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# Introduction to Value of Implementation Analysis: Insights from the UK Experience

Precision Medicine Workshop

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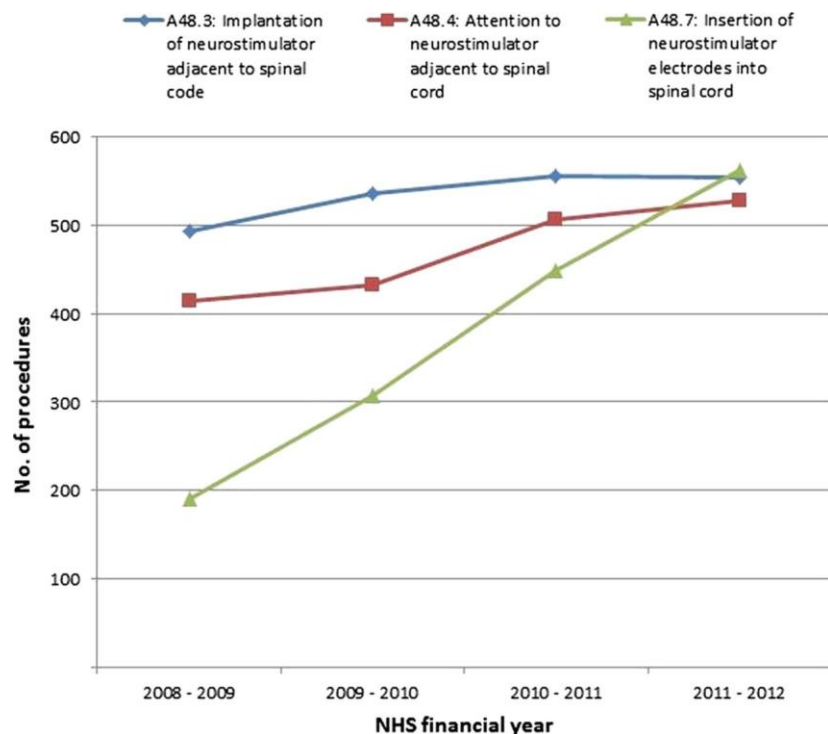
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# What and why?

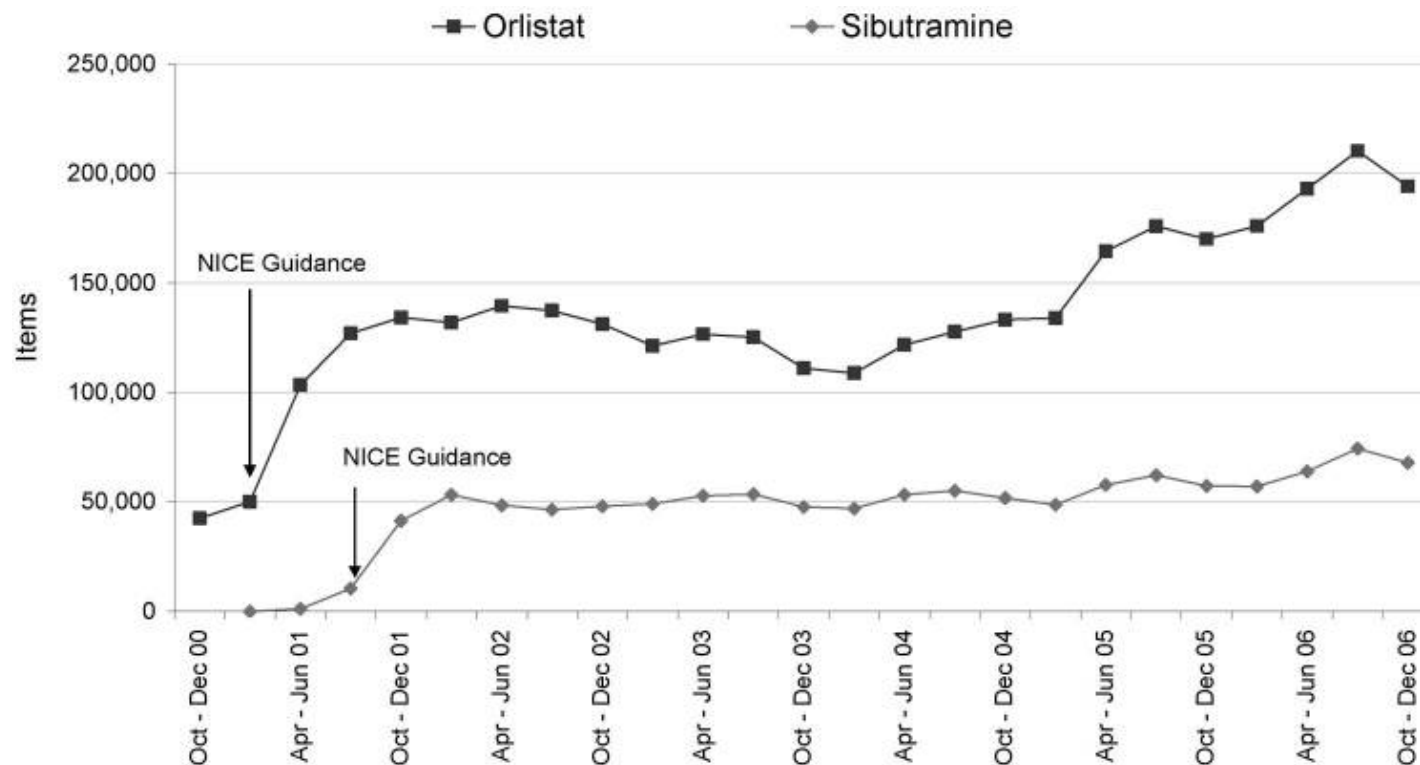
- Uptake/diffusion relate to the degree to which a technology is used in a health system
- Not all diffusion is a good thing...the underlying technology may not be effective or cost-effective
- Not all diffusion is even appropriate, i.e. not for its intended use
- Implementation relates to the uptake of a specific recommendation, and as such, relates to 'appropriate diffusion'
- However, facilitating appropriate diffusion can reduce the barriers to 'inappropriate diffusion'...more of that later
- You can reduce the decision uncertainty to zero, but without implementation, net health benefits are not realised

