PH 458/231
Evidence & Policy
Lecture 9

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Office Hours:
Monday 13.30-14.30
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From evidence to decision (I)

- Saw that controlling for selection bias is an unambiguous virtue of randomization
- But how large an effect is likely to be produced by SB?
- Increasing recognition that the answer may well be ‘quite small’
- Doll & Peto: ‘hardly likely to produce a tenfold artefactual effect [though it] may well produce a two-fold artefactual error’.
- Can only be thinking of practically ineliminable SB
- But their remark
- (a) is “Bayesian-friendly”
- (b) concedes that RCTs may well be unnecessary for large effects
- Glaziou et al (2007) “Some treatments have such dramatic effects that biases can be ruled out without randomised trials.”

From evidence to decision (I)

- But Doll & Peto (and later Peto and others) are not using the likely smallness of SB as an argument for HCT
- On the contrary, as a new argument for randomizing!
- 'Why do we need some large, simple, randomized trials?'
- Doll and Peto "most of the really important therapeutic advances of the past decade have involved the recognition that some particular treatment for some common condition yields a *small but important* improvement in the proportion of favourable outcomes."
- Yusuf et al added: "if any widely practicable intervention had a very large effect, … then ... these huge gains in therapy are likely to be identified more or less reliably by simple clinical observation, by 'historically controlled' comparisons, or by a variety of other informal or semi-formal non- randomized methods" .
- Hence (op cit p.411) "if there remains some controversy about the efficacy of any widely practicable treatment, its effects on major endpoints may well be either nil, or moderate ..."
- NB 'small' here means 'small number of patients getting the (full) +ve outcome'

From evidence to decision (I)

- Need to distinguish between a null and 'moderate' (small!) effect
- HCTs or non-randomized intervention trials, because of (small) SB, cannot be relied upon to do this
- So have to be *R*CTs
- Moreover have to be large:
- "It is chiefly because one [nowadays] usually needs to be able to distinguish reliably between moderate and null effects that trials need to be *strictly* randomized … and much, much larger than is currently usual"
- "the small randomized trials that are regrettably commonplace nowadays have random errors which are often far larger than the real differences to be detected."
- Multi-centre (requires *simplicity*)

From evidence to decision (I)

- In cardiology:
- ASSET (5,200)
- GISSI-2 (12,700)
- GISSI-3 (19,500)
- CURE (12,200)
- ISIS-2 (17,000)
- ISIS-4 (58,000)
- ** Small effects not to be scoffed at:
- Peto et al (1995) claim that the 1988 ISIS-2 study which published an absolute risk reduction of heart attacks of under 2% had probably by 1995 “avoid[ed] about 100,000 vascular deaths in developed countries alone.” (p. 26)

From evidence to decision (I)

- Is *this* a good argument for RCTs?
- Three worries:
- 1. Are there really no more ‘dramatic’ effects to be found? (though argument can be re-jigged)
- 2. External validity
- (esp marked in mega-trials because of
- (a) rigidity of treatment
- (b) possibility of big differences in application of exclusion criteria
- (c) very little difference in the experimental and control groups)
- *3. Don’t forget the ‘down side’

From evidence to decision (I)

- Trials on effects of various statins on subsequent mortality from stroke and heart attack (LIPID, CARE, etc). Here are some representative results

Study	**Outcome**	**Abs RR**	**NTI**
LIPID	mortality	1.9%	98.1
CARE	stroke	1.2%	98.8
GISSI-3	composite	1.4%	98.6

- Relative risk reductions of 30-odd% bandied about ..
- But what if you are the 1 in 100 or so who would benefit?
- Of course if there were no downside ...
- But there is!
- Again not philosophers' possibilities
- Cerivastatin

From evidence to decision (I)

- P(helps) × utility(helps) + P(doesn't help) × disutility(taking it ineffectively and incurring the side effects)
- Given that P(helps) ≈ 0.01 and P(¬helps) ≈ 0.99
- Can't just assume that the expected utility of prescribing the statin is positive
- Lessons for evidence savvy administrators:
- Even if you are confident that the evidence has given you the correct risk assessments
- A. Make sure you are not fooled by relative risk
- B. Make sure you take into account both sides of the utility calculation

From evidence to decision (II): the 'Precautionary Principle'

