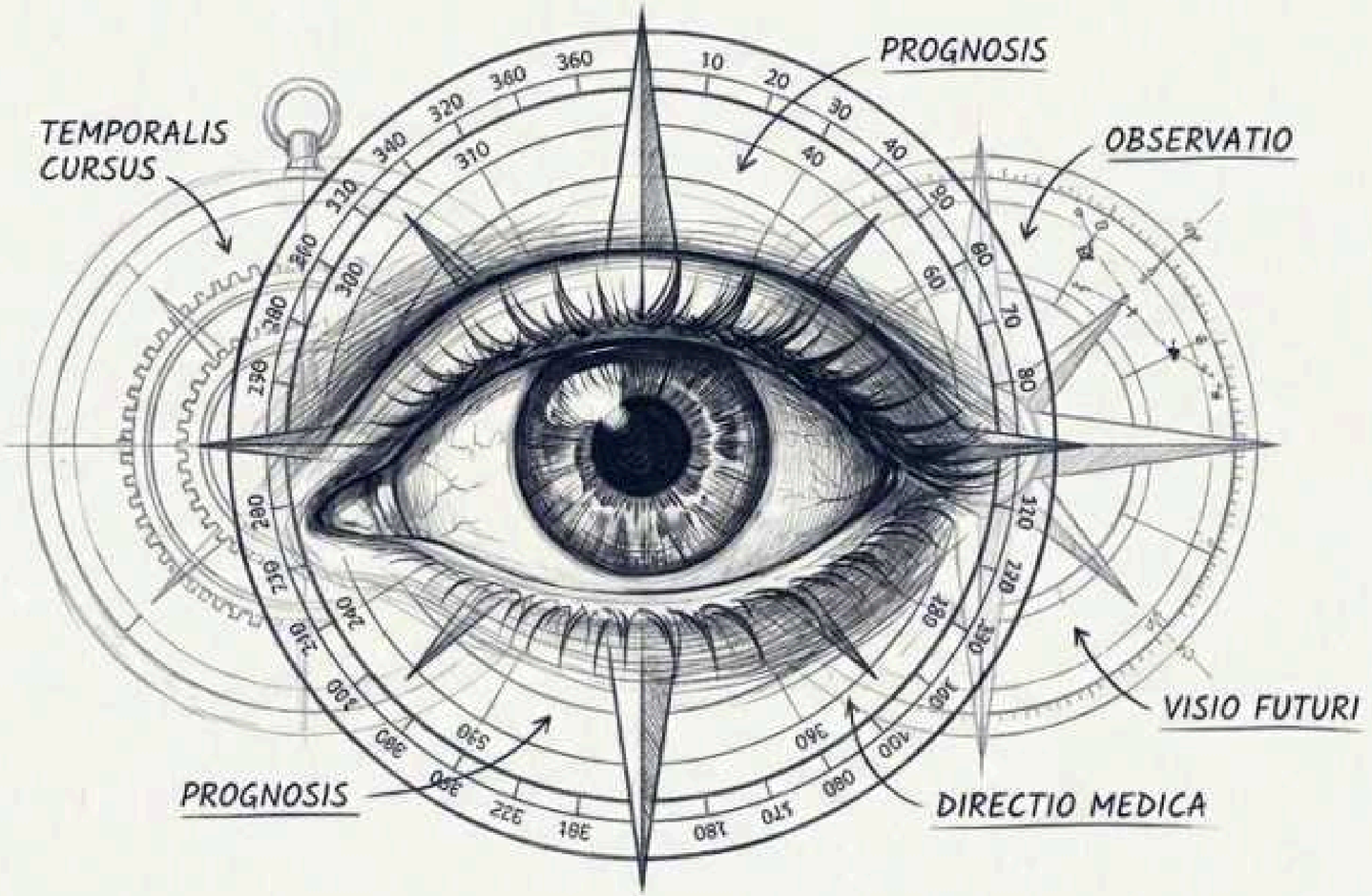
Predicting the Future and Changing Its Course



