On a fundamental level, genetic science is forcing a re-examination of the concept of normality itself, by showing that everyone's genome is different and that we are all in some sense "abnormal." We each carry genetic variants, many of which will have no detectable impact in normal circumstances, but some undoubtedly will alter our risk of disease or may, with a partner carrying similar variations in their genomes, result in the birth of a child with a recessive genetic disorder.

Genetics also raises interesting questions about causation and about responsibility for adverse health events. For example, do people with a genetic predisposition such as factor V Leiden who develop venous thrombosis on long haul flights do so because of genetic susceptibility or because of the flight itself?[9] Is the airline or the person at fault? To what extent should society regulate to ensure a safe environment only for the majority? Or should the standards be set so that all people with susceptibilities are protected?

Seeking commercial rewards from new medical tests or treatments is not new; it is often productive, provided the tests and interventions are effective and the profits are reasonable. But quite often these standards are not met. The enormous investments needed to exploit genetics may have driven a more exuberant set of claims than usual, designed to appeal not only to the public but also to investors. Each new technology brings a crop of exaggerated claims. Even the discovery of radioactivity led to a new batch of "cure all" patented medicines, which enjoyed considerable popularity until the death of the American tycoon E M Byers of radium poisoning in 1932.[10] The appeal of medical "snake oils" is an enduring attribute of human gullibility, not of genetic science.

The antidote to genetics as a driver of medicalisation lies in remaining sceptical and level headed. Genetic claims, tests, and products should be treated in the same way that other medical markers and interventions are increasingly treated: with rigorous evaluation. The successful management of genetic medicalisation will depend on clinical evaluation, integrity, and transparency and on providing accurate information to consumers and patients. Public education about interventions based on genetic science will also be needed to prevent inappropriate social responses that may either lead to discrimination or, conversely, prohibit the adoption of tests and treatments that can reduce or prevent disability. Genetic technologies have the potential to be of major benefit to society, but their introduction must be measured, attentive to the social and ethical considerations of the day, and, most importantly, based on best evidence.

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Medicalisation, limits to medicine, or never enough money to go around?

Spending on preventive treatments that help a few is unaffordable

Ivan Illich, in *Limits to Medicine*, commented: "The more time, toil and sacrifice spent by a population in producing medicine as a commodity, the larger will be the by product, namely the fallacy that society has a supply of health locked away which can be mined and marketed."[1] Rich Western societies are investing in preventive treatments that will benefit only a minority of those who take them for a long time, a situation well illustrated by the statins. Widespread use of statins is scarcely affordable in the developed world and unachievable in developing countries, although the drugs are still marketed heavily there. Using resources to purchase statins means other effective treatments may not be available.

From the perspective of the pharmaceutical industry, statins are an ideal group of drugs. They are, with one exception, safe and free from common side effects. They achieve a premium price and potentially have an increasingly wide market in the primary and secondary prevention of cardiovascular disease. About 11.5 million adults (5.4% of the adult population) in the United States are currently taking either atorvastatin, simvastatin, or pravastatin, all of which are in the top 40 most commonly prescribed pharmaceuticals in the United States.[2] Indeed, atorvastatin (Lipitor) is now the biggest prescription-only drug in the world.

It is paradoxical that while achieving benefits in reducing mortality and major morbidity, the statins are the latest drugs to present a major challenge for health policy.[3] Medical research in the late 20th century has helped define the effectiveness of many medicines, particularly in areas of chronic disease such as cardiovascular medicine and oncology. In developed countries, it is in the prevention of disease that most research now takes place. Treatment for acute health problems, particularly those found predominantly in

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the developing world, is not the subject of such concentrated drug development.[4]

Most treatments that are intended to prevent disease, if they work at all, have only a modest impact on major morbidity and mortality. The increasing number of patients included in the clinical trials of statins bears testament to the increasingly small treatment effects that are of interest. The 4S trial was the first trial to establish the effectiveness of statins in the reduction of major morbidity and mortality, comprised 4444 patients.[5] The heart protection study comprised over 20 000 subjects.[6] The 4S trial had sufficient power to identify a 5% absolute reduction in mortality as statistically significant nine times out of 10. The heart protection study was similarly powered to find a 2% reduction in mortality. Treatment effects in the trials were accrued over a number of years, which may appear to dilute benefits further.