- The orthodox view in decision theory is essentially this:
- You can produce the energy you need either by a nuclear plant or a coal-fired plant
- In both cases you get the energy, but if you choose COAL:
- Definitely problems associated with carbon emissions – leading to increased risk of a number of (slowly developing) bad consequences for the environment
- BUT no chance of (immediate) catastrophe
- If you choose NUCLEAR:
- No problems with carbon emission
- BUT some probability of problems with nuclear waste and (very small) chance of melt-down leading catastrophe
- [The evidence feeds into how bad the problems with carbon emissions are AND what the real probability of waste problems/the melt-down is.]
- We choose C or N depending on the expected (dis)utility of C compared to the expected utility of N = (dis)utility of catastrophe x probability of (waste problems v catastrophe)
- And we choose C v N if the utility of having the energy outweighs whichever is the lower of these.

From evidence to decision (II): the ‘Precautionary Principle’

- However for past several decades many people have advocated a seeming rival in the form of “The Precautionary Principle”
- Intuitions:
- Avoid steps that will create risk of harm.
- Until safety is established, be cautious
- Better safe than sorry!
- Because there is a possible catastrophe associated with NUCLEAR, you should definitely prefer COAL
- Most obvious statement of this as a general view:
- First European “Seas at risk” conference (1994)
- ‘[if] the “worst case scenario” for a certain activity is serious enough then even a small amount of doubt as to the safety of that activity is sufficient to stop it taking place.’

From evidence to decision (II): the ‘Precautionary Principle’

- 1. Is that what the PP really claims? If not, what does it really say?; and
- 2. Is it a defensible/preferable alternative to orthodoxy?
- [If the answers are ‘hard to tell’ and ‘no’ then a subsidiary question arises:
- 3.How come ‘the’ principle has been so widely advocated/ seemed sensible to so many people??]

‘The’ Precautionary Principle

- Sunstein takes it that the way to read PP (strong version) is:
- ‘regulation is required whenever there is a possible risk to health, safety, or the environment, even if the supporting evidence is speculative ..
- And then argues that trying to follow this version would be ‘paralyzing’
- Because ‘ every [action], including inaction, creates a risk to health, the environment or both’.
- E.g. ‘drug lag’: ‘There is a chance that new untested drugs may cause catastrophes: witness thalidomide; so, although the risk is speculative, be very cautious and insist on long, rigorous testing before approving a drug.’
- BUT (of course) you may be withholding a drug of great benefit:
- ‘There is a chance that this drug cures AIDs, in which case you would be causing many unnecessary deaths (catastrophe) if you withheld it ..

‘The’ Precautionary Principle

- Similarly:
- “Ban genetically modified foods, there is a (speculative) chance that they might cause an environmental disaster..”
- “Allow genetically modified foods, otherwise the risks of famine in Africa are greatly increased ..”

‘The’ Precautionary Principle

- So on Sunstein’s construal (‘regulation is required whenever there is a possible risk to health, safety, or the environment, even if the supporting evidence is speculative ..) the ‘strong PP’ leads to paralysis
- I think that a ‘strong’ version more consistent with the original intuitions (‘[if] the “worst case scenario” for a certain activity is serious enough then even a small amount of doubt as to the safety of that activity is sufficient to stop it taking place.’) is
- When confronted with a decision, if there is evidence that one choice C might, with however small a probability, lead to “catastrophe” while the alternative C’ might have risks of harms too, but they are less dramatic, then always choose C
- This is arguably not ‘paralyzing’ (though ‘catastrophe’ is vague) but it would lead to ridiculous decisions.

‘The’ Precautionary Principle

- So if the PP under any ‘strong’ construal is indefensible, how about Sunstein’s follow-up question:
- How come it is so widely advocated?
- Sunstein produces an interesting list of factors, based on the psychological literature on biases in reasoning:
- Loss aversion/endowment effects
- Familiar vs unfamiliar risks
- Myth of the benevolence of Nature
- Availability heuristic
- Probability neglect
- All, arguably, forms of a ‘narrow viewscreen’ approach: concentrating on one part of the effect of a decision/policy and ignoring others (particularly opportunity costs)
- [Heathrow snow equipment]
- When people are forced into a wider-screen view they make more measured, more sensible decisions