Clinical Heuristics for Prognosis and Treatment

Prognosis Maps the Temporal Course of Illness

¶ 5.1



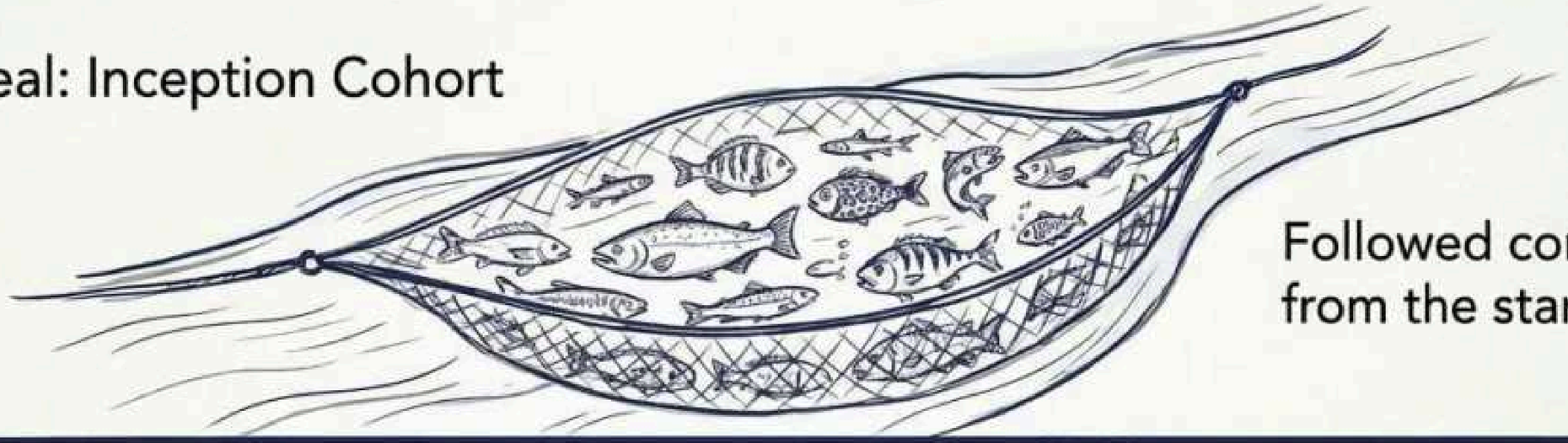


- ✓ Defines aggressive vs. conservative treatment strategy
- ✓ Facilitates life planning

The Inception Cohort Mitigates Referral Bias

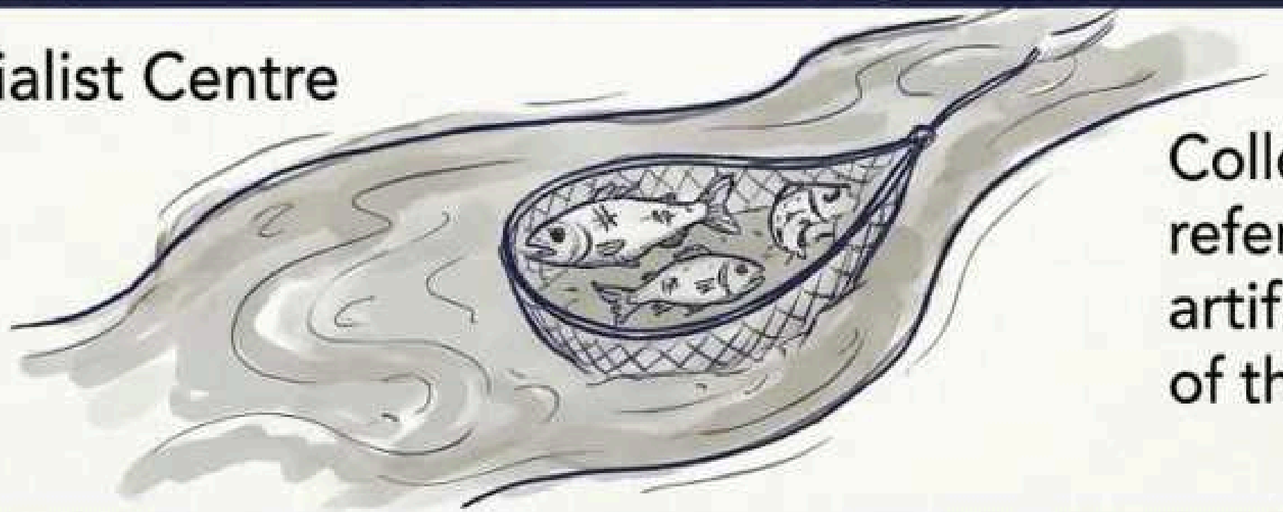
¶ 5.2

The Ideal: Inception Cohort



Followed completely from the start.

