Drugs for Rare and Ultra-Rare Diseases in Europe: Analysis of Budget Impact and Cost Drivers

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Objectives

The objective of the present study was

(1) to review recent studies reporting health care expenditures for (or budget impact of) drugs for *rare* diseases in Europe,
and

(2) to contribute to our understanding of the cost drivers of drugs for non-oncological *ultra-rare* diseases (URDs) by means of an empirical analysis in Germany.

Methods

(1) A systematic search for relevant studies was conducted in PubMed (from 1966 to December 2014) and in abstracts in congress proceedings.

(2) In addition, annual treatment costs of drugs for non-oncological URDs in Germany were analyzed with respect to five explanatory variables: availability of other treatment indications, availability of alternative treatments for the same indication, oral administration, prevalence of the disease, and evidence for a health benefit.

Results

(1) A total of seven studies with specific estimates of the budget impact of drugs for rare diseases for a total of nine countries were identified. Annual per-capita spending for orphan drugs ranges from €0.48 in Russia to €16 in France (see Figure 1). Only one study on URDs was identified.

(2) In Germany, annual treatment costs per patient for drugs for non-oncological URDs varies between €1,175 and €726,890. In all regression specifications, a significant inverse relationship between availability of alternative treatments for the same indication and annual treatment costs was found. In addition, log prevalence was found to have a significant inverse relationship with log annual treatment cost (see Tables 1-3).

Conclusions

(1) Despite annual treatment costs in the range of several hundreds of thousands of euros for some of the URD drugs, per-capita spending for URD drugs is relatively small (see Figure 1).

(2) In this study, using German market data, an inverse relationship between prevalence and annual treatment costs was found specifically for drugs for non-oncological URDs (cf. Table 3).

Discussion

In principle, there are two competing perspectives - incremental costs per patient and budgetary impact - from which costs of treatment of URDs may be looked at. The budgetary impact often represents the primary concern of policy-makers and payers, and it is usually addressed by means of budgetary impact analyses (BIAs). BIAs reflect aggregate spending on an individual or on a group of OMPs, or on the category of URD drugs, and typically are a function of acquisition costs per unit and utilization, i.e., patient numbers and duration of treatment.

The data included in this study do not allow calculating cost effectiveness ratios; yet, the mean annual treatment cost of €235,734 suggests that health gains in the order of several (quality-adjusted) life years were needed for drugs to be considered cost effective by conventional standards. From the standard utilitarian perspective underlying the logic of cost effectiveness, assuming that the goal of collectively financed health schemes ought to be maximization of population health gains (valued on the basis of individual, selfish preferences) within the available resource constraints, drugs for URDs would therefore hardly receive priority.

Rights-based reasoning as well as the "empirical ethics" literature suggest that this approach may be in serious conflict with prevailing social norms and preferences. In this context, we believe it is worth pointing out that on a per-capita basis spending for orphan drugs is generally low as found by our literature search, currently running at €1.50 for non-oncological URD drugs in Europe (projected to rise to €4.04 in 2021 assuming unchanged population size) and a current maximum of €16 per year for orphan drugs in France (projected to plateau at €30 in 2020 – cf. Hutchings et al. 2014).

(1) Budget Impact Analyses

A search algorithm "orphan drugs" AND "('budget impact' OR 'spending')", search period from 1966 to December 2014, supplemented by a search for ISPOR meeting abstracts (year 2014) yielded a total of seven studies. The figure below gives references, year for expenditure data, reported percentage of total pharmaceutical expenditures, and annual per-capita spending [€]:

