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Societal Preferences for Funding Orphan Drugs in the United Kingdom: An Application of Person Trade-Off and Discrete Choice Experiment Methods

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ABSTRACT

Background: It is unclear whether UK National Health Service (NHS) policies for orphan drugs, which permit funding of non–cost-effective treatments, reflect societal preferences. **Methods:** We conducted person trade-off (PTO) and discrete choice experiment (DCE) among 3950 adults selected to be representative of the UK general population. Experimental design was informed by surveys of patients affected by rare diseases, their caregivers, health care staff, and policymakers. Societal preferences were estimated in relation to treating a common disease, increases in waiting lists, or filling of vacant NHS posts. Results of the DCE were applied to recently licensed orphan drugs. **Results:** On the basis of equal cost, the majority of respondents to the PTO (54%; 95% confidence interval [CI] 50–59) chose to allocate funds equally between patients treated for rare diseases and those treated for common diseases, with 32% (95% CI 28–36) favoring treating rare diseases over treating common diseases (14%; 95% CI 11–17), which this reduced to 23% (95% CI 20–27) when rare disease treatments were 10 times more expensive. When framed differently, more respondents prioritized not increasing waiting list size (43%; 95% CI 39–48) than to treat rare disease patients (34%; 95% CI 30–38). **Discussion:** The DCE indicated a greater preference for treating a common disease over a rare disease. Respondents agreed with five of 12 positive appraisal recommendations for orphan drugs, even if their list price was higher, but preferred the NHS not to fund the remainder. **Conclusions:** The general public does not value rarity as a sufficient reason to justify special consideration for additional NHS funding of orphan drugs. This has implications regarding the appropriateness of operating higher thresholds of cost-effectiveness.

Keywords: orphan drugs, person trade-off, discrete choice experiment, rare disease, resource allocation, societal preferences.

Introduction

Orphan medicinal products include treatments for rare diseases that are life-threatening or chronically debilitating, and medicines whose development would not be commercially viable without incentives [1]. Legislations aimed at promoting the development of orphan medicinal products have succeeded to the extent that regulatory approval rates are at their highest. Orphan drugs accounted for 40% of new drug approvals in Europe and the United States in 2016 [2,3]. However, ensuring patient access to these medicines has posed significant difficulties for policymakers, given their high cost [4] and lack of cost-effectiveness [5].

Concerns about inequity of care—patients being denied effective treatment on the basis of the rarity of their disease—has led to specific NHS policies to facilitate access to many orphan drugs. These include the Highly Specialised Technologies program of the National Institute for Health and Care Excellence (NICE), which operates a higher threshold for cost-effectiveness (up to £300,000 per quality-adjusted life-year [QALY]) [6], and the Scottish Medicines Consortium (SMC) and the All Wales Medicines Strategy Group's (AWMSG) permissive policies for appraising orphan drugs [7,8]. Each organization justifies the value of non–cost-effective orphan drugs on the basis of particular patient, disease, or drug feature. These include the magnitude of treatment benefit, the severity of disease, the innovative nature of the drug, and the availability of alternative treatments. There is evidence of general population support for prioritizing patients with greater disease severity as well as interventions that generate larger health gains [9]. There is also evidence that the general population prefers funds to be allocated to innovations that are scientifically proven and have potential health benefits [10]. Unmet need, however, is only considered important from a personal perspective, and not from a public perspective [11]. The implication of considering these factors in choices concerning investment in new medicines but not in the services they displace, however, is the inequitable position of improvements in health being valued higher in orphan conditions than in others [12,13].

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The value judgments of members of society are important in determining the guiding principles of priority setting [14]. NICE involves the public through its citizens' councils, which formulate a view on specific topics. A council discussion on ultra-rare diseases found that rarity is not a factor that, in itself, should warrant additional funding [15]. Previous studies of societal preference conducted in the United Kingdom [16] and internationally [17–20] have also found no evidence of a preference to fund high cost treatments for rare diseases on the basis of rarity alone. Although consistent in their findings, these studies have been criticized for relying on one method of preference elicitation, potential framing effects affecting the sensitivity of respondents' choices to the questions posed or method used [21], inappropriateness of how opportunity cost is presented to those surveyed [18], and consideration of other features of rare diseases besides prevalence.

We aimed to assess whether there is a UK societal preference to support current NHS policies that justify the acceptance of the opportunity cost associated with the funding of treatments for rare diseases. We further tested whether a sample of recently approved orphan drugs would be recommended on the basis of societal preference.

