Personalised medicine: a view from drug discovery

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Plan

- Definition
- Drug discovery context and implications
- Enablers

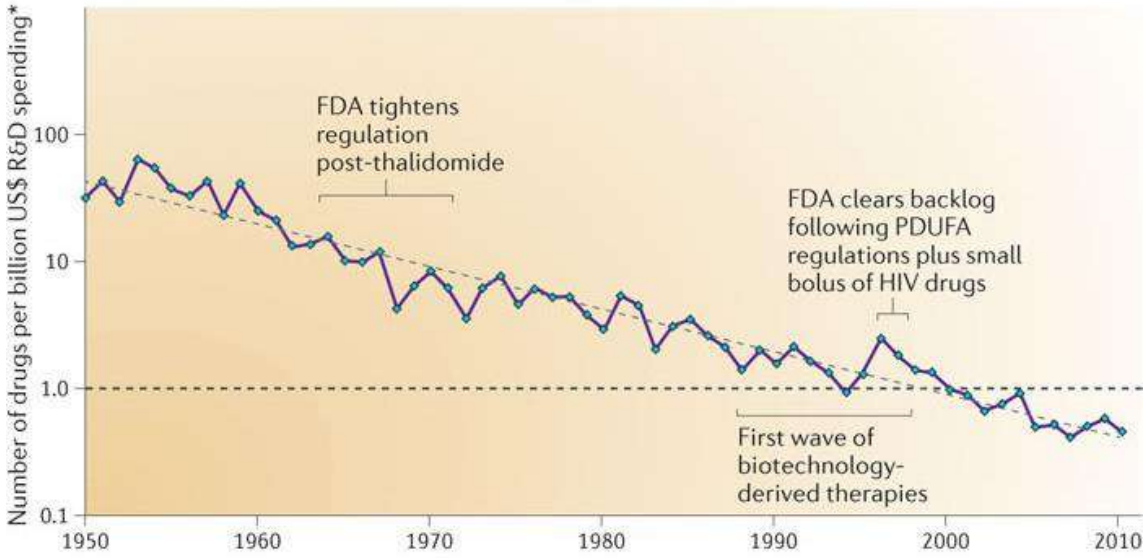
Right patient, right medicine, right time

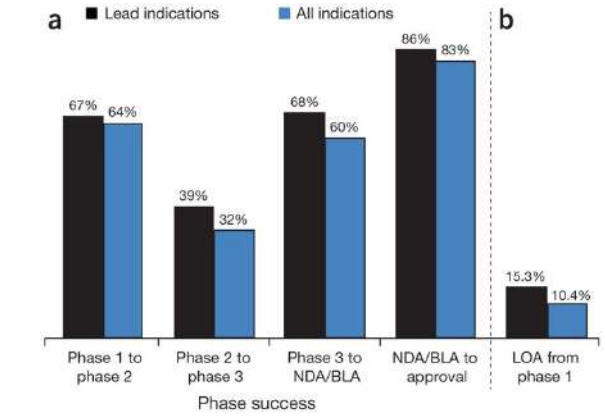
Is this just “medicine”?

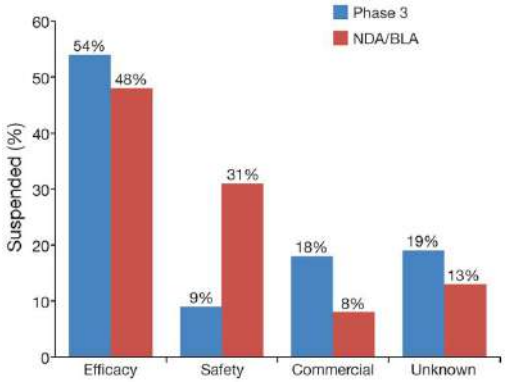
- Often equated with diagnostic biomarker eg academy of medical sciences 2013 report, MRC 2016 framework paper
- AMS report has 8 examples, all DNA/RNA biomarkers.
  - 6 are oncology, 1 HIV (abacavir and HLA B*57:01), one rare disease (CF, kalydeco and G551D CFTR mutation).
  - Only 2 discovered during development, others foundational parts of therapeutic hypothesis
- Too narrow?
  - Eg Asthma sub-populations
- Vaguely: large effect in a selected group
- True personalised medicine?
  - eg cell therapy

