A short intro to causal inference with an example from analysis of linked registries

Jon Michael Gran

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- Not magic: we calculate functions of observed data and interpret the output
- A framework to i) ensure that the outputs answer to well defined research questions and ii) help us avoid methodological pitfalls when answering them, iii) which have led to many new methodological developments

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 - 1 Description (e.g. of disease prevalence)
 - **2 Prediction** (e.g. for prognosis or diagnosis)
 - **3** Causal prediction (e.g. for effects of medical treatments)

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See e.g. Shmueli 2010 and Hernan et al. 2019

Causal versus statistical inference

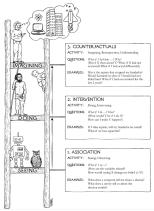
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- See also Pearl's ladder of causation:



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Some follow **Holland's mantra** more dogmatically than others, but most would agree it simplifies things...

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- 2020: ICH E9 (R1) addendum on estimands and sensitivity analysis in clinical trials

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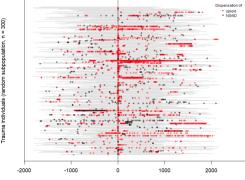
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Can argue that this is a more general principe borrowing the logic of the scientific method

Example using clinical and nation-wide registers

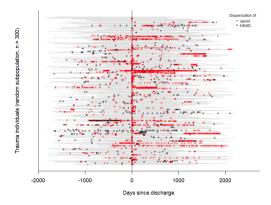
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Days since discharge

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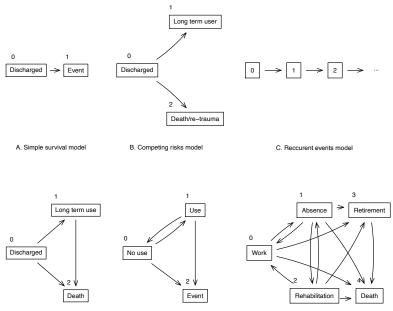
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Write out full protocol as in real RCT: specify eligibility criteria (opioid prescription day 0-14), time zero (14 days after discharge), treatment strategies (as above), baseline adjustment variables (age, sex, income, history of opioid use, geography, injury scores and type, comorbidities, hospital stay characteristics etc), time-varying adjustment variables (health visits in KUHR and NPR, opioids and other drug use) and long term opioid use as outcome (certain amount prescribed over 90 days, followed up by new prescriptions)

Broader outcomes of interest:



E. Illness-death model with recovery

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- Causal inference is not about being overly optimistic about causal claims, but about being transparent and honest