CONTRIBUTIONS to SCIENCE, **8** (2): 167–169 (2012)
Institut d'Estudis Catalans, Barcelona
DOI: 10.2436/20.7010.01.151 ISSN: 1575-6343
www.cat-science.cat

Bioethics and Social Responsabilities

Challenges for industry developers*

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Resum. Cada vegada és més evident que el model actual de recursos i desenvolupament no és sostenible. En aquest context, l'assessorament en tecnologia sanitària (HTA), un camp multidisciplinari d'anàlisi de polítiques que examina les implicacions mèdiques, econòmiques, socials i ètiques de la tecnologia mèdica en l'assistència sanitària, està guanyant importància. Com que proporciona eines que permeten esbrinar el valor de la innovació, pot assessorar en la presa de decisions en el sistema de salut, en l'àmbit clínic, de recerca i de desenvolupament. La sostenibilitat del sistema sanitari està fortament relacionada amb la responsabilitat social i hem de treballar perquè hi hagi aliances entre el sector públic i privat, i tornar-nos més eficaços a l'hora d'integrar innovacions socials, organitzatives i polítiques per tal d'oferir la millor qualitat d'assistència sanitària que el sistema es pugui permetre.

Paraules clau: medicina personalitzada · assessorament de tecnologia sanitària (HTA) · pressions de la indústria sanitària · malalties rares · responsabilitat social

Summary. It is becoming increasingly clear that the current resource and development model is an unsustainable one. Health technology assessment (HTA), a multi-disciplinary field of policy analysis that examines the medical, economic, social, and ethical implications of medical technology in healthcare, is gaining importance in this context. By providing tools with which to scrutinise the value of innovation, it can inform decision-making in the healthcare system, at the clinical, research and development levels. Sustainability of the healthcare system is strongly related to social responsibility, and we have to work towards more effective public-private partnerships, and become more adept at integrating social, organisational and policy innovations in order to deliver the highest quality of healthcare that the system can afford.

Keywords: personalised medicine · health technology assessment (HTA) · health industry pressures · rare diseases · social responsability

The context: pressures and drivers of the health system

Healthcare policymakers and providers are under pressure from various sources. Public expectations, changes socio-demographics, disease patterns, risk factors and scientific knowledge, the globalization of information on healthcare systems, increased patient participation, pressures to achieve financial sustainability and transparency, and the growing awareness of the need for evidence-based decision-making in healthcare are just a few of the most important issues that contribute to increasing pressure on the health system.

But what are the pressures on health industries? There are legitimate pressures, such as increased scientific scrutiny of innovations, but there are also pricing pressures, the threat of biogenerics and biosimilars, the consequences of the loss of patents, obsolete commercial models, and inflexible costs structures. It is becomingly increasingly clear that the current resource and development model is an unsustainable one. It is also clear that society's trust of the pharmaceutical industry has eroded.

In this context, there is a sense of change in health systems as they are once again evolving. What are the drivers of these changes? First, of course, there is innovation in biomedical science. Thanks to complex systems biology and molecular biology, to cell, gene, and enzyme therapy, and to tissue engineering, for example, we have begun to understand health and disease in a new way, one that is certainly very different from how we defined medicine just a few years ago. Moreover, personalised, or stratified, medicine, through genetic research and molecular diagnostics, is changing the paradigms of biomedical and health science research.

But there are also drivers in the healthcare system; these are related to the coverage and provision of healthcare. Currently, there is a debate as to whether we should push for governance or managerialism, in other words, for more strategic or more

* Based on the lecture given by the author at the Parliament of Catalonia, Barcelona, on 23 October 2012 for the annual conference of the EPTA network, 'From genes to jeans: challenges on the road to personalised medicine.'

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tactical approaches. I think we have to do both. But the decision strongly influences the direction in which health systems evolve. Whether doctors can reasonably be expected to become leaders, not just healthcare workers, is another matter of important debate, raising questions about quality and efficiency, but also about professional solidarity and ethical imperatives. Then we have the adversarial relationship between the public and private sectors. I believe that in response to the need for cooperation in matters involving social and institutional responsibility, new public-private partnerships will develop. There is also the driving pressure for healthcare accountability and last but not least, health technology assessment.

