40 years of 'Why Isn't Everyone a Bayesian?" - a regulatory perspective

Andrew Thomson – BAYES 2026



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Reasons to (not) be Bayesian - Part 1

Ease of use: Fisher's theory in particular is well set up to yield answers on an easy and almost automatic basis.

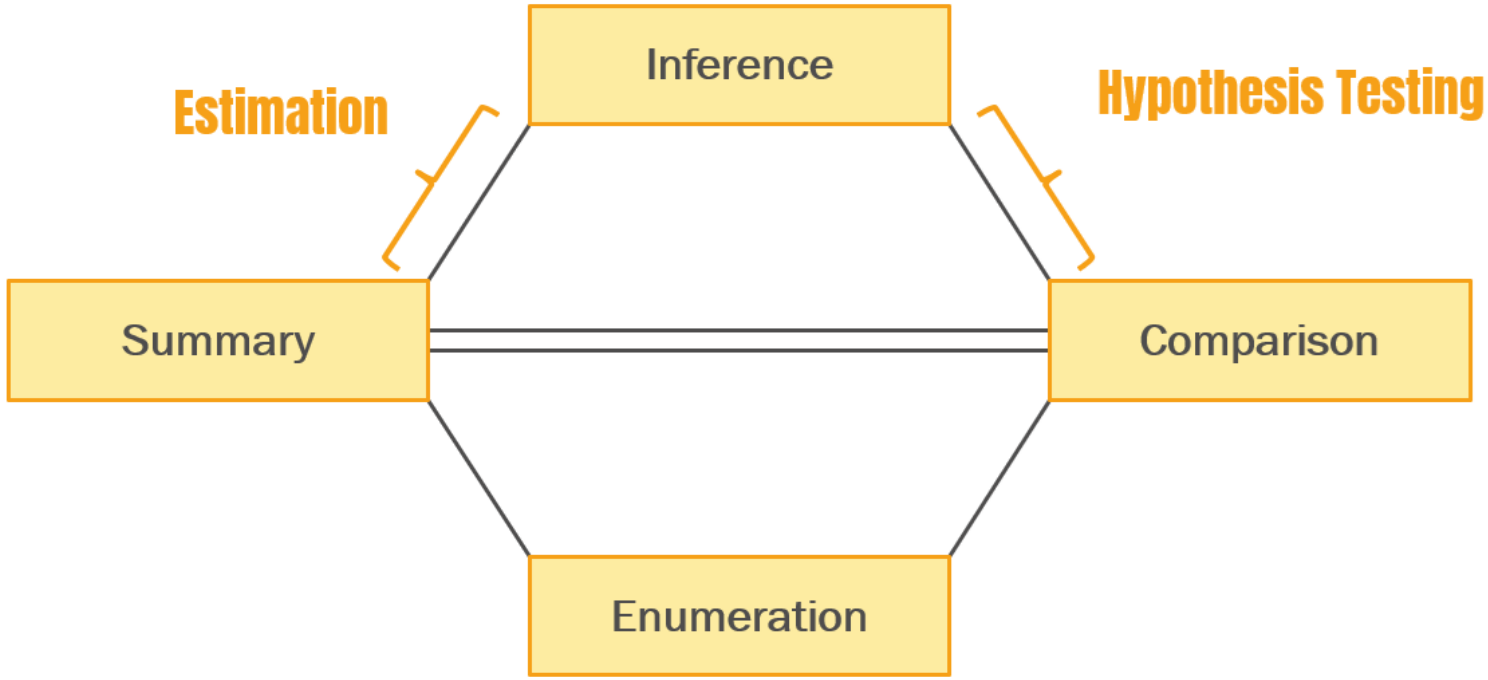
Faced with a new situation, the working statistician can apply maximum likelihood in an automatic fashion, with little chance (in experienced hands) of going far wrong and considerable chance of providing a nearly optimal inference.

Verdict - SOLVED

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Reasons to (not) be Bayesian - Part 2

Model building: Both Fisherian and NPW theory pay more attention to the pre-inferential aspects of statistics.



