

Translational Medicine

Bridging The Gap

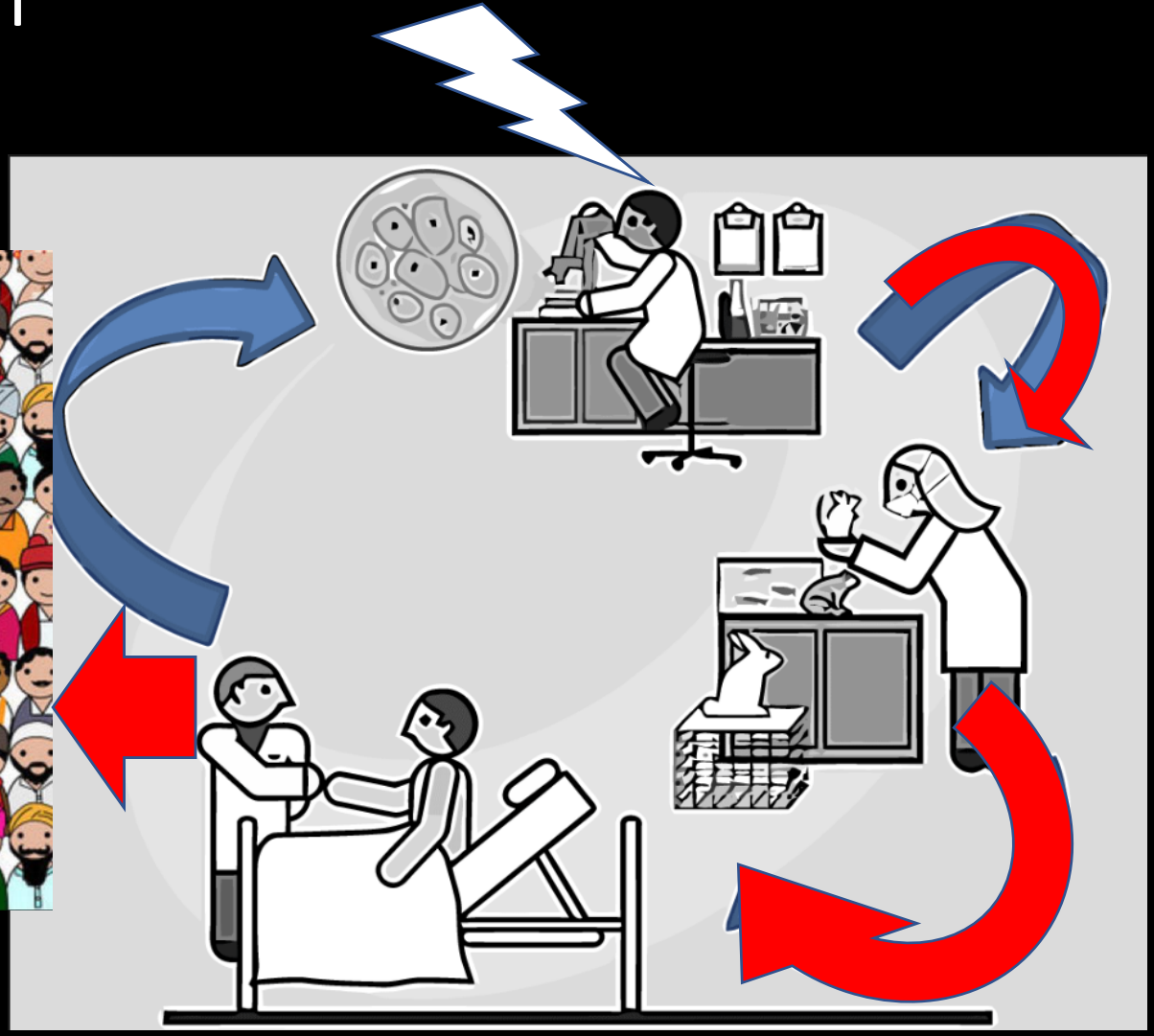
Dr. Tiny Nair, MD, DM, FACC, FRCP.