# Implementation in the UK



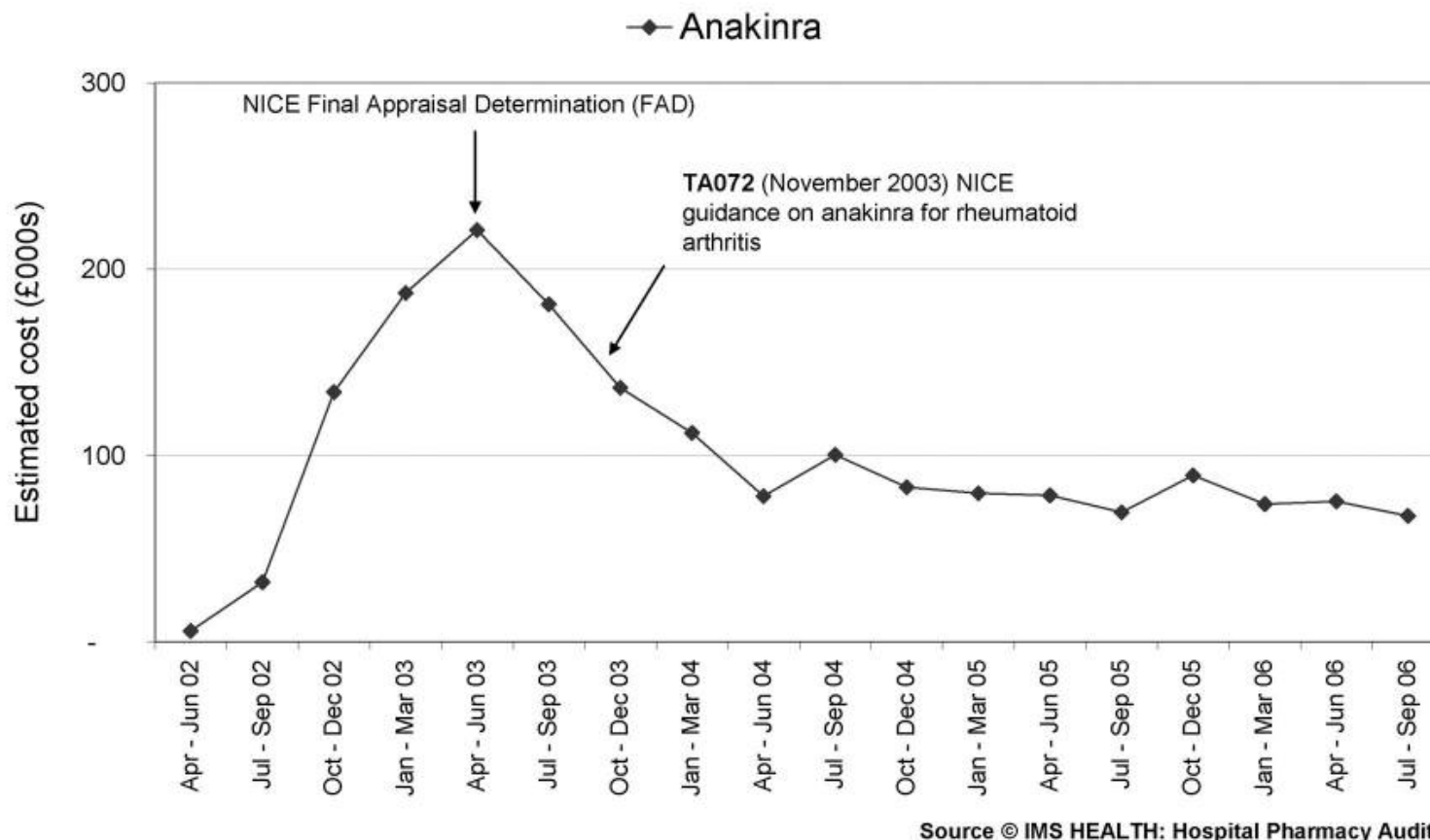
“Despite the positive NICE recommendation for the routine use of SCS, we found no evidence of a significant impact on SCS uptake in England. Rates of SCS implantation in England are lower than many other European countries.”