The Bias: Specialist Centre

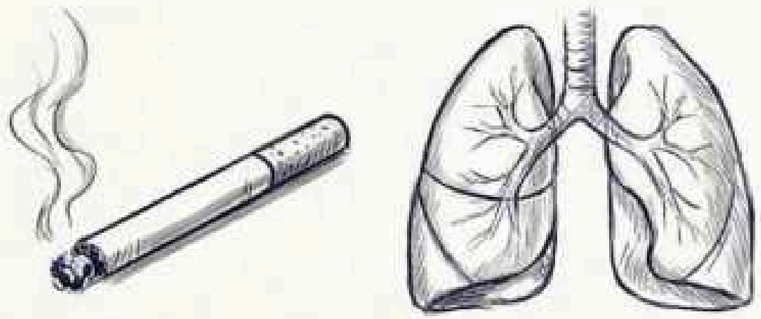
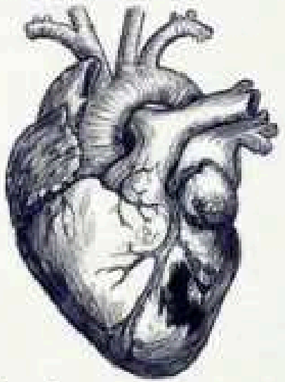


Collects only sicker, referred cases—painting an artificially gloomy picture of the typical course.

The best prognostic studies capture patients at the origin, not at the destination.

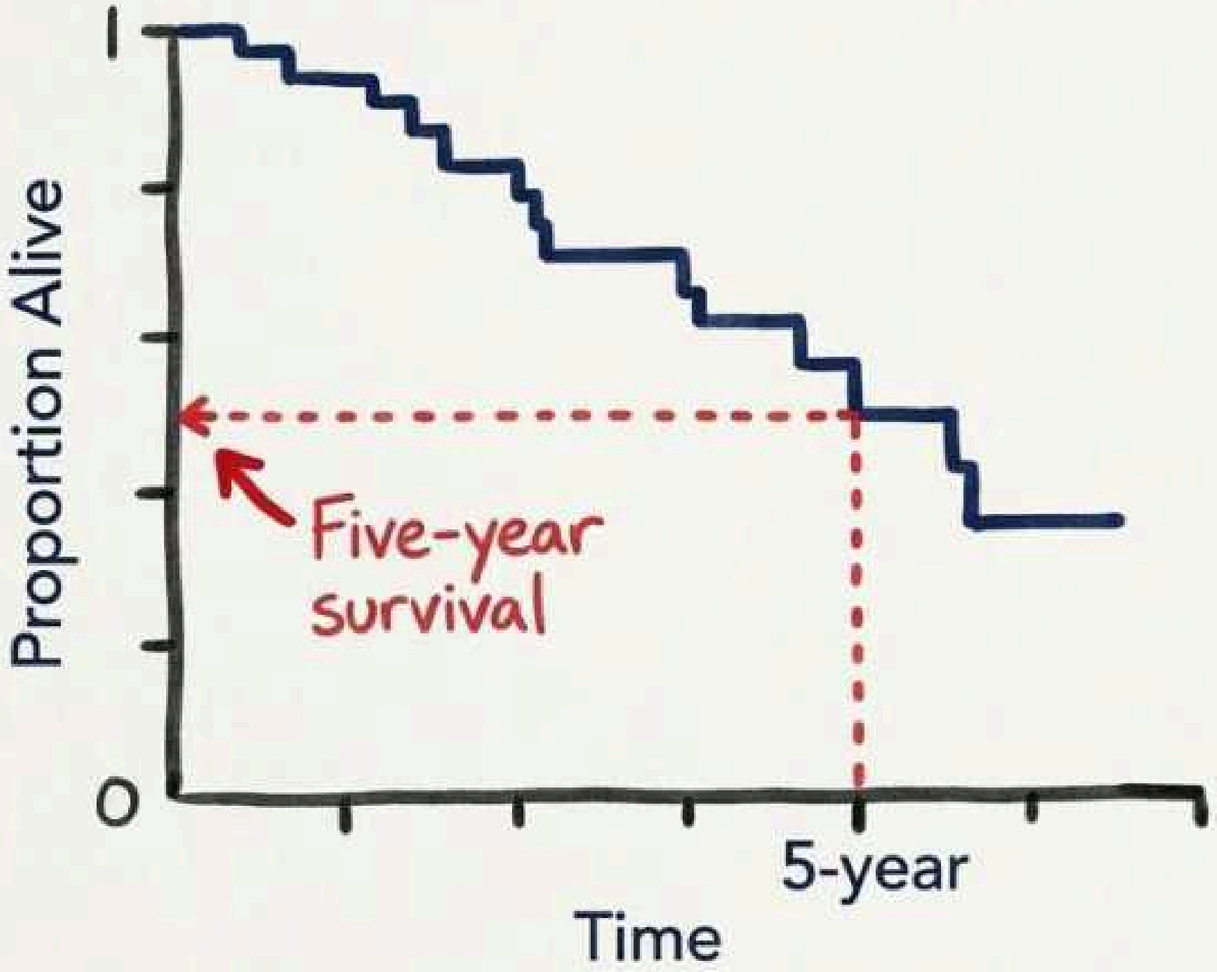
Distinguishing Disease Onset from Disease Course