Head, Dept. of Cardiology,

PRS Hospital, Trivandrum 695002

Kerala, India

Translation



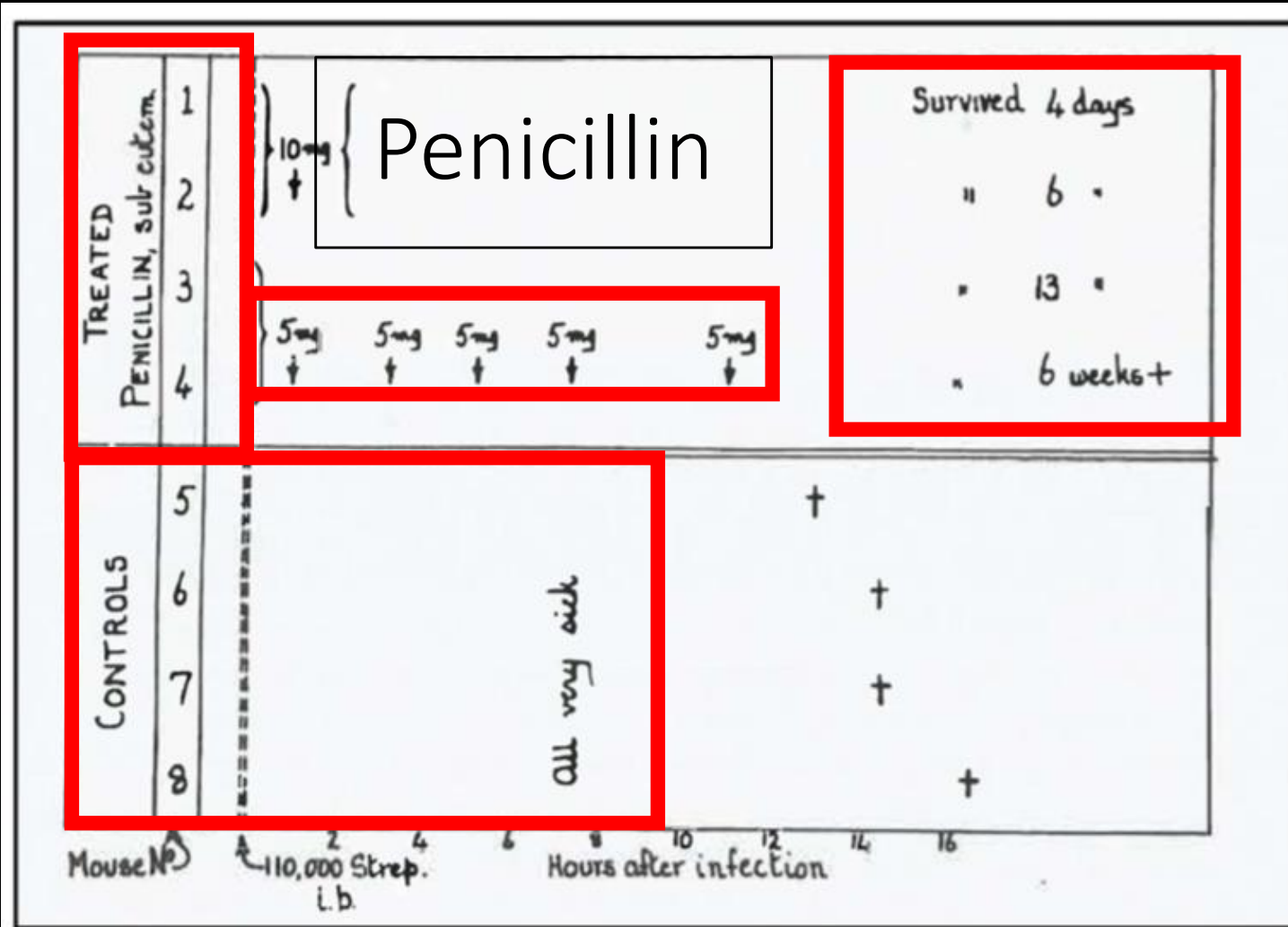
1940

Ernst Chain, Howard Heatley

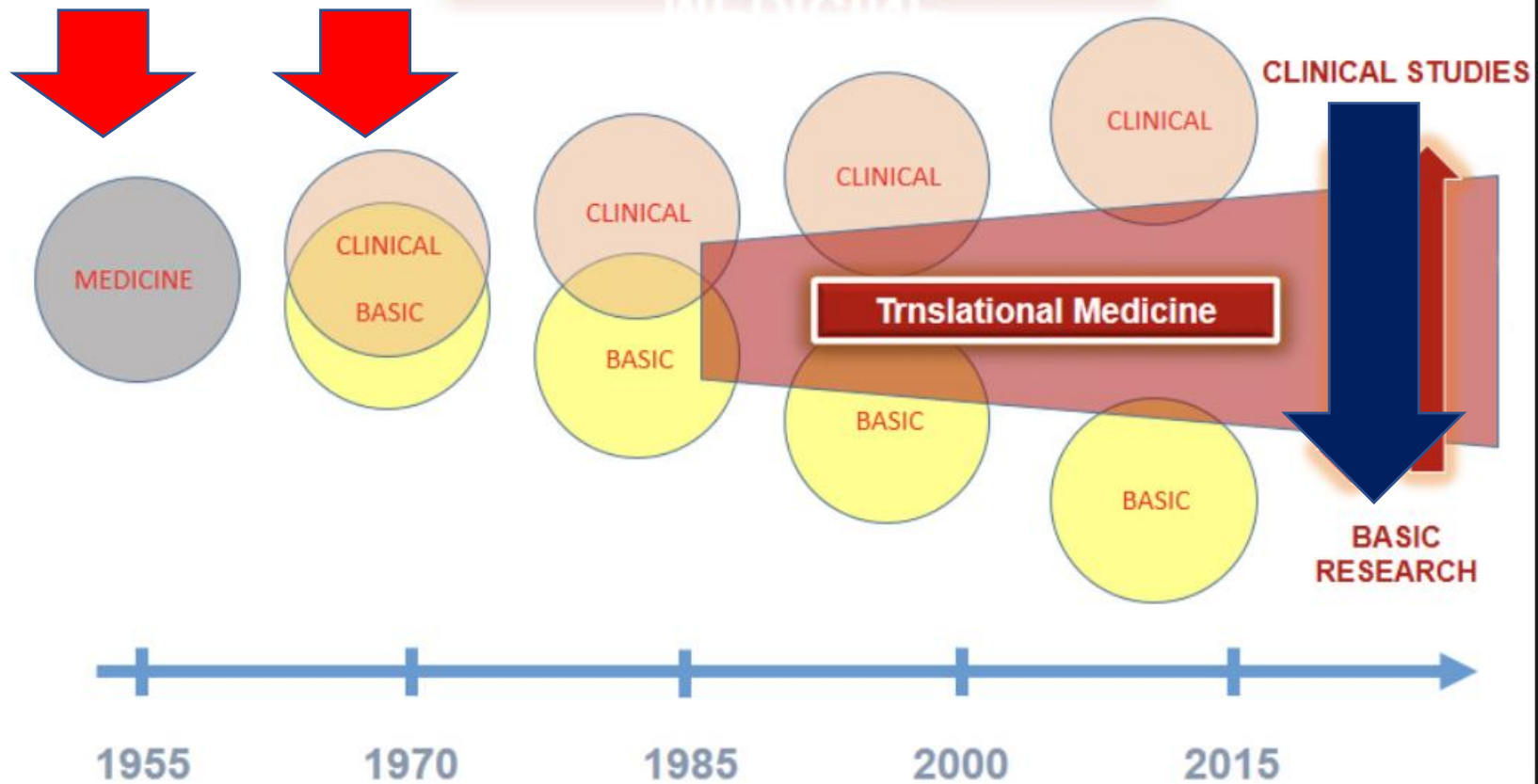
8 Mouse

Streptococcus gr A

Ready for Human Trial



TRANSLATIONAL MEDICINE



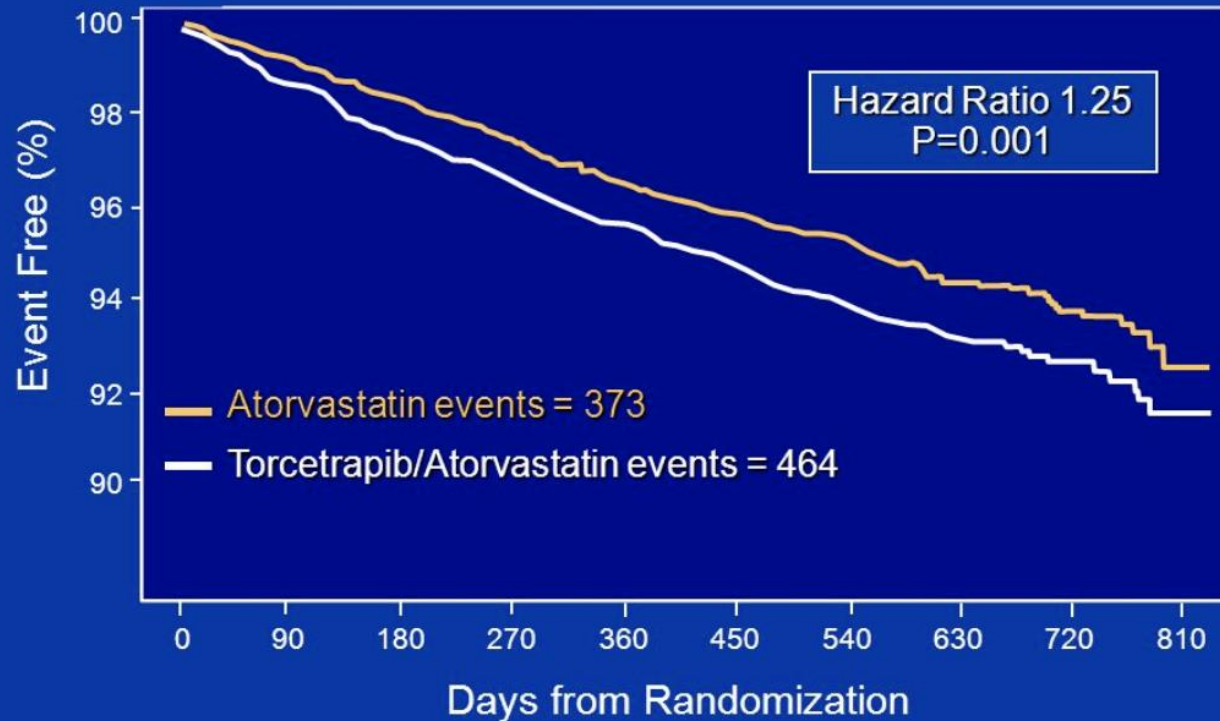
Regulatory Guidelines



RCTs Are
Important

Torcetrapib

ILLUMINATE: Primary Endpoint: Time to First MACE: Kaplan-Meier Plot



CVOT Safety Trial

Empagliflozin and

Bernard Zinman

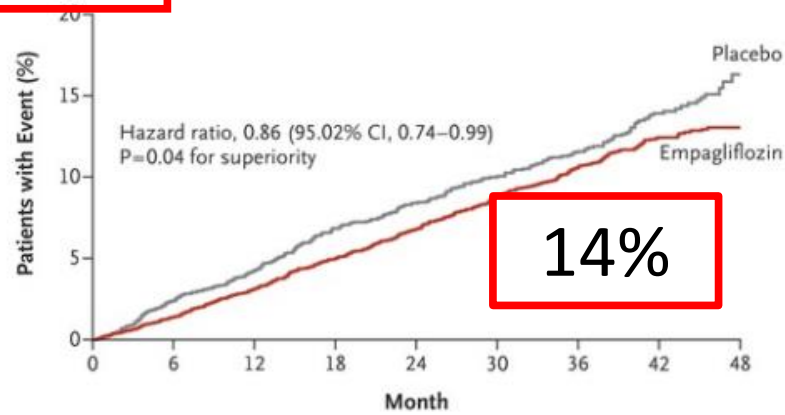
David Fitch

Michael

Odd Erik Johansen