Vyawahare B, Hallas N, Brookes M, *et al.* Impact of the National Institute for Health and Care Excellence (NICE) guidance on medical technology uptake: analysis of the uptake of spinal cord stimulation in England 2008–2012. *BMJ Open* 2014;**4**:e004182.



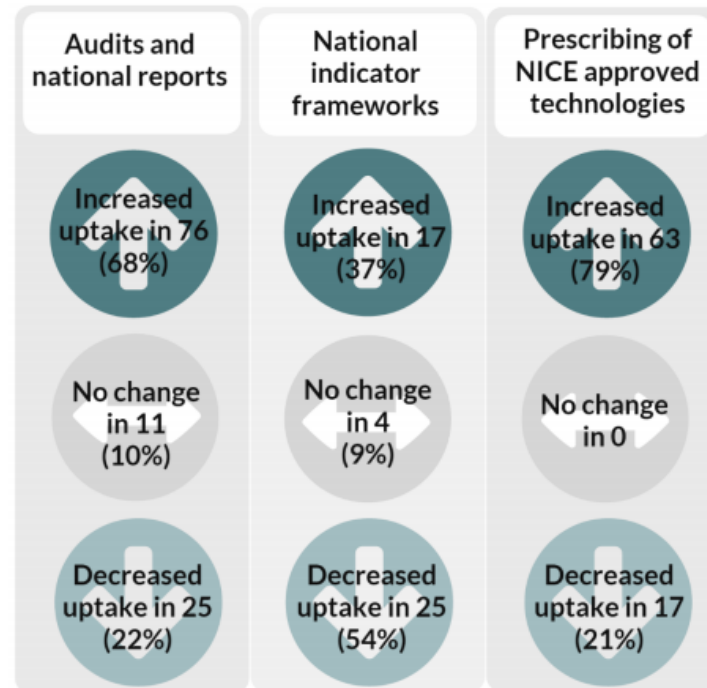
Source: ePACT

Chidgey J, Leng G, Lacey T. Implementing NICE guidance. *J R Soc Med.* 2007 Oct; 100(10): 448–452.



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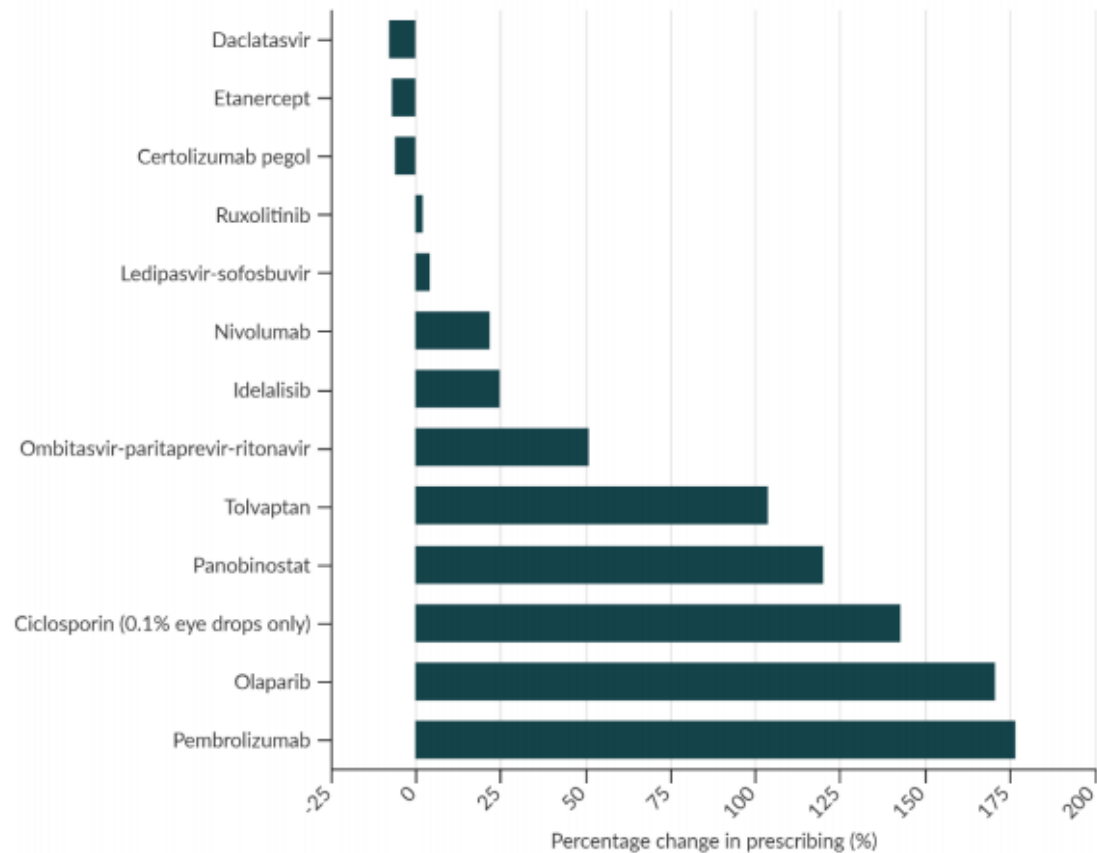
# NICE uptake and impact report



National Institute for Health and Care Excellence. NICE uptake and impact report March 2017. London: NICE, 2017.