¶ 5.3

	Risk Factors	Prognostic Factors
What it Predicts	Who will develop a disease	What will happen to those who already have it
Target Population	Healthy individuals	Diagnosed patients
Visual Example	 Smoking predicting a heart attack.	 Myocardial damage predicting post-attack survival.

Quantifying the Future: Survival Curves and Prediction Rules

¶ 5.4



Clinical Prediction Rules

$$\text{Risk} = f(\text{Factor 1} + \text{Factor 2} + \text{Factor 3})$$



Must be validated in entirely new patient groups before being trusted.

The Sequential Pipeline of Treatment Trials

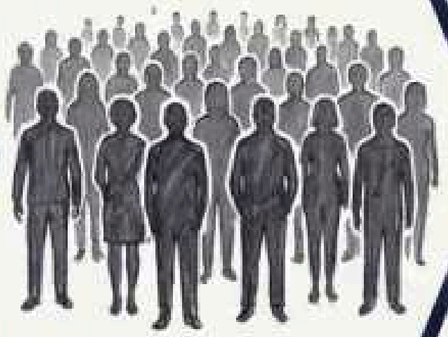
¶ 5.5

Safety & Dosing



Small numbers.

Efficacy



Does the treatment work?

Comparative Effectiveness



New treatment vs. Existing care.

Long-term Surveillance



Watching for rarer harms.