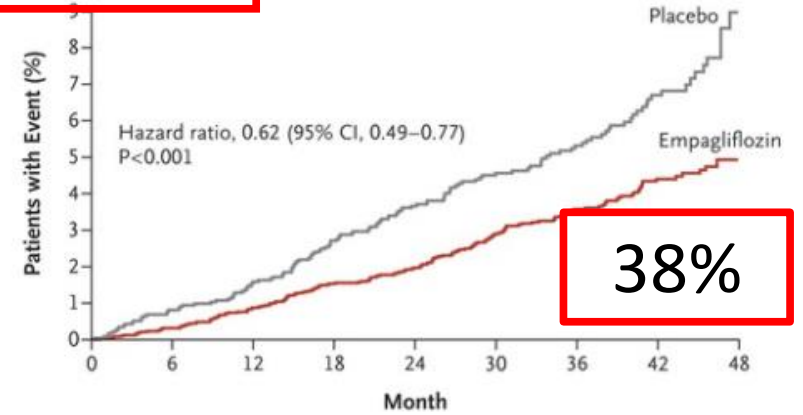
and Silvio E. Inzucchi

A Primary Outcome



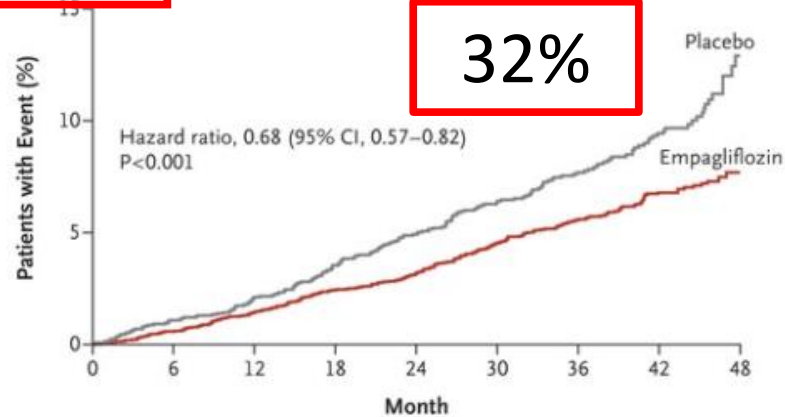
No. at Risk									
Empagliflozin	4687	4580	4455	4328	3851	2821	2359	1534	370
Placebo	2333	2256	2194	2112	1875	1380	1161	741	166

B Death from Cardiovascular Causes



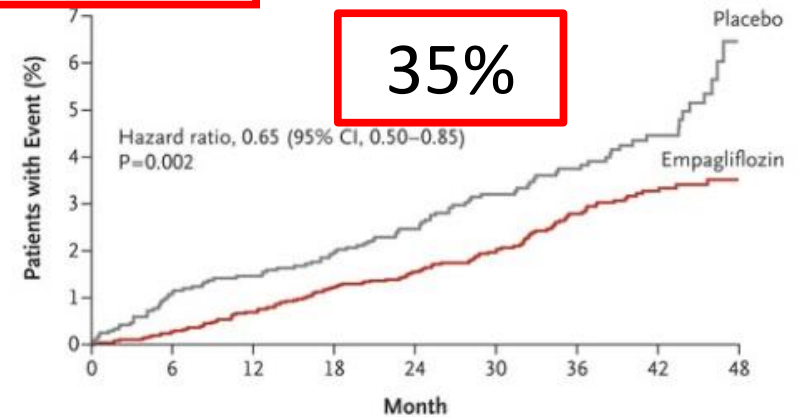
No. at Risk									
Empagliflozin	4687	4651	4608	4556	4128	3079	2617	1722	414
Placebo	2333	2303	2280	2243	2012	1503	1281	825	177

C Death from Any Cause



No. at Risk									
Empagliflozin	4687	4651	4608	4556	4128	3079	2617	1722	414
Placebo	2333	2303	2280	2243	2012	1503	1281	825	177

D Hospitalization for Heart Failure



No. at Risk									
Empagliflozin	4687	4614	4523	4427	3988	2950	2487	1634	395
Placebo	2333	2271	2226	2173	1932	1424	1202	775	168

UD\$

0.5 – 2.4 million

RCT - Time



"This randomized, double-blind trial involving over 20,000 patients was conducted over a 10 year period."

2013; *BMJ*



Chute RCT

2018; *BMJ*

- $n = 44$
 - All jumped out of airplane
 - 22 With Parachute
 - 22 with No parachute
 - PEP – Major Trauma
-
- No difference in primary endpoint of Major trauma.
 - Low Event rate