Personalised medicine and health technology assessment

Health technology assessment (HTA) is a growing movement all over the world. Although it started just a few years ago, it is now a new paradigm in healthcare. But, depending on who you ask, there are different interpretations about what HTA is. For healthcare policy makers and providers, HTA is a tool with which to scrutinise the value of innovation. How? By looking at the scientific evidence in a systematic and exhaustive way and then trying to understand the quality of the evidence, whether published or not, in relation to the projected costs. This information can inform decision-making in the healthcare system, at the clinical, research and development levels. However, the health industry has different perceptions of HTA, as an instrument that either poses barriers to innovations or advocates cost-saving measures.

The current reality, not only for personalised medicine but for every innovation of interest to healthcare systems and industry developers, is that it is important to recognise that an innovation must be more than a scientific novelty; rather, it must, for example, be able to provide therapeutic added value superior to that of already available alternatives or standards of care. Otherwise, it will enter or be maintained in the healthcare market only with difficulty. Growing scientific knowledge often results in our confusion, as the 'yes' or 'no' responses of governments or HTA agencies no longer suffice. Nowadays, the answer is more typically something like, 'yes, but…' Or more specifically, 'I allow you to enter the market but with a policy of coverage with evidence development.' This is a type of conditional coverage in which payers agree to cover new medical technologies, provided that patients receiving care that makes use of those technologies are enrolled in a clinical study to generate the additional benefit and safety information needed to make informed coverage decisions. In fact, coverage with evidence development is a managed-entry scheme designed to address key health policy issues pertaining to the increasing cost pressures, uncertain effectiveness, and greater patient benefit per unit of currency spent. Knowledge is pressuring the system to be more creative, and policies such as coverage with evidence development ensure the preservation of public health safety issues without impeding technological evolution and innovation.

The rules on how these policies should be implemented, who pays for what, etc. are still not clear, but the outcome is of great interest to industry because it offers a path for future investments in research and development. Both the healthcare system and the healthcare industry are being forced to adapt, which requires that they work together. For now, at least, conditional coverage linked to evidence development is a way to do so.

Impacts and difficulties of personalised medicine

Among the impacts of personalised medicine are:

1. Higher probability of desired outcome with a drug
2. Low probability of untoward side effects
3. Preventive strategies
4. Focused therapies
5. Potentially better health outcomes
6. Recognition of the need to change research and healthcare provision paradigms and relationships
7. Recognition of the need for holistic HTA: clinical, economic, social and ethical assessments that include the views of patients
8. Genomics technology that generate massive amounts of information
9. Recognition of the need for alignment between pharmaceutical and diagnostics companies
10. New business models
11. The discovery of genes associated with specific diseases, which for patients with rare diseases and subpopulations of those with common diseases offers novel diagnostic and treatment strategies

Among the main difficulties are:

1. Scientific challenges posed by the lack of validated molecular markers and consensus regarding the kind of evidence needed to prove their value to HTAs
2. How do we get this evidence? Who should pay for it?
3. Operational issues
4. Economic challenges due to poorly aligned incentives
5. Ethical dilemmas not systematically addressed
6. Lack of clarity on how to evaluate clinical validity and utility for decision-making
7. Lack of a revised regulatory framework
8. Opposition by healthcare and industry 'silos'
9. The global recession, which has forced governments to reconcile budgetary challenges. Is there a trade-off between efficiency and solidarity?

Current challenges for industry developers

Below are examples from the field of rare disease, in which I work, but they show that even if we are able to identify a rare disease component, it does not mean that there are few barriers to entering the market. Figure 1 shows the number of or-

Table 1. Percentage of HTA decisions

Agency / Institution	Yes	Yes/Restricted	No
National Institute for Health and Care Excellence (NICE)	67 %	–	33 %
Pharmaceutical Benefits Advisory Committee (PBAC)	4 %	56 %	40 %
All Wales Medicine Strategy Group (AWMSG)	29 %	29 %	43 %
Scottish Medicines Consortium (SMC)	22 %	32 %	46 %
National Centre for Pharmacoeconomics (NCPE)	40 %	–	60 %
CDAC	27 %	–	73 %

phan drug designation applications, designations and approved orphan products per year. Table 1 shows the percentage of HTA decisions by different agencies. 'No' indicates the percentage of components for which market entry was sought but not approved because evidentiary requirements were not met.

