Commentary

Orphan drugs: expensive yet necessary

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Summary

Whether the prices of certain orphan treatments are justified is highly controversial. One argument is that such therapies should not be funded through the public purse or private health plans because a patient with a rare disease requires more than their ‘fair share’ of a limited health care budget. Orphan medications can also be denied because they fare poorly in the cost-effectiveness assessments of drugs. This paper takes the unusual line that life-saving treatments should be provided regardless of their cost. This contention is based on the Harvard philosopher John Rawls’ theory of justice. We offer three rules to limit the use of cost-effectiveness approaches: efficiency assessments should not be deployed (i) when the choice is between an only treatment and no treatment, or to (ii) prioritise between different patients and patient groups. However a well considered cost efficiency calculation may have its place (iii) where a patient has a choice between two or more equally safe and effective treatments. We rebut potential objections to this analysis, and conclude that there has been a tendency to classify appeals for orphan treatments as a minority interest and in conflict with the aims of public health and society at large. Rawls' concept of societal justice shows that a distinction between the individual and society in this context is bogus. The funding of orphan therapies is as much a matter for public health as the funding of treatments for other conditions. Treatment must not be withheld on economic grounds.

Introduction

The vista is gloomy: the impact of the global financial crisis is felt in the UK and European healthcare systems and beyond.1–3 As budgets shrink, expensive drugs for rare (‘orphan’) diseases become a natural target for spending cuts. Orphan drugs have proliferated after the enactment of the US Orphan Drug Act 1983 and its European (Regulation 141/2000) and other national equivalents. Their main attraction is a 7-to-10 year marketing exclusivity which allows a manufacturer to charge an unrestricted sale price for its product. The legislation has resulted in often extraordinary prices for single agents4 and the trend shows no sign of abating.5

One argument is that orphan therapies should not be funded through the public purse or private health plans because a patient with a rare disease requires more than their ‘fair share’ of a limited health care budget. Orphan medications can also be denied because they fare poorly in the cost-effectiveness assessments of drugs, such as the quality-adjusted life years (QALY) which is used in the UK. This is because of their high cost and often small gains in survival or perceived quality of life.6

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Withdrawal of a sole therapy can lead to deteriorating health and inordinate stress to those affected by rare diseases. It is timely at a time of fiscal austerity to reflect on why orphan drugs must be provided to those who need them.

**Why orphan drugs must be funded**

A valid reason is offered by Harvard philosopher, John Rawls, whose vision 'represents the most compelling case for a more equal society that American political philosophy has yet produced'. Rawls asks us to design a society in which we are yet to be born. In this hypothetical position, we would not know whether we were to be rich, talented, handsome, healthy or possess none of these qualities. We would also not know whether we will develop a chronic or debilitating rare disease. If we were to encounter such misfortune, and the disease were left untreated, the condition may hamper development, drastically reduce social and economic opportunities—and probably cause premature death, possibly in childhood or infancy.

Would we design that society to ensure it pays for the only treatment for your disease should you be unwell? At best, the drug would be able to sustain one at full health so that one can attend school and pursue a chosen career path followed, as well as other aspects of one’s life. Put simply, Rawls argued that in a just society, everyone has an equal right to pursue their life plans. Although Rawls did not initially focus on health care, his theory can be extended to state that the more a disease impairs a person’s capacity to pursue their goals, the more urgent it is that their health need is addressed.

Rawls’ fair society concept stems from two powerful arguments: the contractual and intuitive. The societal contract is as described above: citizens decide on the rules behind a ‘veil of ignorance’ before their health and talents are known. Rawls argued that natural caution would lead to the design of a society in which citizens would ensure that the least lucky—such as the most ill—would fare reasonably well, lest they themselves become that person.

Rawls showed that correcting inequalities based only on race, sex, age or social background does not take fairness to its logical conclusion. He concluded that we must also minimize inequalities that originate from the morally random distribution of talents and other personal attributes.

It is, for example, morally arbitrary as to whether a child is born healthy or with a debilitating rare disease. Yet patients with rare diseases often have a drastic loss of social and economic opportunities, and their treatment is often the first to be scrutinised at times of austerity. The only chance of securing equality of opportunity and political liberty is if such patients are offered treatment for their condition.

**Resulting limits on cost-effectiveness approaches**

Some health providers withhold or threaten to deny treatment for rare disorders on account of their high cost and sometimes low effectiveness. We have applied Rawls’ principles to orphan diseases and developed three rules which limit the use of cost-effectiveness approaches:

(i) Efficiency assessments (such as the QALY) should not be deployed when the choice is between an only treatment and no treatment. This is because failure to provide any treatment would entirely deny an individual the right to pursue their life plan. The principle applies even if the drug offers only marginal benefit, given that the treatment may keep the disease at bay until a more effective therapy is introduced. Niemann-Pick disease type C is an example: no specific treatment exists for this devastating condition but a drug approved for Gaucher disease can stabilize some of the manifestations.