Outcomes Matter as Much as Results

¶ 5.6

Patient-Important Outcomes



High Reliability

Death, heart attack, symptoms, quality of life

What patients actually care about

VS

Surrogate Outcomes



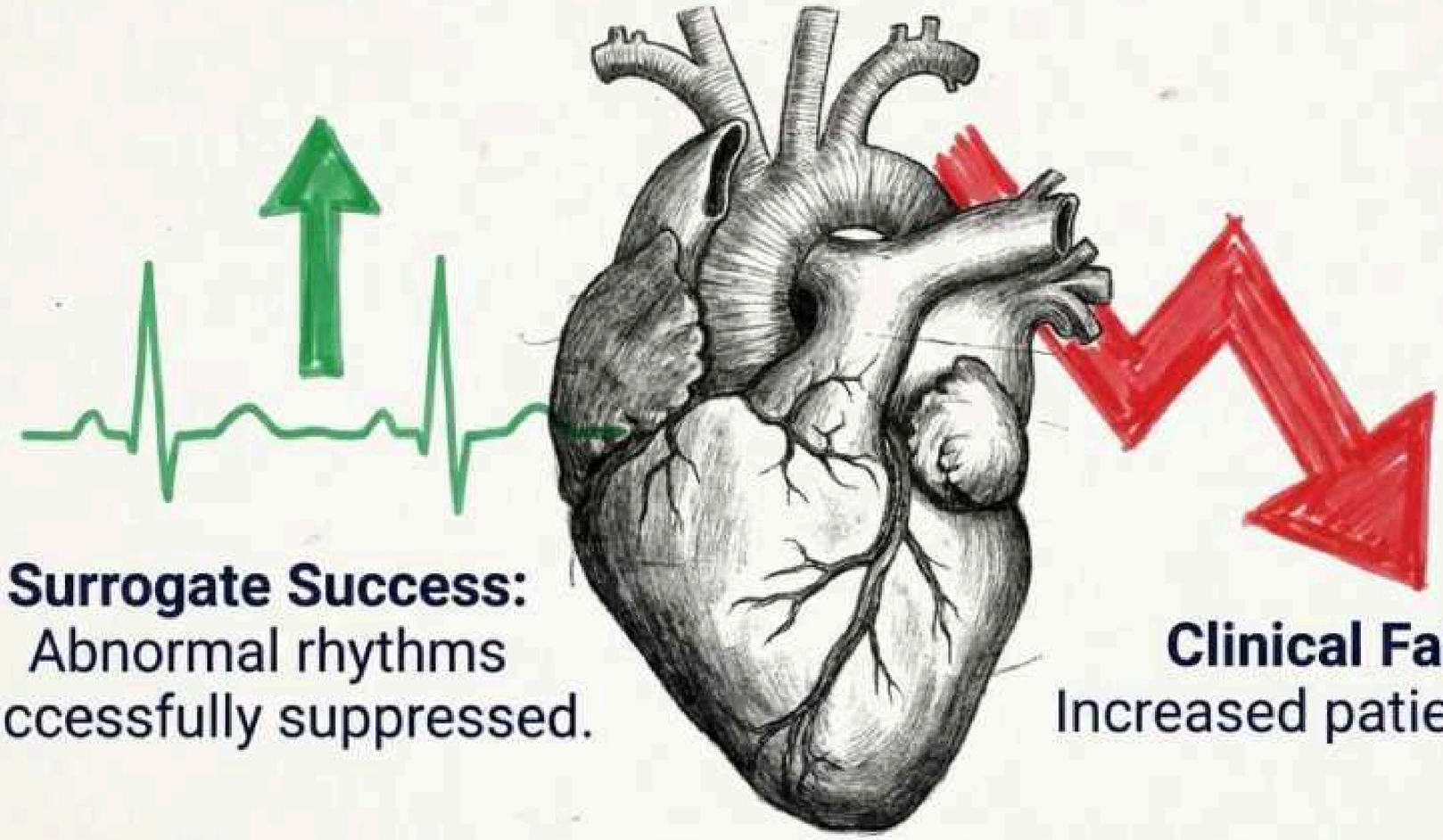