Methods

We utilized two separate preference elicitation techniques: a person trade-off (PTO) study and a discrete choice experiment (DCE). Both methodologies involve respondents trading between options to estimate their preference, but they allow respondents to engage in the decision-making process in different ways. The PTO method asks respondents to select the number of patients for whom they would prefer the NHS to allocate resources, choosing between two populations or scenarios of health service provision. This allows the opportunity cost of the allocation choice to be transparent and unambiguous to facilitate estimation of distributive weighting (i.e., who to treat) [22]. DCEs describe hypothetical but realistic medicines for rare and common diseases by their characteristics (attributes) and associated levels [23]. Respondent choices are then modeled to reveal the importance of the attributes and the willingness of respondents to trade attributes and levels.

Ethical approval was obtained from the Health Care and Medical Sciences Academic Ethics Committee, Bangor University (2015-02-03).

PTO Survey Design

Four PTO scenarios were designed. Two represented a "zero-sum" frame: (1) a scenario based on cost, of trading patients with a rare and common disease; and (2) a scenario in which both treatment costs and benefits were varied; and two represented impacts of additional costs on the provision of health care in terms of (3) an increased waiting list for an unspecified treatment and (4) leaving vacant NHS staff posts unfilled.

In the first two scenarios, the costs of rare disease medicines ranged between 1 and 20 times the cost of medicines for common diseases, to represent realistic values. In the waiting list scenario, we varied the benefits of both the rare disease medicine and the treatment for which patients are waiting, as well as their respective costs. Choices concerning staffing levels were based on the salaries of a health care assistant (1:5) or a nurse (1:3) relative to a doctor. The levels for this scenario were varied by staffing level standards; labeled as normal levels, overstaffed, and understaffed.

A focus group of eight members of the public was convened to examine the face validity of the PTO survey.

DCE Survey Design

We followed good practice guidelines to design the experiments [23,24]. Potential attributes of relevance to rare disease medicines were identified from a systematic review [25]. These were presented to four stakeholder groups by using an online survey (Surveymonkey): patients with rare diseases, their caregivers, clinicians and allied health care professionals, and NHS decision makers. Each participant was also given an opportunity to suggest his or her own attribute and then asked to rank all attributes he or she believed were important for the NHS to consider in funding decisions concerning orphan drugs. Aggregate ranking was summarized by using Borda scores [26], calculated for each group and for all participants.

The identified attributes were presented to a separate focus group of eight members of the public to decide on the final list of attributes and to refine the format and language used in the DCE. Members also discussed options for attribute levels and confirmed the final selection, which was based on criteria for orphan drug designation [1], published evidence on the effectiveness and costs of orphan drugs [4], and change in health status, based on the EuroQol EQ-5D health outcome measure [27].

The DCE attributes and levels are presented in Table 1. A full factorial design would result in 108 profiles and 5778 possible pairwise choice scenarios; hence, a fractional factorial design selected from a design catalogue [28] was selected to reduce the burden on respondents.

Study Sample

Patients and caregivers participating in the stakeholder survey were recruited via support groups for patients with rare diseases. Clinicians and allied health care professionals caring for patients with rare diseases were identified via Orphanet or their membership of NHS rare disease centers of excellence. NHS policy decision makers were defined as members of the NICE, AWMSG, and SMC appraisal committees. Recruitment to the focus group was based on local advertising. Interested persons were included if they were UK citizens, aged 18 years or over, and had no diagnosis of a rare disease or a history of being refused funding for NHS treatment. Target sample size across all groups was 120 participants.

The population survey aimed to recruit 4000 respondents representative of the general population in the United Kingdom, recruited by a market research company (Belindi). Participants were compensated by way of reward points that could be traded for consumer goods.

Survey Administration

In designing the questionnaires, we were cognizant of respondents' likely unfamiliarity with rare diseases and of the high cost of orphan drugs. We were also conscious that respondents may have limited motivation to participate in the study and that an online survey offered no opportunities for clarification and so there was a risk of the questions not being interpreted correctly. Therefore, we designed an animation to accompany the survey, with input from focus group members (available from https://tinyurl.com/OrphansAnimation).

Both studies were piloted among a convenience sample of 12 staff and students at Bangor University. Piloting involved feedback on the instructions, layout, and images used in the PTO and DCE and resulted in some images being subsequently modified.

Participants in the main survey were required to view the animation before proceeding. They were reminded that there were no right or wrong answers and that the research was to determine their views on how the NHS should prioritize treatments. They were directed at random to complete either the PTO