New Learning From RCTs

Translation

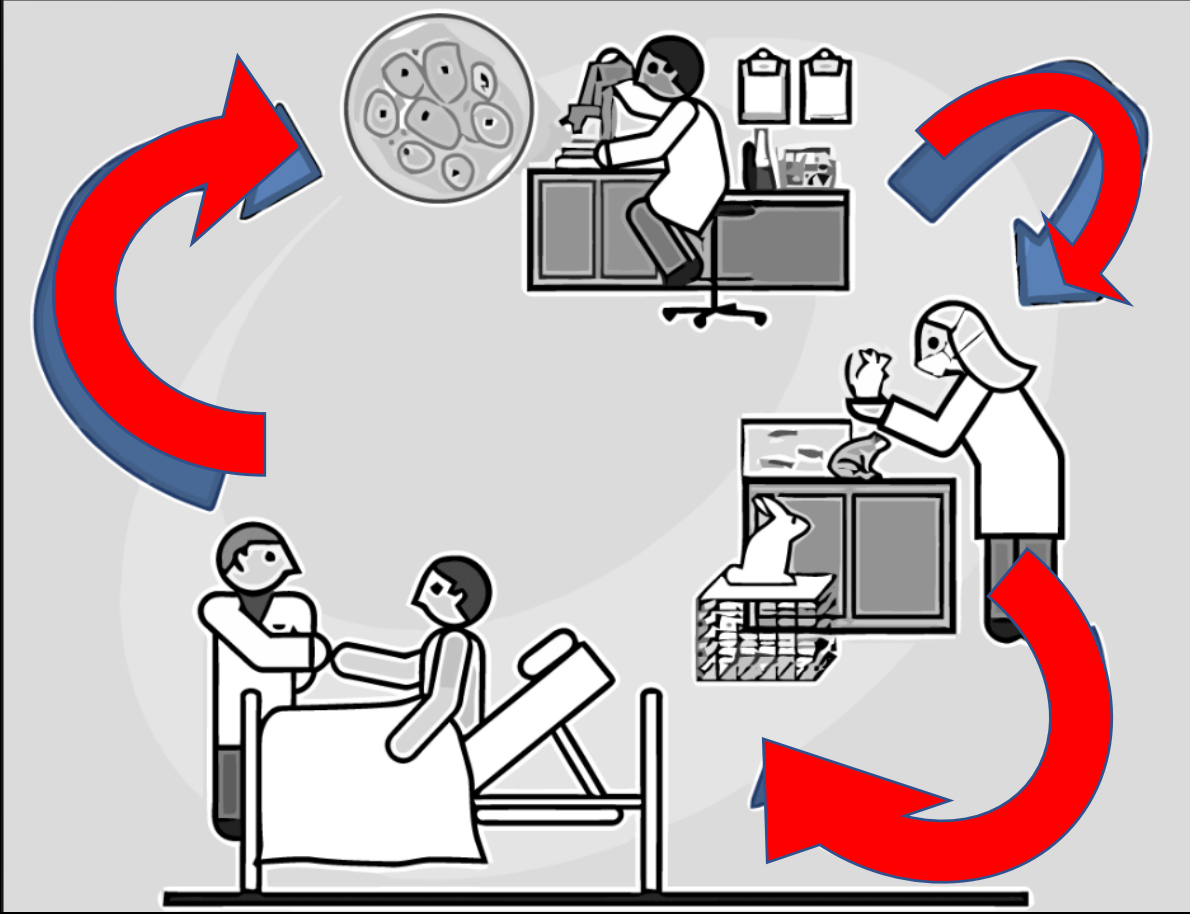
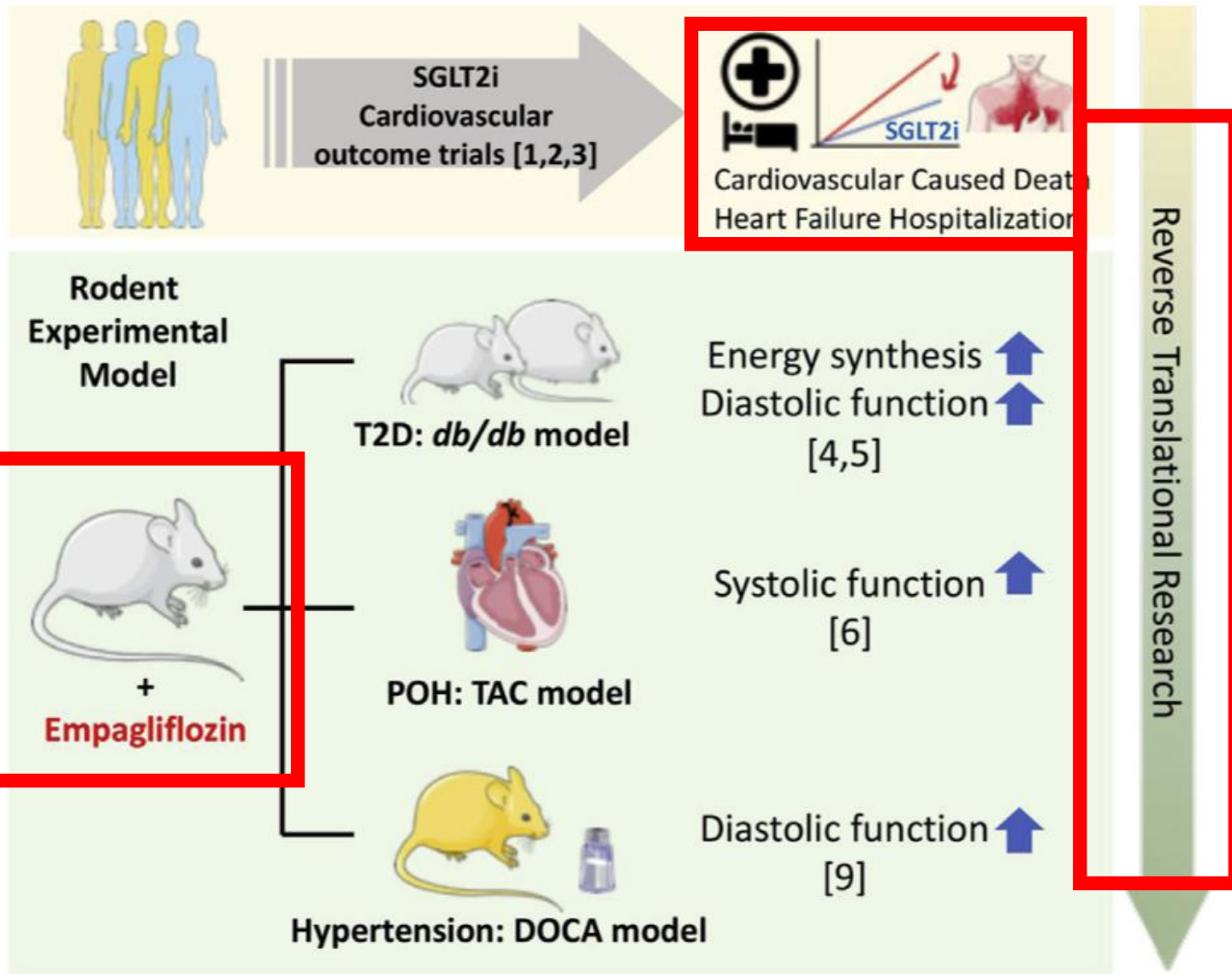
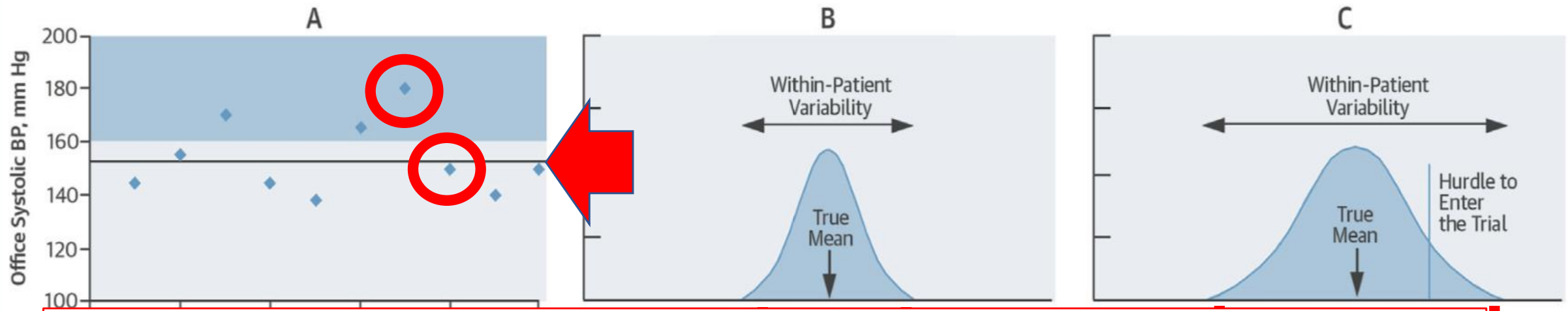