Context

Eroom’s Law



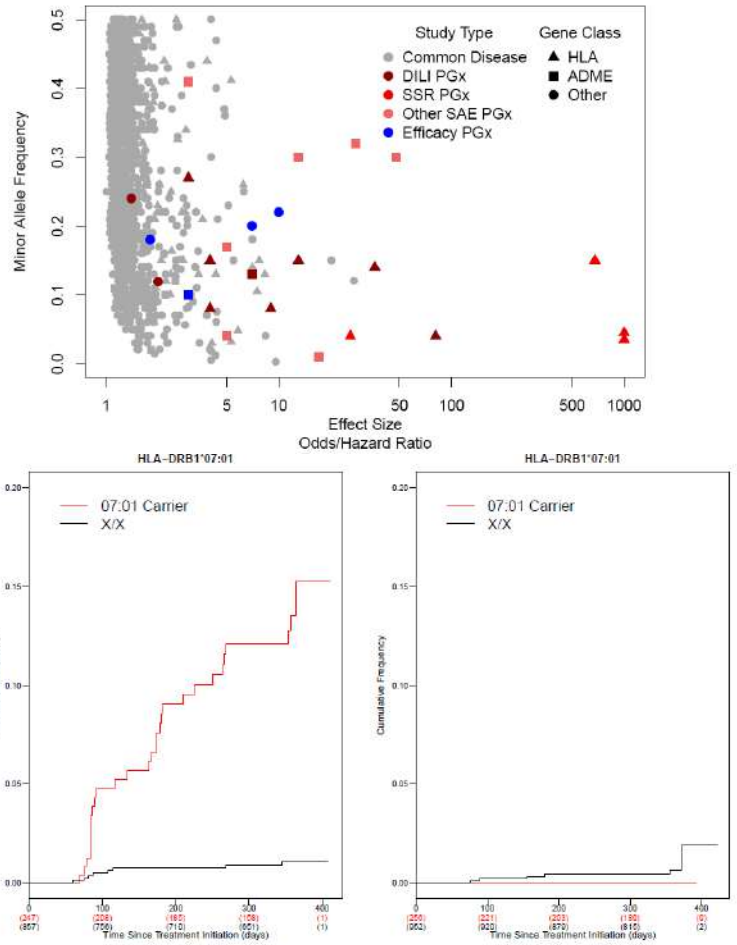




Probability of success at target selection 3%

Stratifying during development is hard

Germline only



Pros:

- Genetic variants affecting safety/efficacy exist
- We expect 10% of drugs to have ‘detectable’ genetic predictors of efficacy
- We do PGx routinely in development

Cons

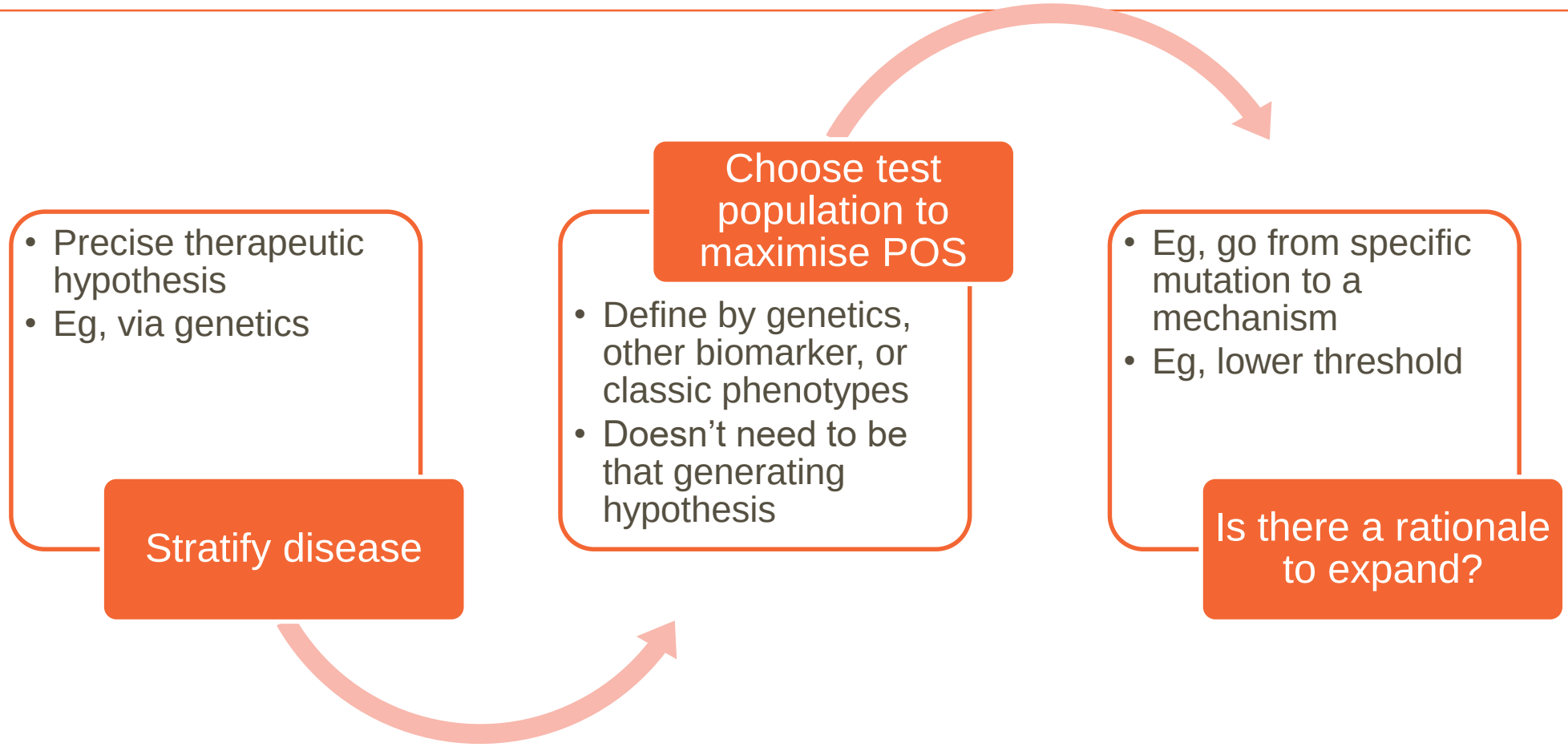
- Trial programs are underpowered for PGx
- Very unlikely that genetics/genomics will rescue failed trials

Future

- EHR/registries + biobanks
  - Polygenic scores?
- Likely best to stratify disease before medicines: *start in the right place*
- *Oncology???*

90% of clinical programs fail

How do we derisk?



Enablers

- Increased causal understanding of etiology
  - Genetics
  - Refined phenotypes
- Ability to recruit stratified populations into trials
  - Biobanks with appropriate consent for recontact?
    - And prospective biomarker measurement?
  - Embedding of trials into healthcare systems?
  - Platform trials with ability to build in stratification?
- Discoveries during development
  - Trials need to collect appropriate data
- Trials that allow expansion of study population?