# Valuing Trial Designs from a Pharmaceutical Perspective using Value Based Pricing (VBP)

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## Introduction

Expected Value of Sample Information (EVSI) and Expected Net Benefit of Sample information (ENBS) consider what data collection is optimal [1].
But traditional methods are not so useful in pharmaceutical industry drug development because,

- EVSI quantifies expected benefits to society - QALY gain net of costs,
- EVSI assumes the price of the intervention is fixed.

We use a novel approach quantifying expected value based price to evaluate trial designs for a hypothetical Systemic Lupus Erythematosus (SLE) drug.

## Methods

In this framework, the trial value is expressed by an expected profit forecast, conditional on the effectiveness and cost-effectiveness of the new treatment . This is a modification of expected profit based on current information proposed by Willan (2008) for VoI from a pharmaceutical perspective[2].

We have uncertain parameters, $\theta$, for cost-effectiveness model of treatments. We denote sample data from a proposed trial of size n with duration d as, $X_{nd}$.

**Expected total profit forecast** for a given sampled dataset, is dependent on
(1) the expected profit per patient per year given trial evidence $\pi(\theta| X_{nd})$
(2) the annual incidence of patients needing treatment k,
(3) the current time horizon of the treatment, h,
(4) the market share of the new treatment, s.

$$PF_{x_{nd}} = \pi(\theta \mid X_{nd}) \times khs$$

**Expected profit per patient** depends on the **Value Based Price**, $P^*(\theta| X_{nd})$, duration of treatment, $t$, and production costs associated with manufacture, marketing and selling the new treatment per patient per year, c.
We assume the pharmaceutical company has a **minimum price** at which they would submit for reimbursement approval, *Pmin*.
Hence, profit per patient is

$$\pi(\theta \mid X_{nd}) = \begin{cases} 0 & if\ P^* < P\min \\ (P^*(\theta|X_{nd}) - c)t & if\ P^* > P\min \end{cases}$$

The value-based price is that which gives an ICER at exactly the reimbursement authority's willingness to pay **λ**. That is, $P^*$ is:

$$P^* = \frac{\lambda \times [Q_2(\theta) - Q_1(\theta)] + C_1(\theta) - C_2(\theta)}{t}$$

where $Q_1$, $Q_2$, are the Quality Adjusted Life Years for treatments 1 and 2 and $C_1$, $C_2$ are healthcare cost consequences (excluding price of the new drug), and t is the duration of treatment with the new drug.

## Method Applied: Systemic Lupus (SLE)

We developed a simple CE model for SLE in which costs and QALYs were estimated analytically conditional on average lifetime disease activity, average lifetime organ damage and mortality.

**Bayesian Clinical Trial Simulation (BCTS)** was developed to sample disease activity and organ damage outcomes for individuals recruited into a RCT. The longest and largest trial was simulated a subsets of the data were analysed for the shorter and smaller trials to reduce variation in the outcomes between trial designs. This was repeated 10,000 times for each trial design. We updated the CE model with trial data using the Brennan & Karroubi Bayesian Approximation method [3].

1. Specify a series of possible trial designs e.g. sample size n, follow-up duration etc.
2. Draw realisation of each parameter $\theta$ from its prior distribution.
3. Generate a sample of n patients in the trial and randomly assign them to treatment 1 or 2.
4. Simulate clinical trial result $X_{nd}$ using sampled parameters from 1.
5. Select patients for analysis according to trial design
6. Estimate a value-based price P* given the sample data $X_{nd}$
7. Repeat 4-6 for all design options
8. Repeat 1-7 for 1000 iterations
9. Evaluate the ENBS_VBP = for each simulated trial
10. Compare ENBS_VBP across trial designs and consider choosing the trial design which has optimal value (i.e. highest ENBS_VBP).

**Case Study Trials: 9 designs**
**n=100, 500, or1500, d=1, 2, or 3 years.**

**Results Table 1: Simulated outcomes for 9 different trial designs**

| | Trial Cost (millions) | Prob. of FDA approval | Probability reimbursed P*<*Pmin* | Mean P* | Expected Profit per patient | Expected Profit (millions) |
|---|---|---|---|---|---|---|
| N=100, d=1 | £1.2 | 57% | 47% | £786 | £2,297 | £406 |
| N=500, d=1 | £2.0 | 85% | 52% | £902 | £2,755 | £469 |
| N=1500, d=1 | £4.0 | 90% | 52% | £912 | £2,790 | £474 |
| N=100, d=2 | £1.35 | 74% | 51% | £866 | £2,614 | £449 |
| N=500, d=2 | £2.75 | 89% | 52% | £906 | £2,767 | £471 |
| N=1500, d=2 | £6.25 | 92% | 52% | £911 | £2,787 | £473 |
| N=100, d=3 | £1.5 | 80% | 52% | £893 | £2,720 | £464 |
| N=500, d=3 | £3.5 | 91% | 51% | £905 | £2,763 | £471 |

## Case Study Results

- Table 1 reports results
- Trial costs increased with sample size and duration of follow-up.
- Probability of regulatory approval is higher because there is greater chance of positive effects being detected in larger longer trials
- Prob. of reimbursement is less responsive because some positive effects have a resulting VBP P* lower than the company's acceptable selling price Pmin (see **Fig 2**). This illustrates the distribution of value-based price for 1 trial design.
- Expected commercial net benefit analysis (see **Fig 1**) shows a short trial of 1 year duration with large sample size (1500) had the highest commercial net benefit this case study.

**Figure1: Commercial Net Benefit of Trial Designs**

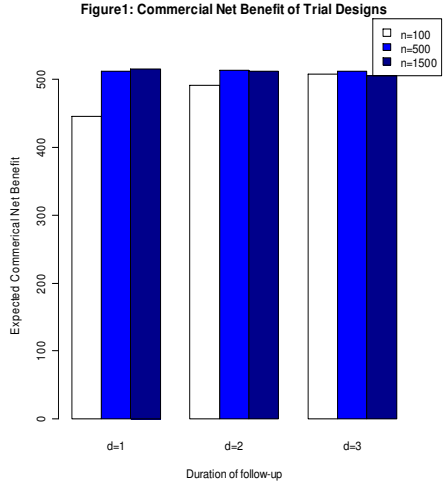
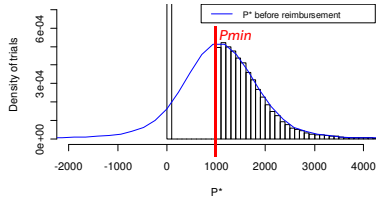



**Figure 2: Histogram of reimbursed Value Based Prices**




## Conclusions

We have illustrated how ENBS can be adapted to value clinical trials in the pharmaceutical industry using expected VBP to integrate price uncertainty into the decision criteria.
Case study analyses indicated larger sample sizes are more efficient than longer trials in SLE. This simple example took 5 days for 10,000 sets of trial results. Analyses can be more time-consuming to run for complex models.

## References

1. Claxton K. The irrelevance of inference: a decision-making approach to the stochastic evaluation of health care technologies. Journal of Health Economics 1999; 18(3):341-364.
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3. Brennan A, Kharroubi SA. Expected value of sample information for Weibull survival data. Health Economics 2007; 16(11):1205-1225.