FIGURE 1 Schematic of Clinical Observations, Promises, and the Future of SGLT2i



CENTRAL ILLUSTRATION Regression to the Mean in a Hypothetical Subject's Serial BP Readings



REVIEW TOPIC OF THE WEEK

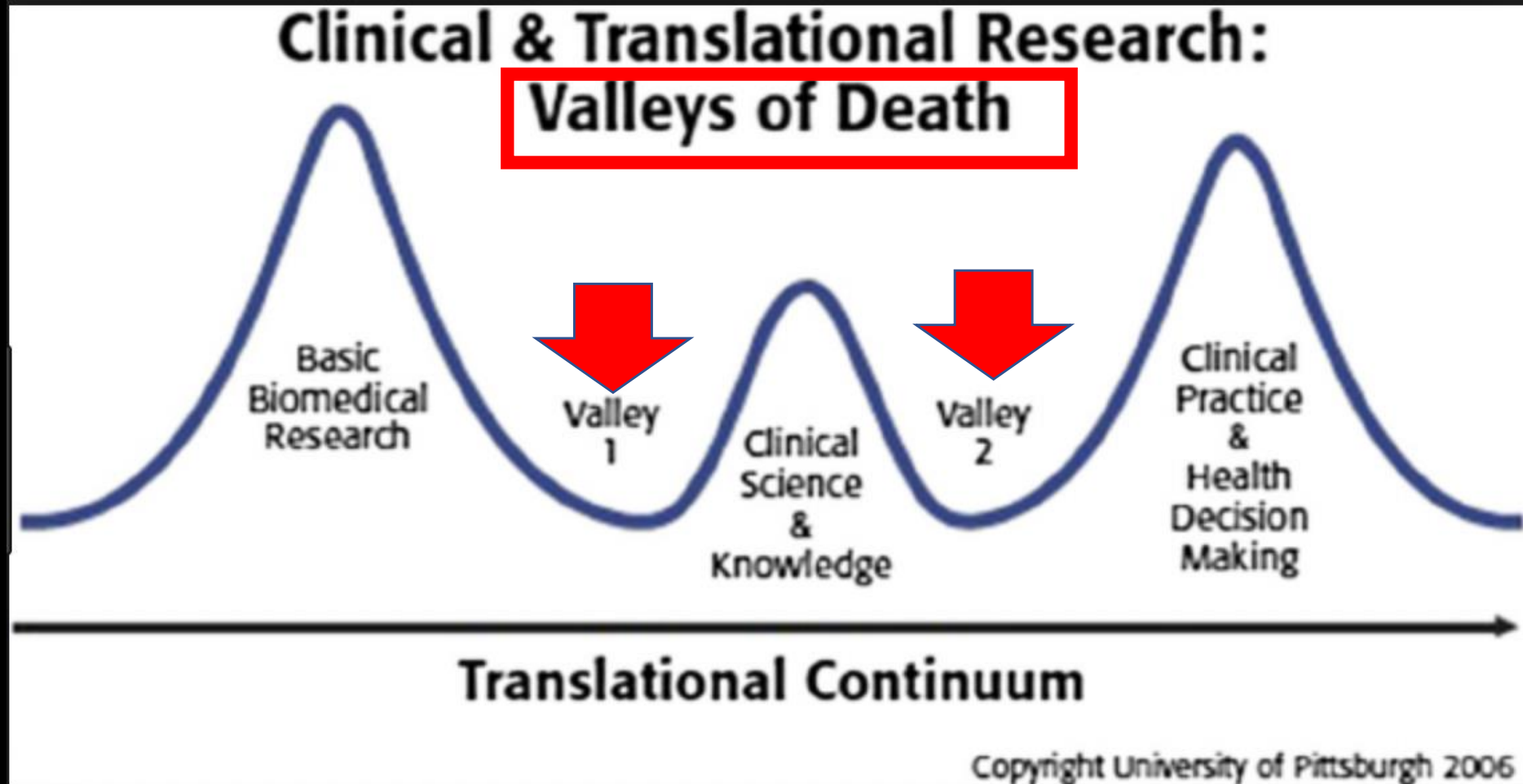
Regression to the Mean in SYMPPLICITY HTN-3