**Chart 18: Medicines newly added to the scorecard October 2016, percentage change in prescribing between October–December 2015 and January–March 2016**

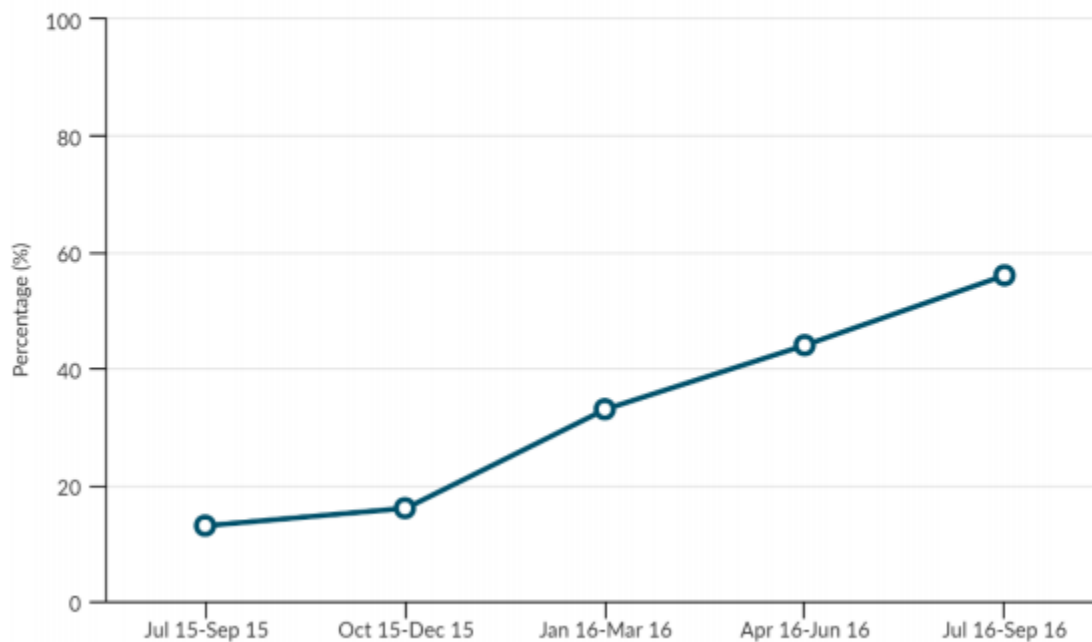


Source: Innovation Scorecard





**Chart 23: Biosimilar infliximab prescribing as a percentage of all infliximab prescribing, July 2015 to September 2016**



Source: Medicines Optimisation Dashboard

# Lessons

- Implementation isn't guaranteed
- Measurement of implementation using routine data isn't always possible
  - Multiple indications
  - Link to highly granular electronic patient record... 'recommended after failure of a platinum based regimen'
- Assessing the counterfactual is difficult
- Assessing increased implementation is a lot easier than assessing 'proportion of eligible population receiving treatment'

# EEPRU work programme

- DH commissioned work in 2013 to support the NICE Implementation Collaborative (NIC)
  - Review the effectiveness and cost-effectiveness of implementation strategies
  - Develop a framework to assess the cost-effectiveness of implementation using the results of CEAs
  - Apply the framework and review findings to two case studies
- Case studies were:
  - B-type natriuretic peptide (BNP) testing in patients with suspected heart failure
  - Novel oral anti-coagulants (NOACs) for patients with atrial fibrillation

# EEPRU review methods

- Non-financial implementation initiatives
- Financial implementation initiatives
- Cost-effectiveness of implementation initiatives
- Diffusion curves
- Frameworks for cost-effectiveness of implementation initiatives
- EEPRU report (Essat et al, 2014)

# EEPRU review results and consequences

- Magnitude of effectiveness is context specific and difficult to predict...as much a qualitative as a quantitative issue
  - Effectiveness needs to be based on ‘indicative estimates’ (see Mewes et al 2017), pilot studies or elicitation
- Cost of implementation initiatives very poor
  - Costs have to be developed locally
- Diffusion is context specific and difficult to predict...as much a qualitative as a quantitative issue
  - Use theory based ‘s-shaped’ diffusion curves, either in their entirety or fitted/calibrated to available data
- Existing frameworks need improvement.....