High Misleading Risk

Blood tests, scan findings

Easier and quicker to measure

The 1989 CAST Paradox: When Surrogates Kill

¶ 5.7



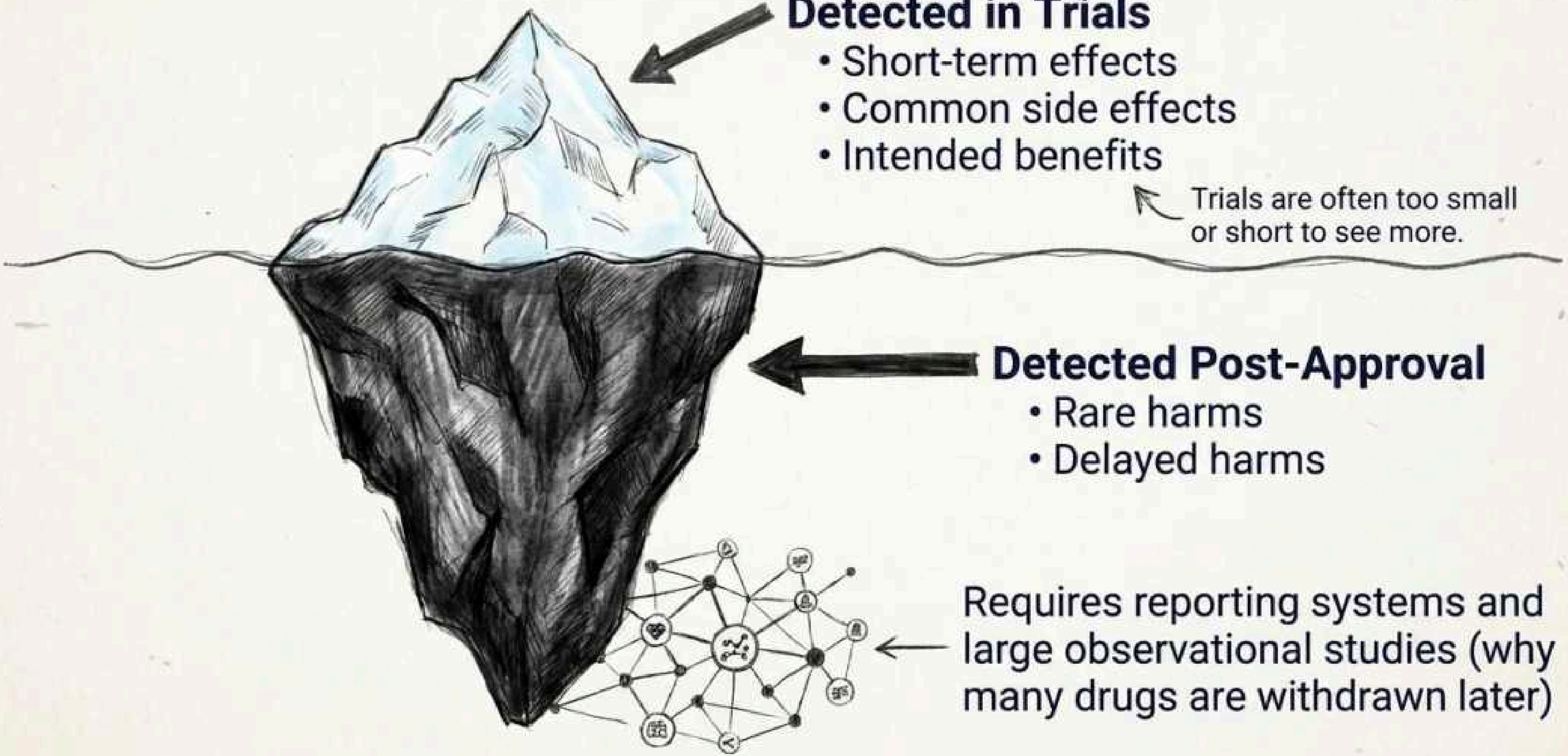
Surrogate Success:
Abnormal rhythms successfully suppressed.