Implications for Design and Reporting of Future Trials

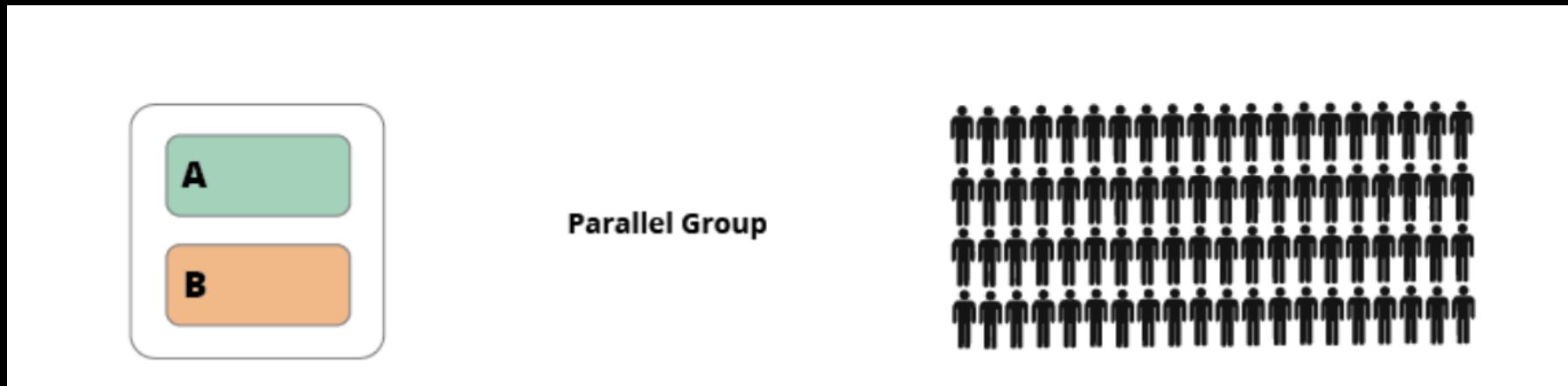
Stuart J. Pocock, PhD,^a George Bakris, MD,^b Deepak L. Bhatt, MD, MPH,^c Sandeep Brar, MD,^d Martin Fahy, MS,^d Bernard J. Gersh, MB, ChB, DPHIL^e