# New framework

- Fenwick framework with a few added extras (Walker et al., 2013)
  - Inclusion of patient sub-groups (NOACs)
  - Inclusion of future patient cohorts (BNP testing)
  - Inclusion of natural diffusion (NOACs and BNP testing)
- Consequences of the framework (ceteris paribus)
  - The more cost-effective the technology, the most cost-effective will any investment in implementation be
  - The higher the baseline level of diffusion and/or the faster its natural rate of diffusion, the less cost-effective will any investment be

# EEPRU results: BNP testing

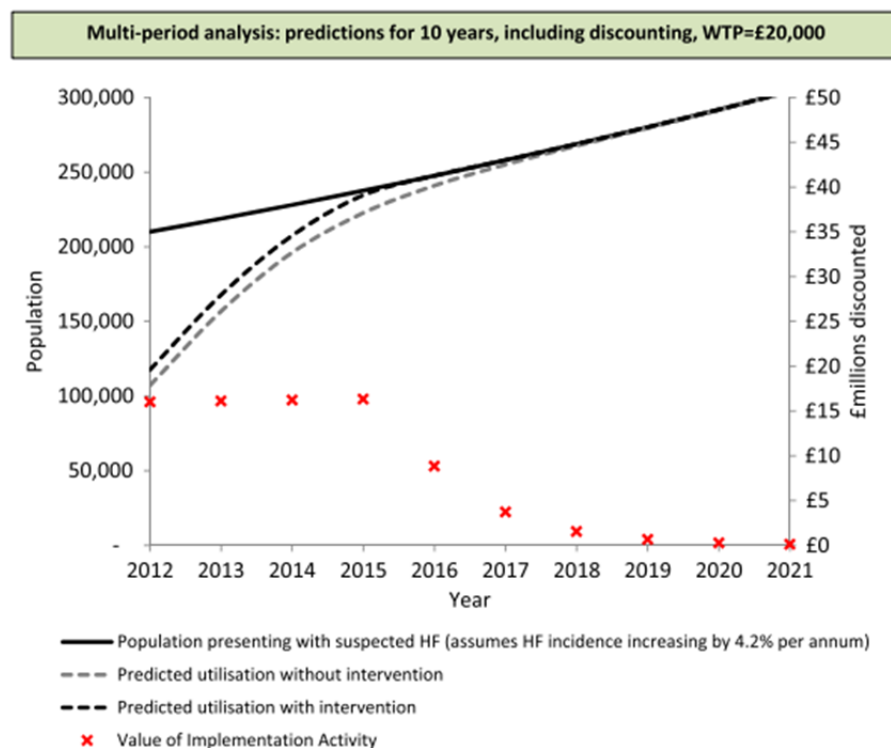
**Table 1 – Static population analysis with base-case assumptions.**

Static population analysis	WTP = £20,000		WTP = £30,000	
	NMB	NHB	NMB	NHB
Net benefit to the NHS (per patient)	£1,518	0.076	£2,282	0.076
Current value of technology given current utilization and population size for England and Wales. Population = 210000, current utilization = 4.43 (51%)	£163,969,752	8198	£246,476,558	8216
Expected value of perfect implementation. Value of increasing utilization from current to desirable maximum. Current utilization = 4.43, desirable maximum = 8.62 (100%)	£154,895,869	7745	£232,836,850	7761
Expected value of actual implementation. Value of increasing utilization from current to achievable. Current utilization = 4.43, achievable utilization with intervention = 4.86 (56%)	£15,943,281	797	£23,965,670	799
Value of the implementation activity. Expected value of actual implementation minus cost of intervention (£28,187)	£15,915,094	796	£23,937,484	798

NHB, net health benefit; NHS, National Health Service; NMB, net monetary benefit; WTP, willingness to pay.

Whyte et al. Estimating the Cost-Effectiveness of Implementation: Is Sufficient Evidence Available? *Value Health* 2016;19(2): 138–144.