As industry developers, we need to receive consistent messages from the healthcare system regarding evidentiary requirements and what is valued by health systems, because this will impact drug development plans. We can be very inefficient in our development processes and very ineffective. If we do not have consistency with respect to the evidence necessary to demonstrate the value of a component, then we are lost.

I would like to transmit the importance of harmonising the method and the criteria for evidentiary requirements for healthcare systems. In the therapy of rare diseases, and similarly in personalised medicine, the challenges for treatment developers are in measuring outcomes. In both cases, we are talking about small, geographically dispersed populations that present recruitment challenges for clinical trials, in that low prevalence limits the ability to perform multiple studies. Also, the heterogeneity of rare diseases poses challenges to uniform treatment paradigms and to study design. The slow progression of the disease means that measurable effects may take years; surrogate endpoints (renal, cardiac, neurological disfunctions, among others) are often more apparent than final outcomes such as mortality. Furthermore, the regulatory agency requirements are not always aligned, neither are the HTAs. Finally, post-approval commitments to perform more real life studies to further understand the clinical outcomes of therapies require continuous significant investments. This means that the standards of evidence-based medicine cannot be easily achieved, and methodological and health technology assessment interpretation and innovation are crucial.

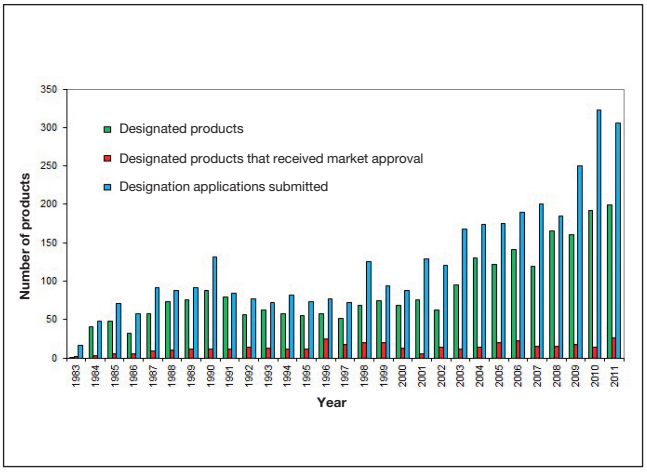

Fig. 1. Number of orphan drug designation applications, designations, and approved orphan products by the FDA Office of Orphan Product Development (OOPD) per year.

Final reflections

Here are just three final reflections. The first one is how can we keep healthcare systems sustainable in a changing scientific and social context? In my opinion, sustainability is strongly related to social responsibility. We need to avoid the 'silo' approach and aim towards more collaborative tools and processes. We have to be more inclusive, working from more effective public-private partnerships, with clear rules. Also, we have to deliver the highest quality of healthcare that the system can afford. We need to have a better vision of integrated care and we must become more adept at integrating social, organisational and policy innovations, not only technological innovations. Technological innovation without the organisational frameworks that allow its effective and efficient implementation is a recipe for disaster.

The second reflection is that we need to keep putting ideas into practice. We need to provide the facilities that promote creativity and cross-fertilization from the public and private sectors. HTA can help us disinvest in what is not effective, what is not efficient. Thus, we have to take greater advantage of the HTA tools we currently have at our disposal, to make informed decisions about investment and disinvestment. And we should always keep in mind that compassion and solidarity should be the principal elements in healthcare systems, not just in Europe but all over the world.

My final reflection is that in this era of networks that we live in today, health system sustainability means, more than ever, social responsibility. Moreover, it will mostly depend on the degree of co-responsibility assumed by healthcare stake-holders.