(ii) Cost-efficiency calculations cannot be used to prioritize between different patients and patient groups, for example between Gaucher disease and diabetes mellitus, both metabolic disorders. This is because from the perspective of fairness, one person’s equal opportunities and liberties cannot be sacrificed for another’s.

(iii) Notwithstanding, a well considered cost-efficiency calculation may have its place in the distribution of health care resources in cases where a patient (or prescribing physician) has a choice between two or more equally safe and effective treatments. For example, there are five treatments for pulmonary arterial hypertension, and there may even be a non-orphan medication based on the same molecule. Here a comparative-effectiveness assessment is a practical solution to reducing costs, as a person’s only chance at equal opportunity is not at stake.

Further to point (iii), scholars of health economics have advocated the importance of comparative-effectiveness research in more efficiently allocating health resources—in particular in situations where it may not be possible to use cost-efficacy as a metric for decision-making. In this connection, we recommend a metric that is developed transparently and through sustained dialogue with and cooperation of patients, other tax payers, industry, insurance and governments; it should take into consideration all the above factors, within the framework of legal arguments which demand provision of these treatments. A sound metric is...
important also because it raises the question as to whether some expensive orphan therapies with low efficacy could be developed further.

Potential objections

It is unrealistic to assume that society will follow Rawls’ principles

Convincing healthcare providers to abide by these rules might appear unrealistic. But they already operate intuitively in society. When funding for the only treatment for Alzheimer disease was withdrawn, a political backlash led the UK government to re-authorize it. In contrast, a policy of switching patients in the UK from atorvastatin (Lipitor) to generic simvastatin proved less contentious. That the US Congress and the European Parliament enacted the Orphan Drug legislation shows that society is reluctant to accept that a group of patients should be left untreated because of a lack of economic incentive.

Limited budgets necessitate cost-efficiency calculations

It is often suggested that because there is a limited pot of money in the health budget, it follows that cost-efficiency calculations should be used to prioritize between treatments. But we contend that this does not follow: a utilitarian distribution of healthcare resources is not the only (or correct) way. For example, that one may have a maximum of £20 to spend in a shop, does not dictate exactly how that money should be spent. A limited budget can be spent according to different principles or habits and the cap on spending is not a reason to opt for cost-efficiency.

Rawls offers no solution

It might be argued that we have failed to solve the tension between treating a small number of patients with very expensive therapies, and treating a large number of patients with moderately expensive therapies. Here, we set out why our proposals represent such a solution:

(i) We have shown that utilitarianism (or cost-effectiveness) is not a sound basis for making treatment decisions. Rawls’ philosophy and utilitarianism are thus not equally sound alternatives from which to choose. The alleged tension is therefore not substantive.

(ii) The tension assumes that it is sound to pit the needs of a minority (rare diseases) against doing the right thing by the majority (common diseases). In fact, the minority/majority divide is a morally arbitrary way to approach resource allocation. Rawls shows that it is morally arbitrary as to whether a disease is rare or common. Hence, the outcome of an allocation based on the majority/minority map will be morally unsound. The question should always be whether a person needs treatment to realize the important opportunities to which all citizens should have equal access.

Healthcare demand is a bottomless pit

The consequential response is that treating everyone on this basis creates a bottomless pit which can drain a nation or health plan’s capital. Clearly, not all treatments can be funded. A related concern may be that ‘equality of opportunity’ is vague and can be defined very broadly in order to secure treatments for serious and less serious conditions. Our principles suggest that life-preserving treatments take priority. Beyond those, the question is society-specific and best decided democratically through open debate. To minimize the influence of our own actual life circumstances in this discussion, we should place ourselves behind Rawls’ imaginary veil.

Indeed, although our analysis may assist patients and their families in securing access to treatment on a case-by-case basis, it is better that systematic and fair rules are agreed through discussion with all stakeholders, i.e., patients, industry and public and private health providers. The National Institute for Health and Care Excellence is in fact using a public consultation process to review its interim methods for evaluating very rare disease treatments.

The debate should also consider whether related budgets are scrutinized with the same rigour. To cite one example, it appears manifestly wrong to seek to make patients affected by rare diseases feel guilty for the cost of an often life-saving treatment while the NHS has simultaneously spent £12 billion on a failed IT system upgrade with the potential for an additional £700 million charge for damages due to system failures.

Conclusion

Hitherto there has been a tendency to classify appeals for orphan treatments as a minority-interest centred on the ‘individual’ patient, and to indicate that these are in conflict with the aims of public health and society at large.

Rawls’ concept of societal justice shows that a distinction between the individual and society in this context is bogus. There is no inherent minority-focus about rare diseases: a society created behind a veil would also choose to develop and
fund a life-saving and expensive treatment for a non-orphan ‘majority’ disease. The funding of orphan therapies is as much a matter for public health as the funding of treatments for other conditions. Those lucky not to suffer from the effects of a rare disease should not use their morally arbitrary good fortune to disadvantage those who do.

While pricing practices for orphan drugs merit scrutiny, in the meantime treatment must not be withheld on economic grounds.

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