

Editorial

How Not to Be a Successful Clinical Pharmacologist

Stockmann C^{1,2*}, Constance JE¹, Roberts JK¹, Sherwin CMT¹ and Spigarelli MG^{1,2}

¹Division of Clinical Pharmacology, Department of Pediatrics, University of Utah School of Medicine, Utah

²Department of Pharmacology and Toxicology, University of Utah College of Pharmacy, Utah

EDITORIAL

Clinical pharmacology has a rich and storied history of many successful clinicians and scientists who have developed novel therapeutic and preventive agents, refined drug dosing regimens, and probed the depths of human physiology and molecular biology [1-5]. Much less is known about how *not* to be a successful pharmacologist. Inspired by Dr. Carole Goble's "Seven Deadly Sins of Bioinformatics" and Corpas et al.'s "How Not to Be A Bioinformatician" [6,7], in this sarcastic editorial we aim to provide a list of 10 guidelines that virtually guarantee that one's quasi-scientific pursuits will be – at worst – confined to obscurity and – at best – enshrined in infamy:

- 1) Assume that your new drug acts in a binary on/off fashion, whereby its effect remains constant until the instant before the next dose is administered, irrespective of its concentration at the effect site. Blindly trust that your drug acts like a light-switch because "your drug is special" (Figure).
- 2) Ensure that dose-response curves result in eye-pleasing shapes. Develop your experimental data by anecdote. Pick and choose only those data points that confirm your prior hypotheses. Use arbitrary cut-offs to derive artificial thresholds that are statistically significant and utterly impossible to reproduce.
- 3) There is an inverse relationship between the number of experiments you conduct and the earth-shattering impact of your results. You already know how this experiment should turn out, right?
- 4) Conduct under-powered non-inferiority trials. Without enough patients to detect a significant difference your drug will always be non-inferior – success!
- 5) Collection of serial pharmacokinetic samples is inconvenient and costly – therefore, replace them with one big sample at the end of therapy. A single snapshot at the end tells you everything you need to know about what came before.
- 6) If a new side effect emerges, simply add another drug to counteract it. Urticaria, nausea, vomiting, hallucinations,

*Corresponding author

Chris Stockmann, Division of Clinical Pharmacology, Department of Pediatrics, University of Utah School of Medicine, 295 Chipeta Way, Salt Lake City, Utah, Tel: 1-801-585-0903; Fax: 1-801-585-9410; Email: Chris.Stockmann@hsc.utah.edu

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irrepressible ticks, a third eye, growth of a new appendage -- there's a drug that can fix that!

- 7) Personalized medicine improves drug safety and efficacy – does your patient prefer the blue, green, or red pill? As patient allocation should be random – let them choose: would they prefer the placebo or active comparator? Additionally, to better model the real-world, why not let clinical trial participants choose their own dosing regimen. Was it 200 mg twice a day or every other day...?
- 8) Rarely include citations – but if you must, only cite irrelevant and outdated literature that does not pertain to the research question at hand. The authors found that "the dense population of brush-tailed marsupials in these skyscrapers suggests that prior to agricultural clearing and timber harvesting, flying sugar gliders may have been much more common in Atlanta than previously thought" [insert citation here], thereby confirming the safety of our proposed dosing regimen.
- 9) Superfluous mathematical equations should always be included to remind your colleagues why you are irreplaceable. The kinetic properties of drug-eluting stents can easily be simulated by coupling a steady-state convection diffusion equation with the steady-state Navier-Stokes equation and Schrödinger's time-dependent equation to yield:

$$Pe \left(\frac{\partial C_f}{\partial z} + \phi \frac{\partial C_f}{\partial r} \right) i\hbar \frac{\partial}{\partial t} \Psi(r,t) = \frac{\partial^2 C_f}{\partial z^2} + \frac{\partial^2 C_f}{\partial r^2} \left[\frac{-\hbar^2}{2m} \nabla^2 + V(r,t) \right] \Psi(r,t).$$

Only you are bright enough to develop unreadable, unparseable equations such as this that don't comply with any known biophysical process.
- 10) When you talk to yourself and develop a break-through idea, cite it as a "Personal Communication". When the data strongly support your conclusions and you never specified any in the first place, call it "emergent science" to lend credibility to your landmark results.

In summary, we have highlighted a series of disastrous practices that will maximize your notoriety and ensure that your research is untrusted and disruptive. By adhering to these

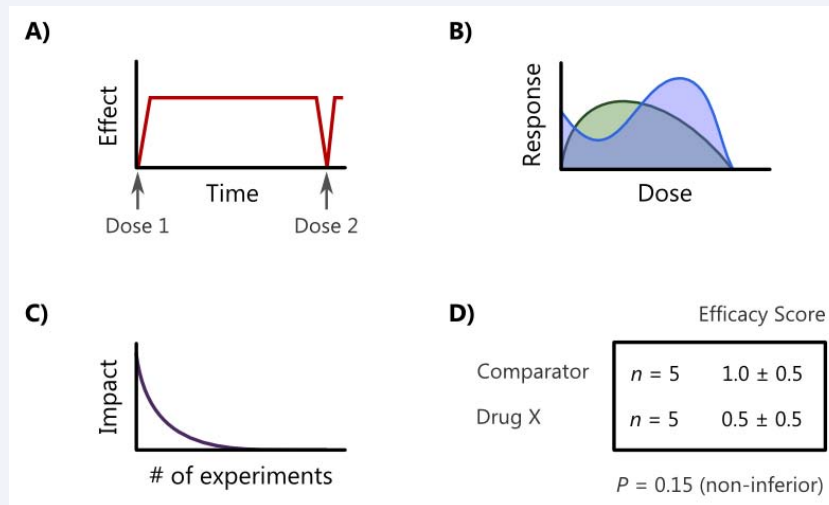


Figure 1 How not to be a successful clinical pharmacologist. (A) Assume that your drug behaves like a light-switch, whereby its effect is immediate upon dosing, remains stable throughout the dosing interval, and is rapidly eliminated the instant before the next dose is administered. (B) When plotting dose-response data, aesthetics should take priority above truth. (C) There is an inverse relationship between the number of experiments you perform and the earth-shattering impact of your results. (D) By under powering your study you can always ensure that your drug is non-inferior.

guidelines we guarantee that your scientific sloth will not go unrewarded.

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