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Original Article

The elephant in the room: ethical issues associated with rare and expensive medical conditions*

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Abstract The treatment of rare and expensive medical conditions is one of the defining qualities of paediatric cardiology and congenital heart surgery. Increasing concerns over healthcare resource allocation are challenging the merits of treating more expensive forms of congenital heart disease, and this trend will almost certainly continue. In this manuscript, the problems of resource allocation for rare and expensive medical conditions are described from philosophical and economic perspectives. The argument is made that current economic models are limited in the ability to assess the value of treating expensive and rare forms of congenital heart disease. Further, multi-disciplinary approaches are necessary to best determine the merits of treating a patient population such as those with significant congenital heart disease that sometimes requires enormous healthcare resources.

Keywords: Congenital heart disease; rare diseases; resource allocation

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THE PURPOSE OF THIS PAPER IS TO FRAME THE discussion of resource allocation in the case of rare and expensive diseases using congenital heart disease as an index case. The argument will be made that the spectrum of diseases within congenital heart disease is each an "orphan disease" by incidence and this "orphan" distinction will be addressed, specifically with regard to how resources are allocated for treatment. The concept of resource allocation and its resulting ethical dilemmas will be explored further from both philosophical and economic perspectives, using Utilitarian interpretations for the former and an introduction to the basic tenets of healthcare economics for the latter.

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"Orphans" and rare diseases

In 2002, the United States congress passed the Rare Diseases Act, which formally established the definition of a rare disease as a disease that affects fewer than 200,000 Americans.[1] The term "orphan" arose from the conflation with this act and the Orphan Drug Act of 1983, whose purpose was to facilitate and incentivise drug development for rare diseases.[2] Thus, the terms "orphan disease" and "rare disease" became interchangeable and share a common legal definition for the ~25 million people in the United States of America affected by an estimated 6000 rare diseases.[3] The Rare Diseases Act of 2002 established, for the first time, an office with statutory authorisation – Office of Rare Diseases of the National Institutes of Health – and a funding strategy for research and treatment of these diseases, and continues to make recommendations for annual funding.[1,3]

There were ~4 million births in the United States of America in 2014;[4] the ~1% incidence of congenital heart disease means that there were ~40,000 new cases

of congenital heart disease in 2014, making it the most common birth defect.[4] There are numerous types and subtypes of congenital heart disease, which range from relatively common to incredibly rare, but even the more common lesions such as septal defects and tetralogy of Fallot are classified as rare or "orphan" diseases by the National Organization of Rare Disorders owing to their low incidence.[5] Practitioners and care providers within the fields of paediatric cardiology and congenital heart surgery may not think that the disease processes they treat are "orphans" by any means, especially because of the immense progress that has been made in treatment over the past century, but the relative rarity of these lesions places them in the same category as hundreds of other, more esoteric, congenital diseases.

Although seemingly just a matter of semantics, the designation of a disease process as an orphan has important implications for healthcare economics and government funding. Government-level resource allocation represents probably the most basic form of healthcare economics, whose primary concern is how finite resources are allocated for maximum benefit to the population. A more nuanced discussion of the basic principles of healthcare economics follows later in the manuscript.

Basic government-level funding strategies

In 2014, the United States of America allocated 2 billion dollars to research in cardiovascular disease and 5.4 billion dollars to research in cancer.[6] Considering that these two disease processes accounted for roughly 600,000 deaths each in 2013, and that each accounted for more deaths than the next four most common causes of death combined, this prioritisation of healthcare resource allocation is unsurprising.[7] In contrast, 3.6 billion dollars were allocated to the category of orphan diseases.[6]

Implicit in this government-level resource allocation is recognition and prioritisation of the major threats to public health based on disease prevalence. Indeed, a further screening of the National Institutes of Health research resource allocation[6] report yields a correlation between disease prevalence and funding amount for research. Other funding mechanisms do exist on both the micro scale – hospital-wide resource allocation and insurance company reimbursement for disease burden – as well as the macro scale – for example, philanthropic organisations, professional societies, etc. – that supplement government resource allocation.