Clinical Failure:
Increased patient deaths.

Improving a number on a test is not the same as helping a patient.

The Hidden Ledger: Weighing Treatment Harms

¶ 5.8



Detected in Trials

- Short-term effects
- Common side effects
- Intended benefits

Trials are often too small or short to see more.

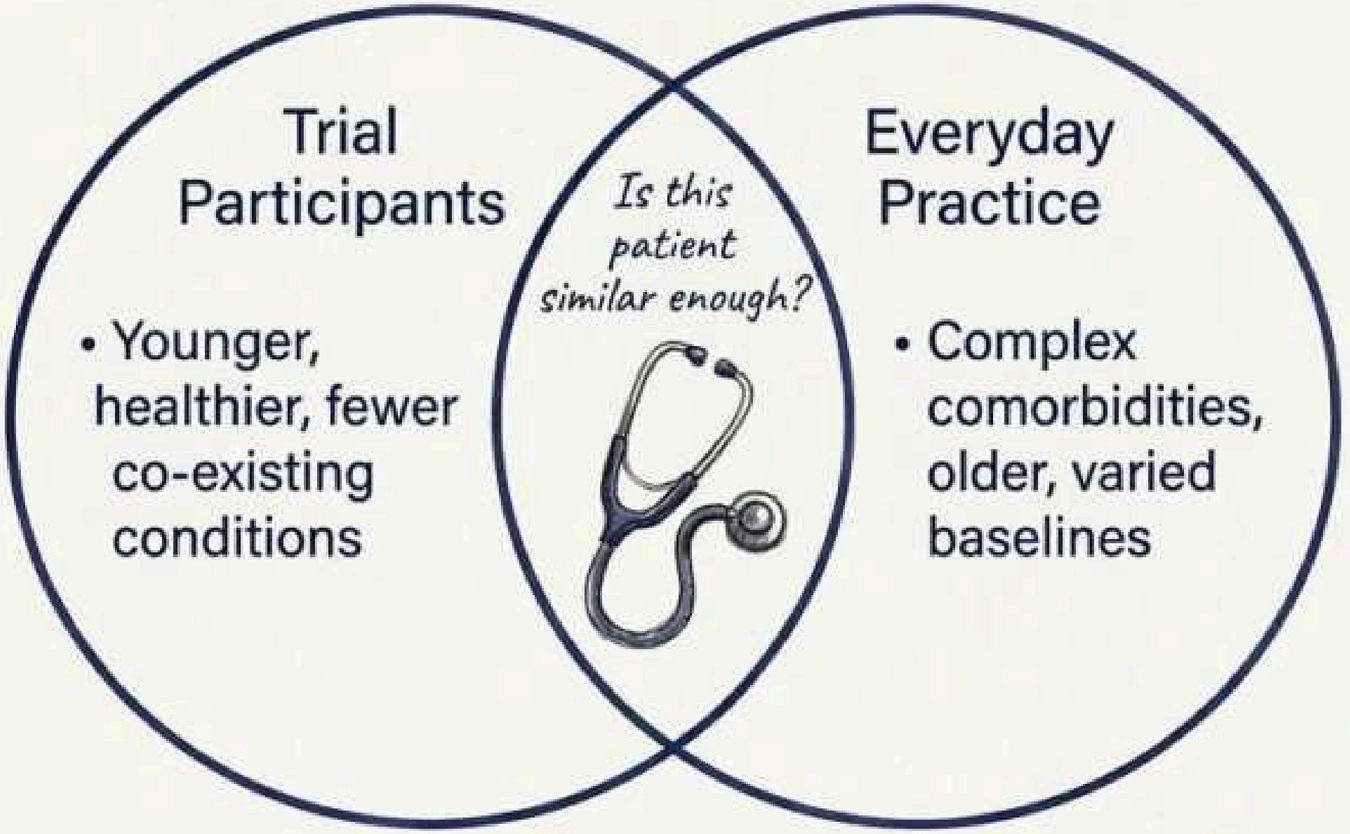
Detected Post-Approval

- Rare harms
- Delayed harms

Requires reporting systems and large observational studies (why many drugs are withdrawn later)

The Generalizability Gap: Trial Cohort vs. Your Patient

¶ 5.9



Absolute Benefit ∝ Patient's Baseline Risk

A doctor must estimate the patient's own baseline risk to know the true absolute benefit.

Bridging the Gap: Pragmatic Trials and Subgroups

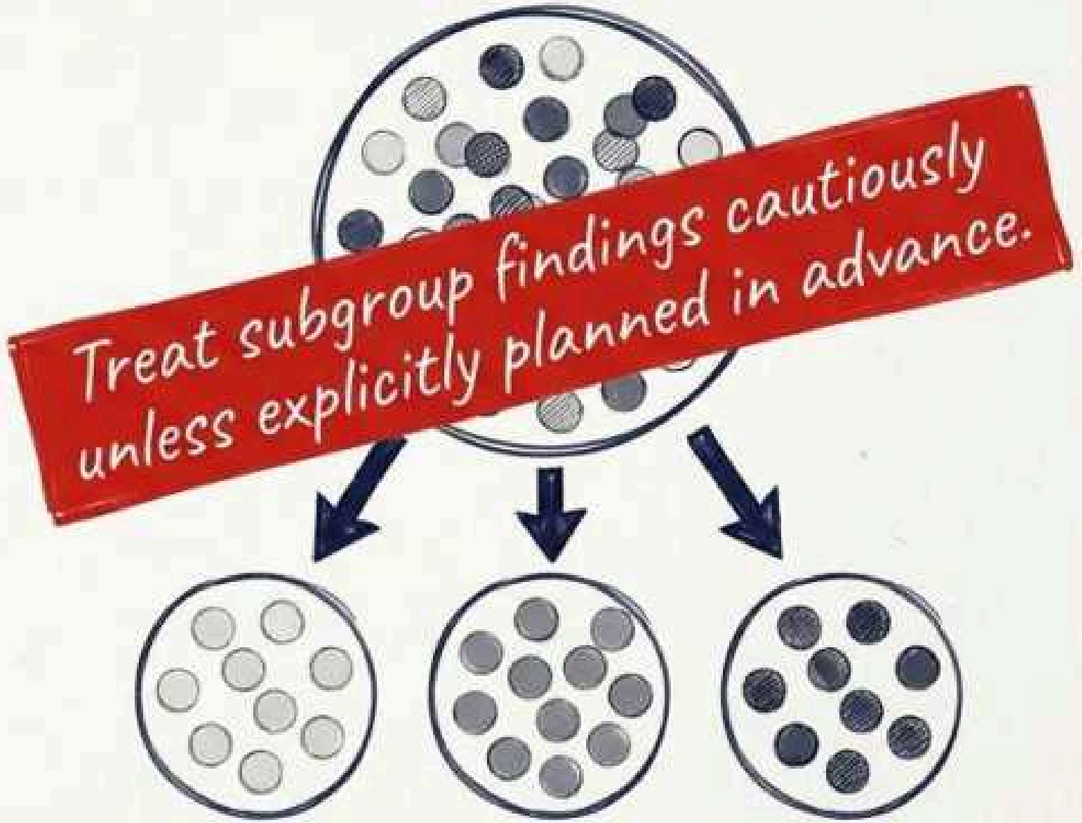
¶ 5.10

Pragmatic Trials



Tests treatments in ordinary clinical settings with typical patients.

