# On Probabilities in Personalised Medicine: 'The Problem of Untestable Treatments'

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# *Aim*

To present a problem with using probabilities that may arise in personalised medicine (but need not in normal evidence-based medicine).

To offer a solution to the problem.

# *Talk Overview*

Preliminaries

(1) The Ethical and Legal Bearing of Epistemic Concerns (in Context)

(2) The Interpretation of Probability

(3) The Reference Class Problem

The Main Dish

(4) 'The Problem of Untestable Treatments'

(5) A Tentative Solution to the Problem

(6) Some Remaining Issues (if time permits)

# *(1) The Ethical and Legal Bearing of Epistemic Concerns*

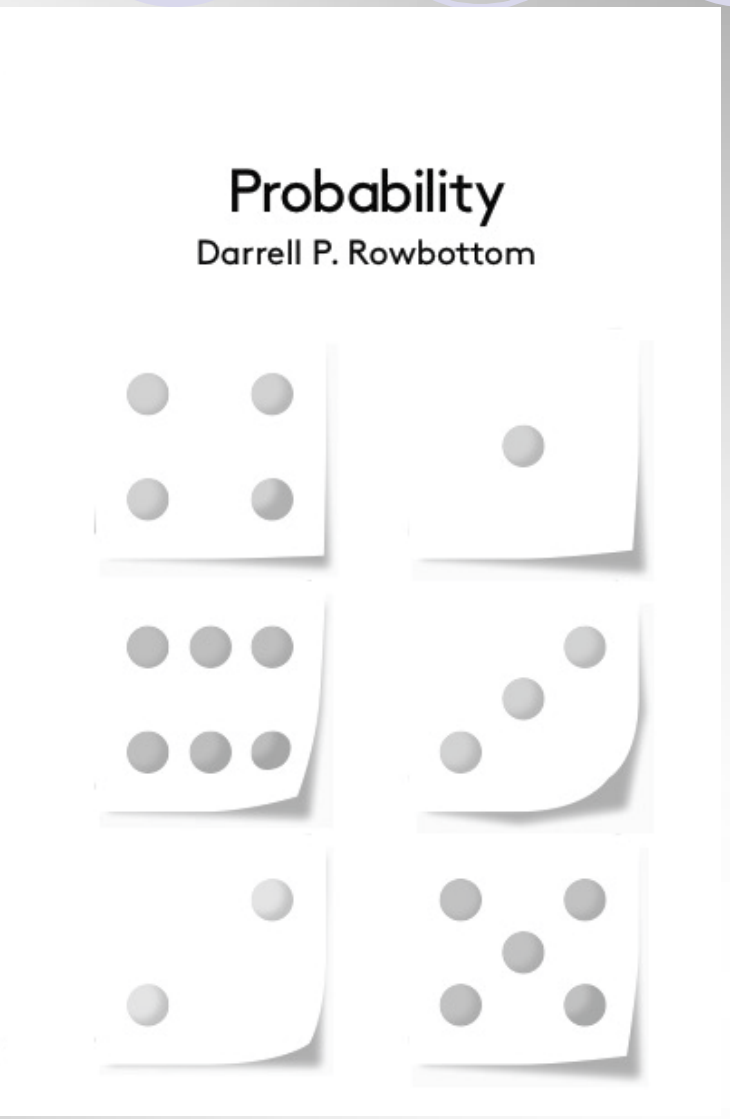
- The primary focus of this paper is epistemic; it considers whether medical practitioners can have 'good reasons' for recommending particular courses of action.

- I take there to be ethical and legal consequences if medical practitioners cannot have, and hence present, such reasons. Consider negligence, or balance of probability considerations.

# *(2) The Interpretation of Probability*

- Probability is Janus-faced.
- There are ‘information based’ and ‘world based’ alternatives.
- There are also many sub-categories.

# (2) The Interpretation of Probability

# *(2) The Interpretation of Probability*

- Today, I'll consider the use of 'world based' probabilities (which are plausibly the appropriate ones to use in evidence-based medicine for independent reasons).

- Very roughly, these correspond to relative frequencies in the limit. (There are better conceptions, but we won't be able to cover them today.)

# *(3) The Reference Class Problem*

- There's a well-known problem about the use of probabilities (so construed), which always concern COLLECTIVES (e.g. some class of coin flips, rather than an individual coin flip).

- The problem is: which is the proper collective to use?

# *(3) The Reference Class Problem*

- Here's an illustration. Imagine you're offering an operation to an elderly patient, and she asks what the probability of success (i.e., recovery with no complications) is.

# *(3) The Reference Class Problem*

- You are aware of two potentially relevant data sets. You know the relative frequency of success for your operations of this kind is around 0.9. (You have performed the operation on many patients, of a wide variety of ages. But you don't have an age-based breakdown.) You also know the relative frequency of success for this kind of operation in a recent large study, involving only elderly patients, but performed by a variety of medics in different hospitals, was around 0.2.

- What should you tell the patient?

# *(4) 'The Problem of Untestable Treatments'*

- Personalised medicine potentially introduces a new kind of problem. (Here I'll discuss only treatments. But similar examples might be constructed which concern diagnosis and prognosis.)

- Imagine we reach a stage at which tailored treatments are devised, on a patient-by-patient basis.

# *(4) 'The Problem of Untestable Treatments'*

- We could not have tested any given treatment before. It's new.

- Moreover, testing it on other people would not be helpful (and could, in fact, be dangerous according to our existing theories). It's personalised. It's not *supposed* to be effective on other people.

- So how could we provide a probability for the treatment being effective (and have reasonable grounds for using / recommending it)?

# *(4) 'The Problem of Untestable Treatments'*

- The example in my abstract concerns individualised drugs. It may be implausible that we'll reach such a stage, at least in the near future. But the treatments need not be drugs. (And the example could be modified, for instance, to involve dosages or drug combinations.)

- Note also that the problem here doesn't depend on there being only *one* patient per treatment type. The number of patients per treatment type might merely be low.

# *(5) A Tentative Solution*

- The solution I propose is to move one level up from the treatment, to the *treatment selection process*, in order to find a suitable collective.

- Specifically, we might consider the relative frequency of successful treatments *being generated by the treatment selection process*.

# *(5) A Tentative Solution*

- Data on this *can* be collected (e.g. in trials, *inter alia*, using standard techniques such as random sampling).

- Moreover, double blind trials remain possible. (The patient and medic need not know if a patient has received a treatment *selected by a given process*, as opposed to no treatment, a placebo, etc.)

# *(6) Some Remaining Issues*

- Nevertheless, a whole treatment selection process is typically much ‘bigger’ – in terms of complexity – than a treatment administration process.

- For instance, it might involve a diagnostic step, or steps, such as DNA sequencing.

- Thus a *treatment selection process* typically has more potential sources of error than a *treatment administration process* does.

# *(6) Some Remaining Issues*

- There's a way of demonstrating this via a well-known result in philosophy of science, namely Duhem's thesis.

- This says that a hypothesis cannot be tested in isolation.

- Or in other words, generating any prediction from a theory requires auxiliary hypotheses.

# *(6) Some Remaining Issues*

- Does this present a new difficulty?

- On the one hand, some treatment trials are only valid *provided* the diagnoses of the subjects, performed before the trial, were reliable. (Consider, for example, the misclassification of patients in psychiatry. The DSM definitions change noticeably, on occasion, between editions.)

- On the other hand, they may be constructed with recourse only to patient symptoms…