Acquired cardiovascular disease healthcare costs amounted to ~$444 billion in 2010,[8] making this disease a paradigm of high incidence and high cost. The significant resource allocation to this disease process is, thus, easy to justify because it is a common disease that kills a large percentage of Americans and represents a significant fraction of healthcare spending. It is difficult to assess healthcare costs of the 30 million Americans affected by rare diseases, because there is considerable variation in healthcare costs. Neonatal surgery for some of the more rare forms of congenital heart disease such as hypoplastic left heart syndrome and transposition of the great arteries carries the most expensive hospitalisations among birth defects.[9] Furthermore, six out of the top 10 most expensive birth defect-related hospitalisations are congenital heart defects.[10,11] From a resource allocation standpoint, congenital heart disease represents a significant problem because of the small population affected and the high cost of disease treatment. The philosophical and economic framework within congenital heart disease follows.

Utility, economics, and other attempts to solve healthcare resource allocation

Although the specific issue of government-directed healthcare resource allocation is a relatively recent ethical and public policy problem and would have been foreign to its initial proponents, the philosophical school of Utilitarianism offers key insights and appears to have had a significant impact on modern healthcare economics.[12] The Utilitarian school of thought was first described by Jeremy Bentham and later by John Stuart Mill, and its central thesis is described in Mill's 1863 work "Utilitarianism" as follows:

> actions are right in proportion as they tend to promote happiness, wrong as they tend to produce the reverse of happiness … happiness … is not the agent's own happiness, but that of all concerned. As between his own happiness and that of others, utilitarianism requires him to be as strictly impartial as a disinterested and benevolent spectator.[13]

Utilitarianism espouses a kind of detached maximisation of utility, or happiness, of the many even if it is at the expense of the few or the individual. The resulting utilitarian ethics become strictly democratic and provide little, if any, consideration of the needs of the minority or of groups that may require more resources to achieve the same level of utility as the majority population. The ethical issues associated with this school of thought have been debated since its initial publication and are far from the scope of this manuscript.

Although the origins of utilitarianism and healthcare economics are separated by roughly a century, the kind of detached maximisation of

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societal benefit that Utilitarianism espouses represents one of the fundamental goals of healthcare economics. Healthcare economics start off with the familiar preface that resources are finite and must be rationed. Three main questions follow: "what goods and services shall be produced?", "how shall they be produced?", and "who shall receive them?". Although basic economics might defer to the market to answer these questions, one of the most important problems and basis of enquiry for both economics and healthcare economics is how to manage so-called "market failures". Having market forces determine healthcare resource allocation has several potential problems stemming from information asymmetry (physicians have greater knowledge than patients regarding medicine and could use this to their advantage), from the desire that healthcare should be provided based on need and not on ability to pay, the desire that even diseases whose treatments may not be profitable should be treated, and others. These problems form the basis for the myriad economic models that attempt to answer the three main questions while maximising the wellness of society.[14]

The conflicts associated with prioritising the interests of many over the interests of few while maintaining equitable access to healthcare form the basis of market failures, and the science and practice of healthcare economics involve creating economic models to describe and ultimately address these market failures. Examples of such economic models include cost–benefit analysis, cost-effectiveness analysis, needs assessment, marginal analysis, and quality-adjusted life years. These models are designed to inform policy decisions by quantifying aspects of resource allocation that are often difficult to quantify, such as benefits to society of treating certain diseases, the value of an individual life, the difference in a human life's worth in the case of significant morbidity, the point at which resources should no longer be allocated to a disease process treatment because of futility. These topics may seem more *a propos* to an ethical discussion and the approach of ethicists and economists may seem completely different at first, but the strongly Utilitarian ethos behind healthcare economics places the resulting economic arguments within an ethical framework. Quantification and evaluation of seemingly ethical variables and problems become just other ways to inform the fundamental ethical problem of resource allocation. A summary and evaluation of the economic models that inform the healthcare resource allocation debate follow.[14]