Treating for one year 1000 people who had previously experienced a myocardial infarction would be expected to avoid four deaths, six non-fatal myocardial infarctions, and two non-fatal strokes.[7] Statins seem to exert a similar relative benefit (relative risk or hazard ratio) for patients at different levels of cardiovascular risk. This means that patients at higher risk face the prospect of larger absolute benefits. Conversely, those patients who face a lower risk, such as those without established coronary heart disease, stand to benefit to a lesser extent in absolute terms. Extending therapy to a non-diseased population may also have important ethical implications, as treatment with statins may lead to perceptions of illness. The trial of pravastatin for primary prevention by WOSCOP (the west of Scotland coronary prevention study) would indicate that of 10 000 patients treated with a statin for five years, 9755 would receive no benefit.[8]

The benefits from statins seem similar to the absolute reduction in deaths attributable to antiplatelet therapy in high risk subjects, supporting the notion that statins may be "the new aspirin." Many may argue that treatment with a statin is best practice. However, for a health system, the cost of achieving these benefits among the minority of patients who avoid serious events is staggering, and the resources consumed may be better used elsewhere. In the United Kingdom, the acquisition cost of statins is about £1 ($1.4; €1.6) a day—compared with a fraction of a penny for aspirin. Health economics may seem to go some way to justify the acquisition costs of statins, but economic analyses are often dependent on strong assumptions and hypothetical benefits not observed within the time periods of the trials. For example, although the WOSCOP trial followed 6595 men for mean 4.9 years,[9] the benefits for therapy included in the economic analysis were derived mostly from extrapolations at the end of the trial, rather than the very modest benefits estimated from within it.[8]

Whereas the longer term benefits of therapy beyond the period covered by the randomised trials are unknown, the acquisition costs are more immediate and assured, providing support for the adage that the two certainties in life are death and taxes. Although the costs of widespread therapy with statins in the United Kingdom are considerable, they may still be affordable. Costs in other health systems, such as those in the central and eastern European countries, may be crippling,[10] especially as statins are similarly priced in those countries as in the much richer, western European countries (ostensibly to avoid parallel importing). The Baltic states of the former Soviet Union have around £30 to spend per capita each year on pharmaceuticals, about 20% of that available to countries in western Europe.

The implications of medicalisation and the increasing use of pharmaceuticals are clear. In the United Kingdom—and other countries in the Organisation for Economic Co-operation and Development (OECD) on average—the percentage of public expenditure on pharmaceuticals as a percentage of gross domestic product has increased from 0.4% in 1970 to 0.7% in 1996.[11] During this time total expenditure on pharmaceuticals has also increased as a percentage of all health spending in the United Kingdom, from 12.5% in 1970 to 16.1% in 1996. Jacobzone comments: "The average share of GDP [gross domestic product] has increased in most OECD countries by around 50% since 1970, which means that pharmaceutical expenditure in real terms has increased on average 1.5% more than GDP growth."[11] As a consequence, pharmaceutical companies are also increasing in size and wealth. Using market capitalisation as a measure, the larger companies are now competing directly with countries as financial entities on the world stage—Pfizer is ranked 17 compared with Australia (11), Sweden (19), and Singapore 39.[12]

Regardless of the available resources, all countries are making difficult choices between treatments—for example, the current debate in the United Kingdom about the availability of interferon beta on the NHS. In the lower income countries, questions may be qualitatively different. Knowing man cannot choose but pay, how have we cheapened paradise?

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