Subgroup Analysis

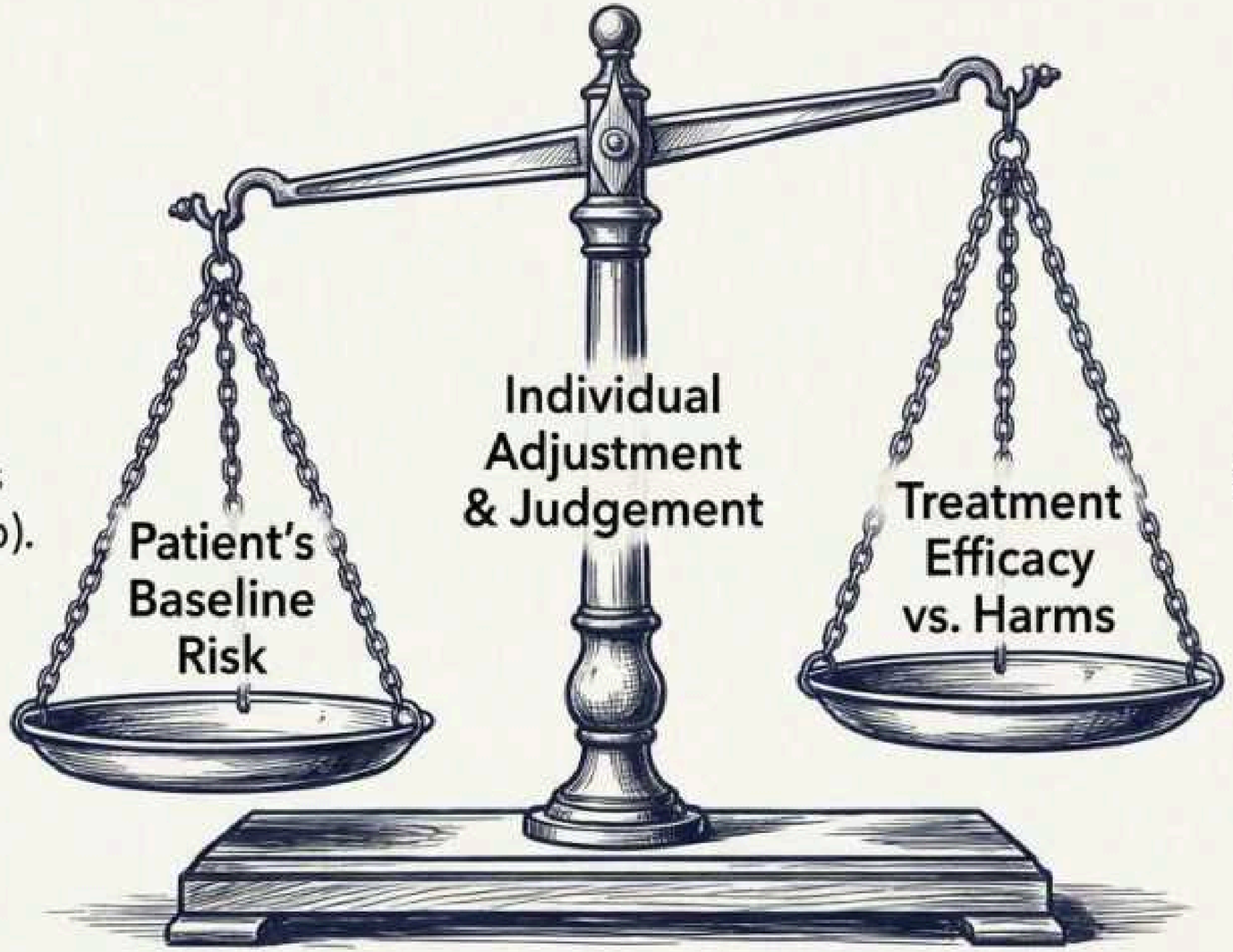


Reports results for specific, important patient profiles.

The Clinical Decision Equation

¶ 5.11

(Derived from inception cohorts and early follow-up).



(Derived from trials measuring patient-important outcomes).

Prognosis informs the risk. Trials inform the tool. The clinician balances both.

Next: Integrating this into Evidence-Based Medicine and Public Health.