Personalised Medicine: The Way of the Future?

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Big claims for personalized medicine

- *We are in a new era of the life sciences, but in no area of research is the promise greater than in personalized medicine.*— Barack Obama, as a Senator introducing US Genomics and Personalized Medicine Act 2007
- But US presidents tend to make large claims—JFK even claimed to be a Berliner!
- So let's hear from a genetic scientist...

Francis Collins, The Language of Life (2010)

- *We are on the leading edge of a true revolution in medicine, one that promises to transform the traditional "one size fits all" approach into a much more powerful strategy that considers each individual as unique ... Although the scientific details to back up these broad claims are still evolving, the outline of a dramatic paradigm shift is coming into focus…[Y]ou have to be ready to embrace this new world.*

Do I? Questions to ask

- 1. Are these predictions justified by the evidence base?
- 2. If so, are there still ethical debates about how to implement personalized medicine?
- 3. If not, why are these claims being made?

1. What's the evidence, past and present?

- Plans to spend $416 million on a four-year PM plan were announced in December 2011 by the US National Institutes of Health. Private sector interest is also intense.
- But Human Genome Project (HGP) was also very generously funded, without having so far produced correspondingly weighty results for translational medicine.

Another ‘paradigm shift’?

- “Indeed, after 10 years of effort, geneticists are almost back to square one in knowing where to look for the roots of common disease” (Wade 2010 on HGP).
- Productivity in drug development actually *declined* after the HGP announced its completion, as did new license applications to the US Food and Drug Administration (Kimmelman 2010).

A necessary reality check

- Current genetic tests and molecular diagnostics only apply to about two per cent of the US population (United Health 2012: 3).
- Poll of 2760 US patients and physicians in 2012 indicated that doctors had only recommended personal genetic tests for four per cent of their patients.
- Gradual process of incremental change, consistent with past trends in diagnostic innovation, but not yet paradigm shift .

The strongest evidence base: pharmacogenetics

- Pharmacogenetic drug regimes could spare patients overtreatment that will do them more harm than good by minimising adverse drug reactions and adjusting treatment to cancer's genome as well as patient's.
- Not limited to oncology: H3 Project (Human Heredity and Health in Africa) applies genome scanning and sequencing to HIV/AIDS, tuberculosis and malaria.

Example of PM from cancer care

- Gene-specific drug Vemurafenib (Zelboraf) for aggressive melanoma extended life span of **25%** of patients 16 months (9 months in conventional treatment); 75% didn't benefit. (Sosman et al. 2012, NEJM)
- However, a genome-wide analysis study on kidney cancer patients (Gerlinger et al. 2012, NEJM), published a month later, was much more pessimistic.

Why second study is discouraging

- Single tumour found to have many different genetic mutations at different locations.
- Two-thirds of genetic faults identified not repeated in same tumour, let alone in others metastasized through body.
- If pharmacogenetic drug targets one mutation, it may not work on others.

Non-pharmacogenetic success

- Conversely, progress in cancer care is still possible with ‘one size fits all’ treatments, even for genetically linked cancers.
- Single daily 600mg dose of aspirin resulted in 63% reduction in colorectal cancers in patients with hereditary Lynch syndrome. (Geddes et al. 2011)

Me Medicine: the full range

Personalised medicine comprises very wide range of procedures:

- 1. Direct-to-consumer genetic tests
- 2. Pharmacogenetics
- 3. Private umbilical cord blood banking
- 4. Enhancement technologies such as neurocognitive and drug treatments to produce ‘the best me I can possibly be’

Me vs. We Medicine

- Pharmacogenetics, have a good evidence base, but other forms of MM are largely unproven and sometimes harmful.
- By contrast, We Medicine (vaccination, screening and other public health measures) produced greatest expansion in life expectancy but is now threatened by austerity cuts and public distrust

Hostility to vaccination worldwide

- Vaccination programs are in profound trouble: US and UK campaigns against MMR vaccine.
- India: reaction against vaccination of young girls against the human papillomavirus implicated in cervical cancer.
- Muslim areas of northern Nigeria, which accounts for about 45% of polio cases worldwide: WHO polio vaccination campaign was boycotted as Western plot to spread HIV and AIDS through adulterated injections.

2. Economic and ethical questions

- Gene-specific drugs will probably be very expensive because of small market (e.g. Xalkori for lung cancer, price $115,200 p.a.)
- If patients who can benefit will be minority, would it be fair to devote majority of our scarce resources to them? Not just rhetorical question.

Social justice and individual health

- In 19th c., rich and poor alike were vulnerable to epidemics such as cholera, smallpox and typhus, so public health measures served all equally
- This is still true of pandemic flu, but more typically, infectious disease has been replaced by cancer and cardiovascular disease as main cause of mortality; illness has been individualised.

Stratified medicine in two senses?

- 1. Clinical 2. Economic and social
- Will personalised medicine increase social and economic inequality?
- It’s not obvious that the poorest will necessarily be the have-nots if PM gains ground, but publicly funded systems will find themselves denying some patients treatment.

3. If evidence for PM is uneven, why are such large claims being made?

- In our society, where individualism and choice are highly valued, ‘personalised’ is automatically assumed to be good
- Perhaps the favourable term is being used to prejudge the debate about whether we should put our available resources into Me or We Medicine?
- Except perhaps in pharmacogenetics, science alone doesn’t explain rise of Me Medicine

Four other explanations for PM

- 1) Threat and contamination
- 2) Growth of narcissism
- 3) Corporate interests and government policies favouring them
- 4) Sacredness of personal choice
- Not all equally convincing

1. Threat and contamination

- Eurobarometer survey: nearly half of respondents reject public banked blood
- 25% of European population would only accept own stored blood for transfusion; another 23% would only accept from family
- Public blood bank contamination scandals in France and UK
- Does sense of threat from public medicine leads to interest in personalised medicine?

2. Narcissism

- Is it only a coincidence that the words “me” and “my” are part of the brand for so many genetic testing companies? – such as 23andMe, Knome, deCODEme and MyGenome.
- Or is retail genetics part of a more generalized trend towards narcissism and self-absorption, with a decline in social capital and communal solidarity?

3. Corporate interests

- Facing patent expiry on blockbuster drugs, pharmaceutical industry needs to find a new business model: ‘niche’ personalized drugs
- Personal genetic firms pursue strategy of accumulating genetic and lifestyle data and claiming valuable patents (e.g. 23andMe Parkinson’s disease patent)
- ‘Personalisation is sometimes represented as a response to demand, but in some cases at least it seems to be a case of supply looking for demand’ (e.g. private cord blood banks).

4. Personal choice and autonomy

- Dominant values in Anglo-American medical ethics (less so in Scandinavia, France and Germany, but personalised medicine less advanced there)
- Pharmacogenetics does enhance patient choice to some degree, but not when it results in denial of treatment

Conclusions

- Good practitioners have always relied on close observation of the particular patient. As Hippocrates said, “It is far more important to know what person the disease has than to know what disease the person has”.
- Personalised medicine was already the way of the past. Jury is out on whether Me Medicine will be the way of the future.
- But we need to think carefully about how to balance its claims against those of We Medicine.