Healthcare economics

As it is easier to quantify treatment costs rather than more abstract concepts such as quality of life, many of the initial and simple healthcare economic models involve an assessment of healthcare costs. In its most basic form, a cost of illness study is just that, and it is used for this purpose. Treatments can then be assessed based on both direct costs of treatment as well as any decreased healthcare resource utilisation after treatment. Although these are among the more simplistic measures of healthcare resource allocation, they inform additional models that balance cost of disease with either strictly monetary benefit to either individuals or society, as is the case in cost–benefit analysis, or with non-monetary measures of treatment efficacy as is the case in cost-effectiveness analysis. In presenting an objective assessment of the costs associated with a treatment, cost-based analyses can help supplant sometimes subjective and political decisions with mathematical and economic decisions. Opponents of these models argue that these analyses are rarely thorough and comprehensive and that they have the potential to be just as subjective and political as the decisions they try to replace depending on the data they use.[15]

Rare and expensive disease resource allocation provides a significant challenge to such analyses, particularly in the case of treatment equipoise and uncertain prognosis. Sample size is paramount to establishing the assumptions and basis for the cost necessary for analysis; in the case of complex congenital heart disease, sample size is generally low, and there are often significant discrepancies with healthcare costs, as evidenced by recent analyses on the subject.[9] Post-operative morbidity suffered by patients can also be highly variable in the case of complex congenital heart disease, further confounding analyses of outcomes to provide any prospective, normative guidance regarding preferred or economically beneficial treatment options. Furthermore, the time frame of such an analysis may confound analysis of disease processes that require timely, early, and expensive surgical intervention if it does not sufficiently take into account the years of hospitalisations and untimely death of a patient who does not undergo corrective surgery.

As the alternative for critical congenital heart disease is often death, cost-based analyses and healthcare economics in general must at least implicitly place a value on a human life for the purposes of analysis. The most common form of so-called cost-utility analysis is the quality-adjusted life years. The basic premise of this metric is that if a year of additional life in good health is worth one then a year of additional life in poor health must be worth less than one.[16] Varying degrees of disability and morbidity are associated with a decimal value – utility value – that corresponds with how studied individuals would rate quality of life associated with a given condition. If the degree of

human suffering carries with it a detrimental cost to quality of life, it is implied that healthy life also has a value associated with it.

Such implicit valuation of human life becomes problematic when it is made explicit, as is the case in the debate over the value of a single quality-adjusted life year and whether or not treatments shall be offered or paid for. To be sure, there is a point of healthcare resource spending beyond which no further benefit can be achieved, either because the patient has been cured or because futility of care has been reached. Marginal analysis, the healthcare economic model dedicated to defining such a point, has been very helpful in establishing guidelines and informing medical decision making.[14] The debate over what constitutes an appropriate amount of healthcare resource allocation to an individual in a given year is contentious and the origins of what are generally considered acceptable figures for quality-adjusted life years are somewhat murky. A common figure cited is $50,000 as an appropriate amount per year to justify treatment for an individual with a good quality of life.[17] The origin of this figure is said to have arisen from the per annum cost of haemodialysis as it was in the 1970s, but this point is debated. The $50,000 per quality-adjusted life year gained widespread acceptance in the early 1990s in the world of healthcare policy, and it has endured as a benchmark figure for healthcare policy decisions.[17] It should be noted that this figure is used primarily as a model, and that the favourable economic environment of the United States of America healthcare system has not forced the issue of using such a value to deny treatments to individual citizens to this point. The fact that the $50,000 per quality-adjusted life years has not been formally adjusted for inflation as it remains a benchmark of ethical and economic enquiry is mathematically perplexing, but different organisations have proposed higher quality-adjusted life year values of $100,000 and even $300,000.[17]