Verdict – SOLVED

(as much as we can)

Adapted from Why Isn't Everyone a Bayesian, Four Basic Statistical Operations and How They Relate to Estimation.

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Reasons to (not) be Bayesian - Part 3

Division of labour: The NPW school in particular allows interesting parts of a complicated problem to be broken off and solved separately. These partial solutions often make use of aspects of the situation, for example, the sampling plan, which do not seem to help the Bayesian.

Kopp Schneider at al have shown that for small specific problems – pre-specified primary endpoint, control of false decision declaring, frequentism wins.

Verdict - SOLVED

Although not necessarily to the satisfaction of Bayesians. And what about the bigger picture?

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Reasons to (not) be Bayesian - Part 4

Objectivity: The high ground of scientific objectivity has been seized by the frequentists.

Subjectivity... has failed to make much of a dent in scientific statistical practice. The nature of scientific communication makes me doubt that it ever will. "Scientific objectivity" is more than a catch-phrase. Strict objectivity is one of the crucial factors separating scientific thinking from wishful thinking...
... A prime requirement of any statistical theory intended for scientific use is that it reassures oneself ***and others*** *that the data have been interpreted fairly.*

Verdict – UNSOLVED

Possibly unsolvable

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A Short Interlude - 2 Questions

1) Has anybody here ever asked a regulator *why* they don't like Bayesian statistics?

2) Has anybody here ever uttered the statement "I don't understand why regulators don't like/accept/understand Bayesian methods"

If you want to answer the question "what do I need to do to convince you?", you need to understand why regulators may not be currently convinced.

And in order to understand that 'why', another step back is needed, and to appreciate why Phase 3 adult de novo randomised clinical trials in common disease are different. From now on, "Phase 3".

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Why are Phase 3 Trials different?

- Designed for regulators, who make absolute decision is made on them, within a strict legal framework, in which there is no opportunity cost.
- Legal framework requires a level playing field.
- The decision is adversarial.
- This is as good as it gets:
  - Evidence Base;
  - Treatment Effect.
- There is genuine equipoise.

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What are the consequences?

- Confirmatory trials are important.
- Often the decision is a two-step process – show it ‘works’ and then evaluate benefits and risks.
- Regulators are genuinely interested in data given hypothesis.
- Hardest decision set at the margins. Consistency needed for a functional legal framework.
- At the margins, sensitivity analyses are often crucial.
- Huge amount of focus on the enumeration, estimation and comparison parts of that diagram.
- Preference for methods that likely do not over-estimate the treatment difference
- When faced with a bias-variance trade-off, the position has very often been “variance”

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What is the impact?

There are good reasons: philosophical; practical scientific ones; practical legal ones; practical operational ones, that all hold back the use of Bayesian statistics in regulatory decision making. It is not (just) a lack of understanding of Bayesian methods, and if you just explain it to them a little bit more then regulators will come round to your way of thinking.

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How to move forward?

Given all of this, what could and should people who would like Bayesian methods to be used more frequently in regulatory decision making *actually do* to make this happen?

- Stop telling them they are interested in hypothesis given data – they aren't.
- Stop telling them Bayesian statistics is easier to understand and explain to clinicians than frequentists statistics.
- Appreciate the legal framework – regulation is where law and science meet.
- Acknowledge it is a bias-variance trade-off oftentimes on the side of bias.
- Work out the areas where everything I have said is not the case, and focus on these.

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What are those areas?

Where could and should Bayesian statistics be used more in regulatory decision making where it is currently underused?

- Rare diseases
  - Type 1 Error – Sample Size – Type 2 Error dynamic breaks down. Bayes may not be the answer.
  - **Totality of evidence** – moving away from the small part of the problem.
  - **Relative decision making** - Significant benefit discussions for Orphan status.
- **Not about comparison, but estimation** - secondary endpoints, subgroups.
- Paediatric Extrapolation - r**elevant prior data exists** – combined with a model linking adults to paediatrics.
- **One party owns both decisions –** Phase 1, 2 some parts of Phase 4.

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Conclusions

For Phase 3 clinical trials there is frequentist decision making, for everything else there is Bayesian.

And keep up the good work.

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