The 12 members of the management committee were keen that all participants should share equally in this honour, so at the committee's request, no photographs of the lead authors are reproduced, as is usually customary here for Paper of the year. This spirit of selflessness is also evident in the commitment to make the study's software and data available to other research groups.

What remains to be determined is the extent to which the statistical significance of genome linkage studies translates into clinical significance for patients and populations, either through enhanced diagnosis or more effective treatments. Furthermore, future studies must address the multiethnic and fluid nature of contemporary populations if such work is to become generalisable. But a new era in genomic research has begun, an era in which such questions are being asked.

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Hugging the kilogram

The best way to "get any insight into the nature of those parts of the creation, which come within our observation", argued Stephen Hales (1733), "must in all reason be to number, weigh and measure". And to illustrate the point he invented the manometer. Nonetheless, a good many years were to elapse before medicine was willing or able to adopt the Reverend Hales' advice. When *The Lancet* hit the streets for the