



Why Do Some Countries Approve a Cancer Drug and Others Don't?

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Why do some countries approve a cancer drug and others don't?*

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- ❖ Social Health Insurance systems tend to make more Favourable decisions than tax-based systems
- ❖ Cost-effective drug-indications have a higher probability of reimbursement
- ❖ Other countries are more likely to make a Favourable decision if NICE also make it
- ❖ A requirement for Economic Evaluation reduces the number of Favourable decisions
- ❖ A lower proportion of Favourable decisions during the global financial crisis

Findings

- Found support for each of these hypotheses e.g.
- in SHI countries 301/439 [69%] decisions were Favourable (without restriction) compared to 260/436 [60%] in tax-based countries ($p = 0.0027$)
- For drug-indications where NICE made an unfavourable decision 72/223 [33%] were unfavourable in other countries, whereas drug-indications which NICE made a favourable decision 172/230 [75%] were favourable in other countries
- Clearly testing hypotheses one at a time is not ideal. The next step was to consider a wider range of factors potentially influencing a decision in a single model

Variables considered for inclusion in the model

System-wide	Product-specific	Time dependent
Evidence	Type of patient	GDP growth rate
Body independence	Orphan	Health expenditure per capita
Decision level	Number of patients	Public health exp. (%GDP)
Health system	Disease stage	Adult female mortality rate
Initiator	ICER	Adult male mortality rate
Stakeholders	End-of-life treatment	% population 0-14 years
Transparency	Managed entry agreements	% population >65 years
Appeal	Alternative	Crisis dummy
Economic evaluation	Time difference	
Budget impact	Therapeutic area	
Pricing location		
Pricing decision		

Data

- We have analysed the drug reimbursement decisions from 10 European countries (Scotland, England, Belgium, Sweden, Portugal, Germany, Poland, Spain, Netherlands and France)
- Included drugs for Cancer, Multiple Sclerosis & Rheumatoid Arthritis. 199 drug-indication pairs analysed.
- Sample includes the drug reimbursement decisions from 2002 to April 2015 (Germany from 2011)
- 1077 decisions (not all drug-indication pairs have been assessed in each country)

Cabazitaxel: Hormone refractory metastatic prostate cancer previously treated with a docetaxel-containing regimen

Country	Decision	Date
Belgium	Restricted	20-Apr-12
England	Unfavourable	11-May-12
Germany	Favourable	29-Mar-12
Poland	Unfavourable	25-Jun-12
Portugal	Not Assessed	
Scotland	Unfavourable	7-Nov-11
Spain	Favourable	29-Aug-11
Sweden	Restricted	18-Dec-13
France	Favourable	22-Mar-12
Netherlands	Favourable	08-Nov-11

Decision outcome by therapeutic area

Decisions	Cancer	Multiple Sclerosis	Rheumatoid Arthritis	Total
Unfavourable	122 (14.3%)	7 (7.6%)	6 (4.5%)	135 (12.5%)
Restricted	190 (22.3%)	32 (34.8%)	56 (42.4%)	278 (25.8%)
Favourable	541 (63.4%)	53 (57.6%)	70 (53.1%)	664 (61.7%)
Total	853 (100%)	92 (100%)	132 (100%)	1077 (100%)

Data availability & meaning of decision outcome differs across countries

- Spain & France, do not report negative decisions. Not possible to know if a particular drug has been assessed but has subsequently not entered the positive list.
- The Netherlands database only records positive decisions
- In France & Germany the assessment of the drug is used to define the pricing decision procedure rather than to accept or reject the new technology.
 - e.g in France if the new technology is adding value, the price is set based by negotiation. Conversely, if it is not adding value, the price is set using a reference pricing procedure.

Decision outcome by country

	Scotland	England	Belgium	Sweden	France
Unfavourable	42 (29%)	40 (33%)	5 (3%)	5 (7%)	8 (4%)
Restricted	59 (41%)	38 (32%)	78 (50%)	8 (10%)	4 (2%)
Favourable	44 (30%)	42 (35%)	72 (47%)	65 (83%)	172 (94%)
Total	145	120	155	78	184

	Poland	Portugal	Germany	Spain	Netherlands
Unfavourable	28 (23%)	7 (13%)	0 (0%)	0 (0%)	0 (0%)
Restricted	72 (60%)	3 (6%)	0 (0%)	16 (11%)	0 (0%)
Favourable	20 (17%)	43 (81%)	28 (100%)	128 (89%)	50 (100%)
Total	120	53	28	144	50

Econometric analysis

- Interested in the effect of the explanatory variables on the probability of reimbursement (which is unobservable). Use a categorical variable corresponding to the final decision
 - 0 unfavourable
 - 1 restricted
 - 2 Favourable
- Hierarchical Random Effects Ordered Probit selected in order to be able to take account of different time periods, spatial distribution and heterogeneity of the model
- Bayesian inference using Integrated Nested Laplace Approximation

Results

- The requirement of economic evaluation for all drugs, an external review of evidence, the manufacturer being the initiator of the process, price based on reference pricing, and a budget impact being required were all associated with a lower probability of reimbursement
- A drug considered cost-effective by NICE/SMC is associated with a higher probability of reimbursement
- A drug-indication with a NICE favourable decision has a higher probability of also being considered favourable by other countries
- No evidence of systematically different decision making by therapeutic area

Additional analyses

- France and Germany were removed from the sample. This new model improves in terms of efficiency (DIC and CPO). Similar sign and significance. However, initiator and time dependent variables not significant.
- Hypothesis: the effect of the explanatory variables on the final decision may differ according to the pricing system (create interactions).
- The main result that there is a statistically significant effect when the price is set by the manufacturer (NICE, SMC, Sweden, Netherlands and Poland) compared to the price based on a negotiation (France and Germany, drug is adding value). The pricing system of each country has an effect on the decision outcome.

Implications

- There are differences between these ten European countries with respect to their decisions but they can be explained using a combination of system-wide, product-specific and time dependent variables
- This is potentially important for a wide range of stakeholders (from patient groups through to manufacturers)
- There are marked differences between countries regarding the transparency of decision making and the accessibility of information regarding both the processes and the outcomes
- One spin-off from our research is that we have identified the best way for each country to locate what data are available (a benefit not just for other researchers but for anyone with an interest in these important decisions)