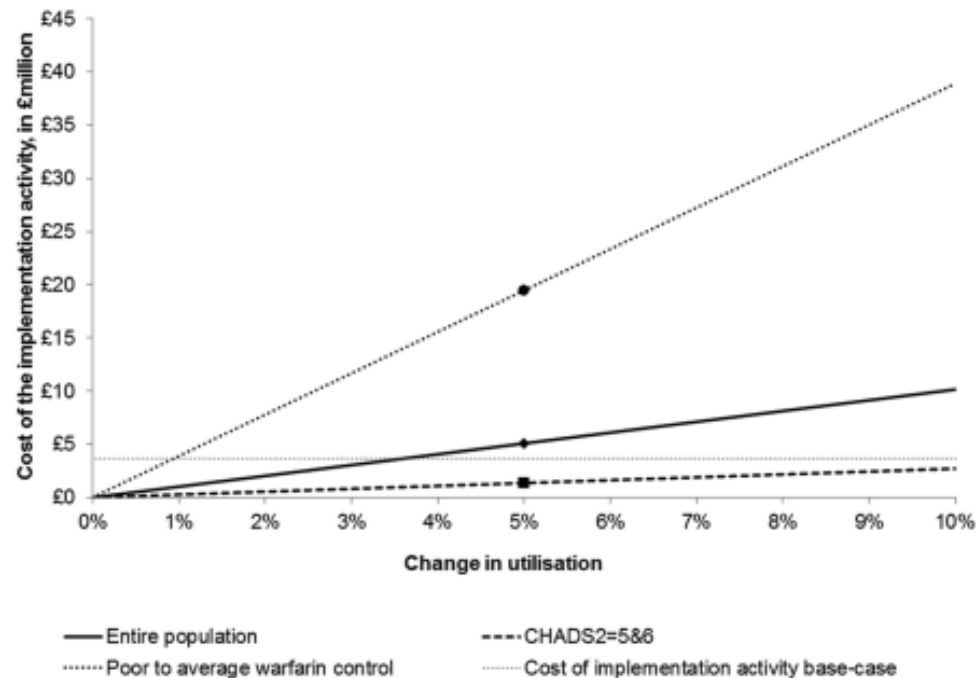
# EEPRU results: BNP testing



Whyte et al. Estimating the Cost-Effectiveness of Implementation: Is Sufficient Evidence Available? *Value Health* 2016;19(2): 138–144.



# EEPRU results:NOACs



Faria et al. How to Invest in Getting Cost-effective Technologies into Practice? A Framework for Value of Implementation Analysis Applied to Novel Oral Anticoagulants. Medical Decision Making 2017;37:148-161.

# Lessons

- Evidence on effectiveness of implementation strategies isn't very good...planning and predicting implementation is problematic
- Data are not always available
  - Most plausible ICER
  - Expected diffusion in terms of shape, gradient and maximum uptake (with the latter being especially problematic in the presence of multiple substitute technologies)
- EVImp can vary by sub-groups

# Implementation dynamics

- Characterised ‘static’ EVPI and EVPImp by:
  - Assumption of (immediate) 100% uptake of technologies
  - Assumption that the ICER is not influenced by the level of implementation
- Relaxing these assumptions would require an exploration of:
  - Diffusion
  - Price changes as a consequence of diffusion (experience curve effects)
  - Effect changes as a consequence of diffusion (learning curve effects)

# “as a consequence of diffusion”

- Price (and effectiveness) changes that happen irrespective of diffusion, such as price reduction in the face of generic competition are not relevant here
- However:
  - Some *price* changes may only happen if the technology is implemented....economies of scale can only happen if implemented, competition will only appear if there is a ‘non-zero market’
  - Some *effectiveness* changes may only happen if the technology is implemented....learning effects can only happen if patient throughput is sufficiently high

# Case study

- Technology for predicting pre-term birth
- Diffusion curves generated using the Bass diffusion model parameterised through SHELF
  - Two separate curves were generated relating to different types of research being made available...diagnostic study and a clinical study
- Experience curve parameterised using a surrogate technology
- Learning curve not deemed relevant and so not incorporated into the model

# Diffusion curve modelling

- The Bass model:

- $$P(t) = p + q * \frac{N_{t-1}}{m}$$

- Where  $P(t)$  is the probability of adoption in period  $t$ ,  $p$  the coefficient of innovation or external influence,  $q$  the coefficient of imitation or internal influence,  $m$  the number of attainable adoptions, and  $N_{t-1}$  the number of cumulative adoptions up to the previous period  $t-1$ .

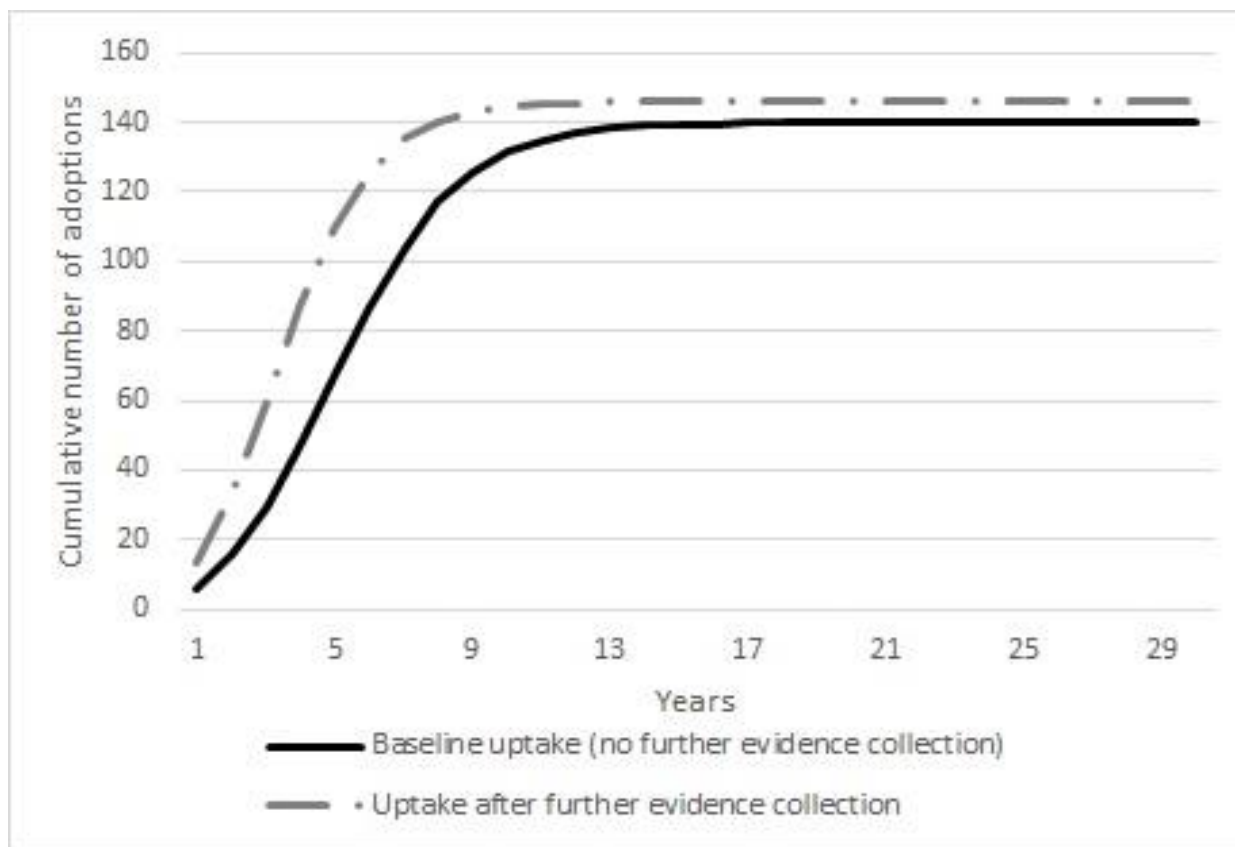
- Values for  $p$  and  $q$  are available from the literature (believe it or not)