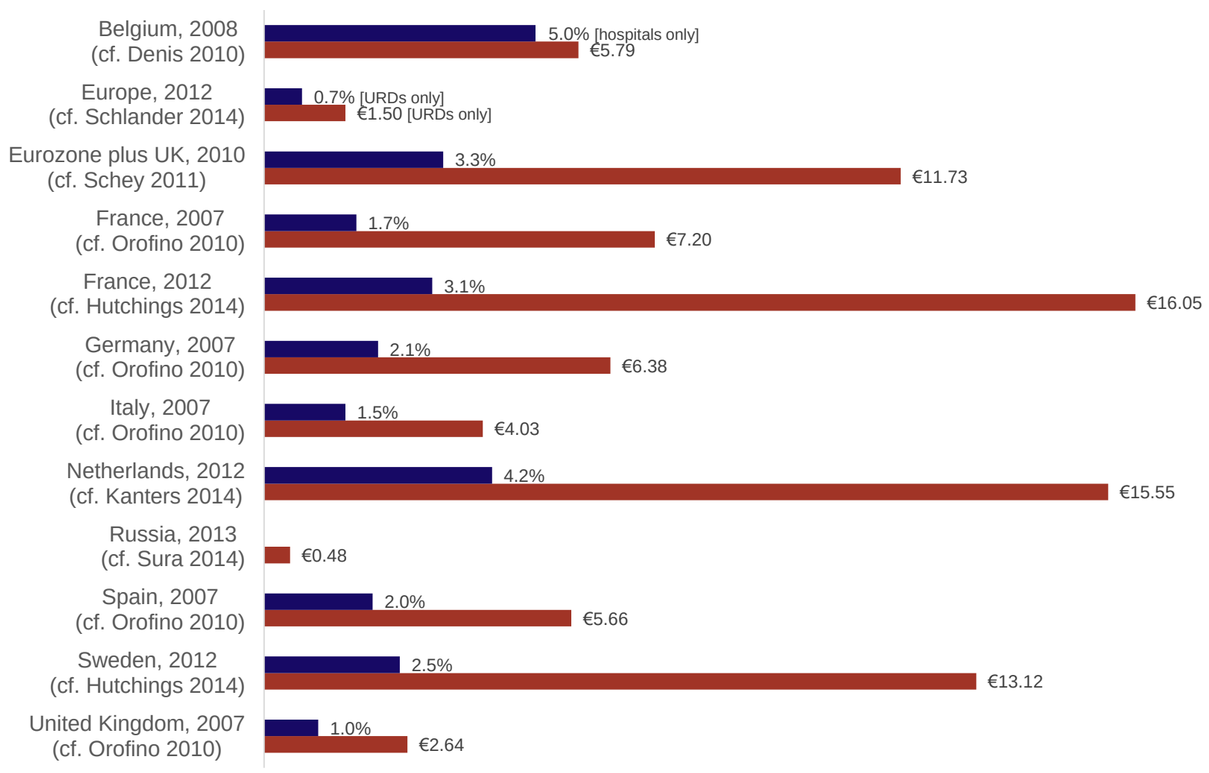

Figure 1: Budget Impact of Orphan Drugs in Europe

(2) Drivers of Cost per Patient for URDs

We found 17 drugs for non-oncological drugs with a marketing authorization and an active orphan drug designation in Europe. Annual treatment costs per patient varied between €1,175 and €726,890. Mean cost was €235,734.

In the correlation matrix the highest correlation was found between availability of other treatment indications and prevalence (r = 0.65). The chi-squared contingency table analysis showed no significant relationships, indicating absence of multicollinearity.

In all regression specifications we found a significant inverse relationship between availability of alternative treatments for the same indication and annual treatment costs (Tables 1 to 3, below). In addition, log prevalence was found to have a significant inverse relationship with log annual treatment cost (Table 3). According to this log-log specification, a 1% increase in prevalence leads to a 0.1% decrease in annual treatment cost.

Table 1: Regression Model Using Untransformed Variables
(dependent and independent)

	Coefficient	Std. Error	t-ratio	p-value
Constant	252,963	92,042.5	2.7483	**0.01895**
Other indications	120,180	92,553.7	1.2985	0.22068
Alternative treatments	−230,998	104,140	-2.2181	**0.04852**
Oral treatment	63,631.2	142,647	0.4461	0.66420
Prevalence	−111,357	156,324	-0.7123	0.49108
Quality of evidence	145,598	156,107	0.9327	0.37101

P-values marked in bold are significant at a 0.05 level.

Table 2: Regression Model Using Log Annual Treatment Costs
as the dependent variable

	Coefficient	Std. Error	t-ratio	p-value
Constant	11.9894	0.52839	22.6904	**<0.00001**
Other indications	0.19669	1.14884	0.1712	0.86717
Alternative treatments	−2.51025	0.925136	-2.7134	**0.02017**
Oral treatment	0.940004	1.08352	0.8675	0.40417
Prevalence	−0.31739	0.883374	-0.3593	0.72618
Quality of evidence	0.398531	0.693321	0.5748	0.57698

P-values marked in bold are significant at a 0.05 level.

Table 3: Regression Model
Using Log Prevalence and Log Annual Treatment Costs

	Coefficient	Std. Error	t-ratio	p-value
Constant	11.2015	0.575911	19.4500	**<0.00001**
Other indications	0.0110252	1.43227	0.0077	0.99400
Alternative treatments	−2.37977	0.920428	-2.5855	**0.02534**
Oral treatment	0.982519	0.947924	1.0365	0.32222
Prevalence	−0.113487	0.0488416	-2.3236	**0.04032**
Quality of evidence	0.824779	0.503497	1.6381	0.12966

P-values marked in bold are significant at a 0.05 level.