The explicit valuation of human life, although perhaps ethically troubling, is, nonetheless, an important aspect of healthcare resource allocation in a society with finite resources. Such valuation is important in evaluating different treatment modalities for common diseases, but its use is much more challenging in the case of rare and expensive medical problems such as critical congenital heart disease. Maximising quality-adjusted life years places a premium on preserving life years, not necessarily individual lives. Critics of quality-adjusted life years argue that there is a fundamental conflict between a cost-effectiveness approach similar to the maximisation of quality-adjusted life years and the "Rule of Rescue – people's perceived duty to save endangered life when possible".[18]

Many forms of congenital heart disease treatment fall within the scope of rescue. Patients can be in extremis and treatment initiation is often time sensitive. Failure to initiate treatment may result in patient death, and thus deprivation of their life plan. Hyry et al argued that quality-adjusted life years should not be used in cases where the debate is treatment versus no treatment because of the ethical issues associated with withholding treatment from a certain group for strictly economic reasons.[12]

Within the valuation of human life proposed by the limits of quality-adjusted life years and their use in healthcare economic policy are numerous ethical debates beyond the obvious valuation of human life. Depriving a patient of treatment because of cost violates patient autonomy, and depriving a healthcare worker the right to initiate treatment to a patient violates the bioethical principle of beneficence. The bioethical principle of justice becomes a matter of debate regarding the proper distribution of healthcare resources, but it is difficult to fathom denying expensive treatments for treatable conditions such as congenital heart disease based solely on economic concerns. Moreover, having limitations on expensive treatment distribution would stifle further development of these treatments that may ultimately lower the cost of treatment. The cost of sequencing the human genome has fallen precipitously owing to technological advances, as have costs for once experimental medications and complicated surgical procedures. Setting cost limits on treatment for otherwise life-threatening conditions not only commits those afflicted to death but it also prevents research and development of better and perhaps less-expensive treatments. Worse still, research regarding currently expensive technologies and treatments has potential ramifications to benefit more than just those afflicted with the disease by improving medical knowledge and research methods. A society that prioritises quality-adjusted life years and uses it as a basis for healthcare resource allocation may allow for the current majority to have access to the currently most economic treatment for the currently most prevalent disease processes. Nevertheless, by limiting resources for research into rare, expensive, or difficult-to-treat disease processes, such a society has the potential to be ill-prepared to deal with new disease processes and may ultimately not be able to accommodate the future needs of the many by having ignored the past needs of the few.

Healthcare cost is becoming increasingly important as demand for, and access to, medical care is increasing both domestically and internationally. The debate on healthcare resource allocation and resulting healthcare economics has its roots in utilitarianism through their shared telos of prioritising the utility of the many over the utility of the few. Although healthcare economic models can provide a framework by which to make difficult decisions regarding

healthcare resource allocation, the treatment of rare and expensive diseases such as congenital heart disease present a significant challenge to currently used healthcare economic models. The shortcomings of various healthcare economic models to inform the healthcare resource allocation for rare and expensive diseases debate are similar to the shortcomings of their "philosophical parent"[19] as a basis for a universal ethical system. Putting aside the needs of the few for the needs of the many is a simple idea in concept, but becomes significantly more challenging when it is often difficult to quantify the quality and quantity of life gained through the oftentimes urgent surgical interventions necessary to correct critical congenital heart disease in infancy. Further attempts by economists, ethicists, and clinicians alike will be needed to best inform the practice of treating rare and expensive disease processes such as congenital heart disease. Such policies might combine the objective quanitification of healthcare costs and human morbidity that healthcare economics provides while maintaining the bioethical principles of justice, beneficence, nonmalfeasance, and autonomy. Growing populations and increasing access to healthcare resources will continue to push this and other important healthcare resource allocation debates to the fore, and a multidisciplinary approach will be vital to ensure that the needs of the many are satisfied, but not always to the detriment to the needs of the few.

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Conflicts of Interests

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