- Reported ranges in a variety of industries were (0.000021; 0.03297) and (0.2013; 1.67260) respectively (Sultan et al, 1990)
  - Note that  $q/p > 1$

# Diffusion curve elicitation

- Eliciting “coefficient of innovation” and “coefficient of imitation” difficult, so alternative parameters are required
- Decided to use the attainable number of adoptions ( $m$ , as before), the number of adoptions in the first year after technology introduction (denoted as  $N_1$ ), and the point of inflection, described as the number of years after which the number of adoptions starts to decline ( $t'$ )
- No algebraic solution that allows us to generate a diffusion (logistic) curve from this, so....
  - Used Excel solver to sample  $p$ s and  $q$ s for the given  $m$ , to identify a combination that best fitted the  $N_1$  and  $t'$  elicited
  - Repeated 1,000 times for repeated draws from the distributions of the elicited distributions of  $N_1$  and  $t'$

# Result.....



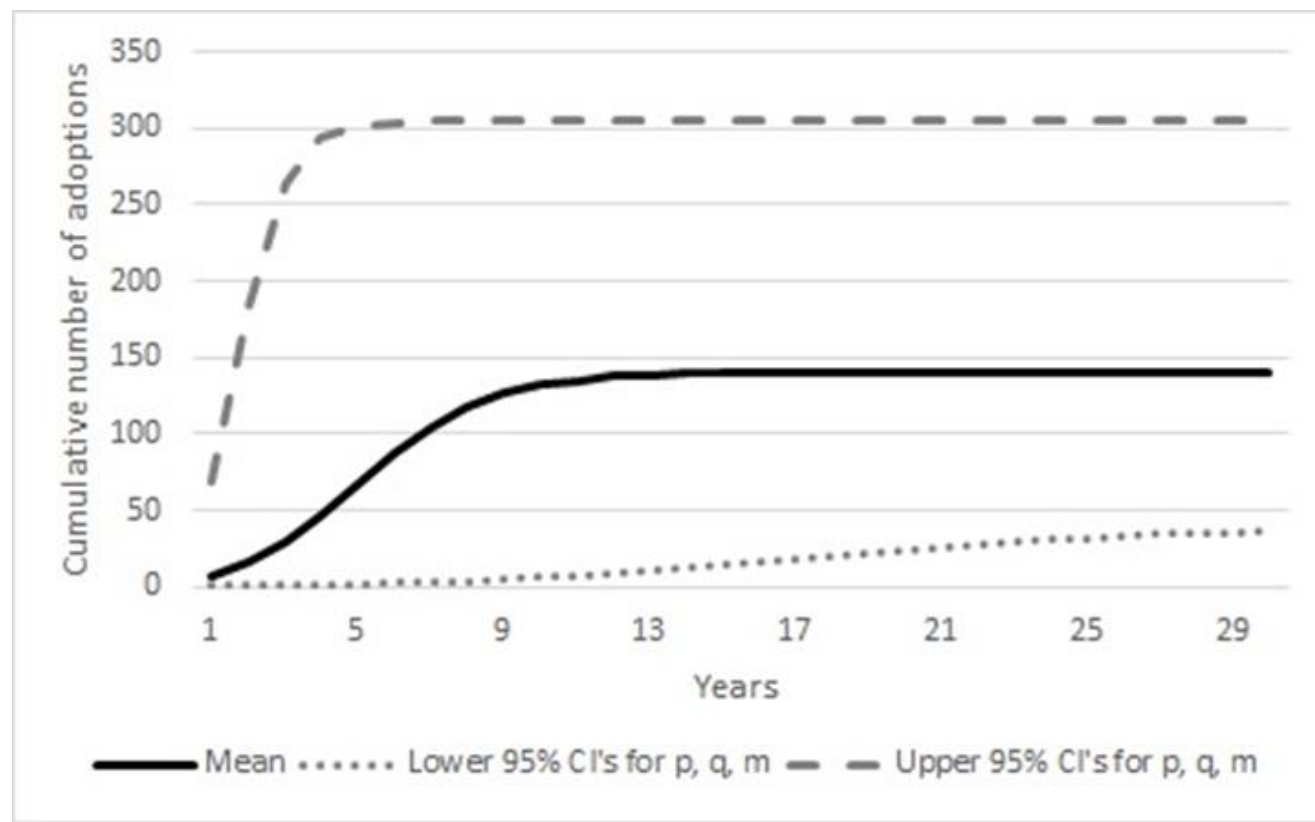




# Curves from the individual experts



# 95% confidence intervals...



# Lessons

- We can parameterise theoretically grounded diffusion curves that can be incorporated into EVImp analysis
- Research can have an impact on implementation
  - Formal research
  - Observational data....*ad hoc* research and audits, registries and managed access data collection stipulations
  - But, can it only be collected with access? Longer term trial follow-up will happen anyway. No access, doesn't mean zero uptake.
  - In other words, we need to know whether access is necessary, and if it is, what data are important

# Managed access in the UK

- Managed access has been formalised through the Cancer Drugs Fund (CDF)
  - Aims to resolve uncertainties through the collection of (up to) 2 years of data in the NHS, followed by a re-appraisal
- It has also been introduced ‘informally’ for direct-acting antivirals for the treatment of hepatitis C
  - “It is recommended that the decision to treat and prescribing decisions are made by multidisciplinary teams in the operational delivery networks put in place by NHS England, to prioritise treatment for people with the highest unmet clinical need” ....in other words, patients with cirrhosis first and a cap on the number of new patients and with treatment outcomes being closely monitored

# Access and re-appraisal (1)

- Access has the potential to provide information on parameters that are relevant to the estimation of cost-effectiveness
- The rate of implementation will determine when sufficient data are collected to re-appraise
- Forecasting implementation is essential for planning re-appraisal
- Purchasers have an incentive to encourage implementation otherwise sufficient data may not be collected for a robust re-appraisal

# Access and re-appraisal (2)

- Data collection needs to be planned
  - Diffusion (appropriate and inappropriate)
  - Parameters of interest for the re-appraisal....QoL, % meeting stopping rules, outcomes, etc.
- Data analysis needs to be planned
  - Observational studies are open to biases
  - How do you analyse the data collected, and synthesise it with the trial data, in a way that is valid?
  - If the analysis isn't believable, neither will the re-appraisal

# Access and re-appraisal (3)

- Dynamic effects are possible, but difficult to include
  - Access has the potential to influence price (when market entry is easy)
  - Access has the potential to influence effectiveness, for example, patient selection, use of concomitant medications
- Rapid diffusion can lead to inappropriate use
  - This isn't normally included in economic evaluation, but should be considered when assessing value of implementation
  - Specific strategies with good data collection will reduce inappropriate use...do they exist?....how much do they cost?

# Access and re-appraisal (4)

- The PTB study suggested that quicker diffusion and a higher overall level of diffusion was possible following further research
- If a managed access scheme generates information that reduces decision uncertainty, this too may increase diffusion in the event of the technology being recommended for use, and therefore, increase population net benefit
- This provides another reason for purchasers to invest in MEAs
- Given the role of MEAs in future implementation, they should be designed not just to reduce decision uncertainty, but to identify and resolve barriers to uptake



# Other literature

- Related to the notions of EVImp and Managed Access are other literature linking uncertainty to data collection
  - Approval with Research
  - HTA Risk Charts
  - Risk Sharing
  - Outcomes based contracting (or payment for performance)
- These all link and provide different perspectives and lessons, e.g. the role of irrecoverable costs, quantifying uncertainty and pricing
- Linking access, risk and contracting needs to be considered
- All of these require a 'sensible' estimate of opportunity cost ( $\lambda$ )

# Summary

- EPRU work showed us that applying a simple framework can be far from simple
- Diffusion is highly unpredictable, but for a rational framework, ex ante forecasting using a Bayesian framework is possible
- Diffusion, data collection and re-appraisal are all connected
- Data collection reduces uncertainty and can increase implementation
- Inappropriate use should be considered within implementation design and evaluations
- Value of implementation links to other concepts both academically and practically...data collected during managed access can form the basis of outcome-based contracting

# Acknowledgements

- The EPRU modelling was undertaken by Sophie Whyte and myself (Sheffield) and Rita Faria, Mark Sculpher, Simon Walker and Stephen Palmer (York). The work was funded by the Department of Health.
- The work on diffusion and its link to EVI and EVImp was the focus of doctoral thesis by Sabine Grimm (and supervised by John Steven and myself)
- All errors have nothing to do with me.

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