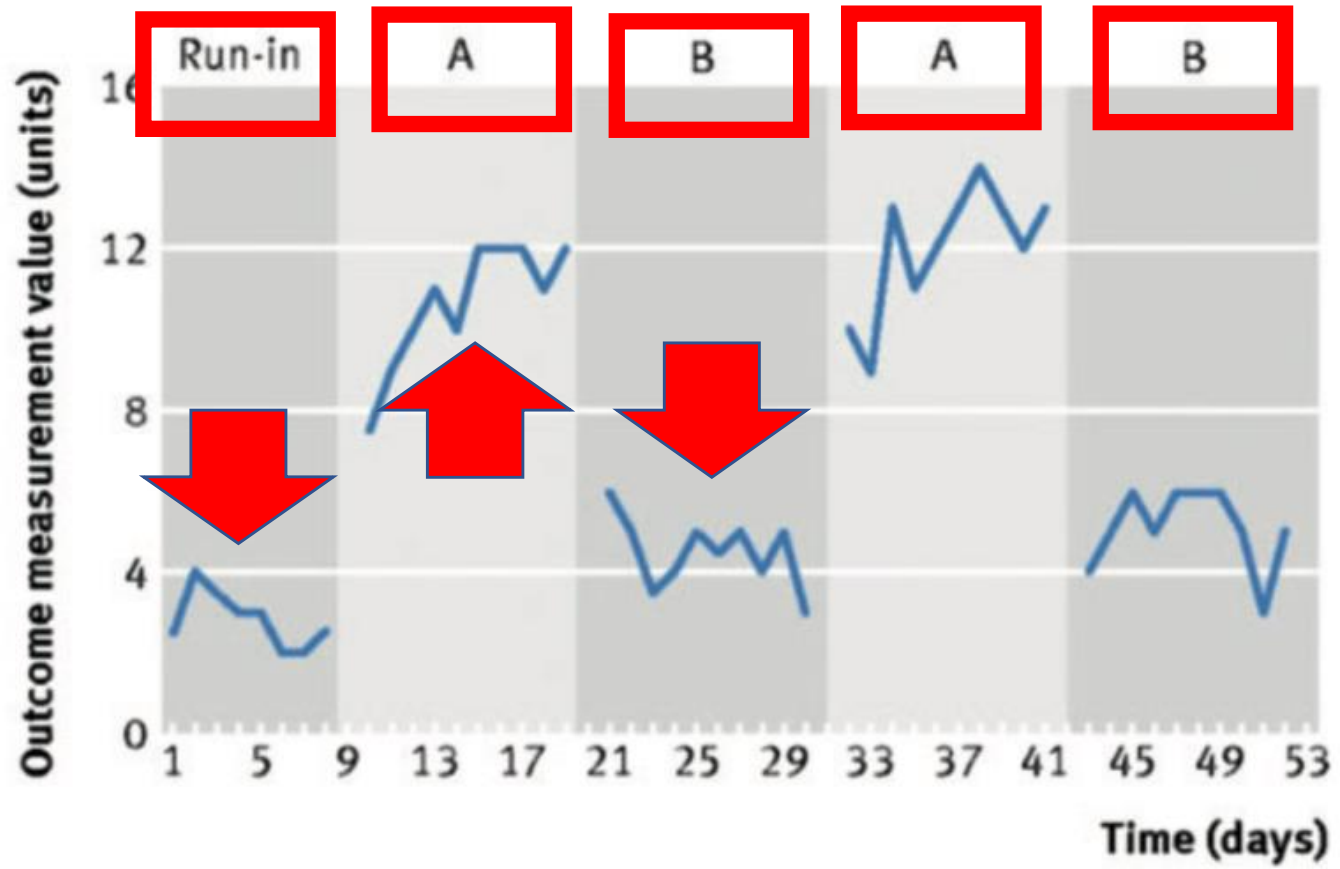


Real-Life Gaps



Change in Trial Designs





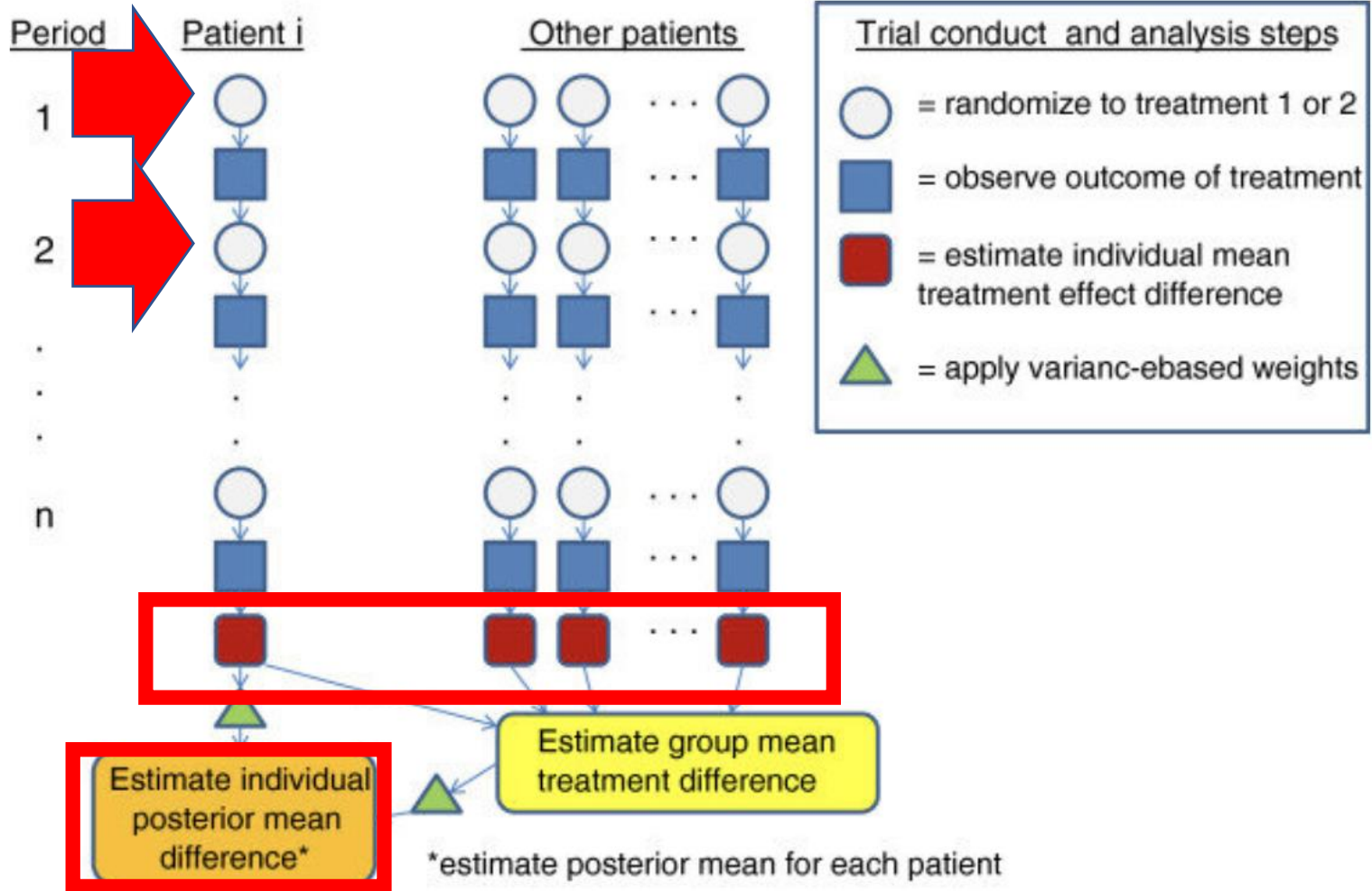


ILLUSTRATION BY GREG CLARKE



Time for one-person trials

Precision medicine requires a different type of clinical trial that focuses on individual, not average, responses to therapy, says **Nicholas J. Schork**.

Every day, millions of people are taking medications that will not help them.

US\$215-million national Precision Medicine Initiative. This includes, among other things,

may prescribe one drug for hypertension and monitor its effect on a person's blood pres-

IMPRECISION MEDICINE

For every person they do help (blue), the ten highest-grossing drugs in the United States fail to improve the conditions of between 3 and 24 people (red).

1. ABILIFY (aripiprazole)
Schizophrenia



2. NEXIUM (esomeprazole)
Heartburn



3. HUMIRA (adalimumab)
Arthritis



4. CRESTOR (rosuvastatin)
High cholesterol



5. CYMBALTA (duloxetine)
Depression



6. ADVAIR DISKUS (fluticasone propionate)
Asthma



7. ENBREL (etanercept)
Psoriasis



8. REMICADE (infliximab)
Crohn's disease



9. COPAXONE (glatiramer acetate)
Multiple sclerosis



10. NEULASTA (pegfilgrastim)
Neutropenia



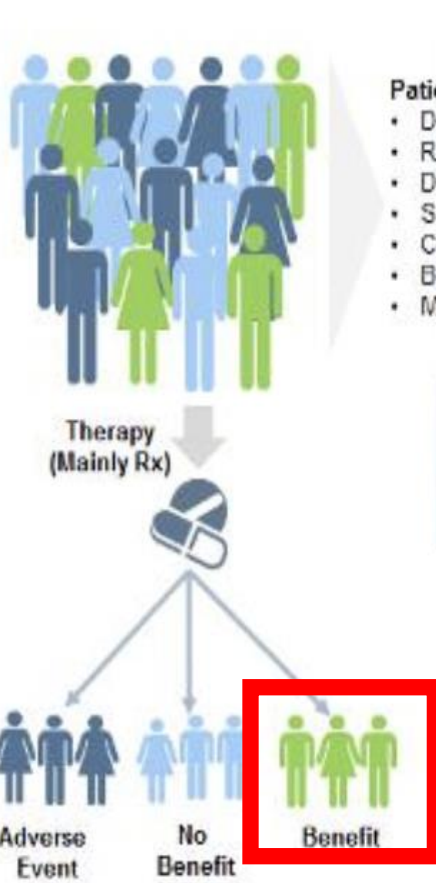
One-size-fit-all
Medicine

From

Stratified Medicine

To

Precision Medicine



1 Patients are grouped by:

- Disease Subtypes
- Risk Profiles
- Demographics
- Socio-economic
- Clinical Features
- Biomarker
- Molecular sub-populations

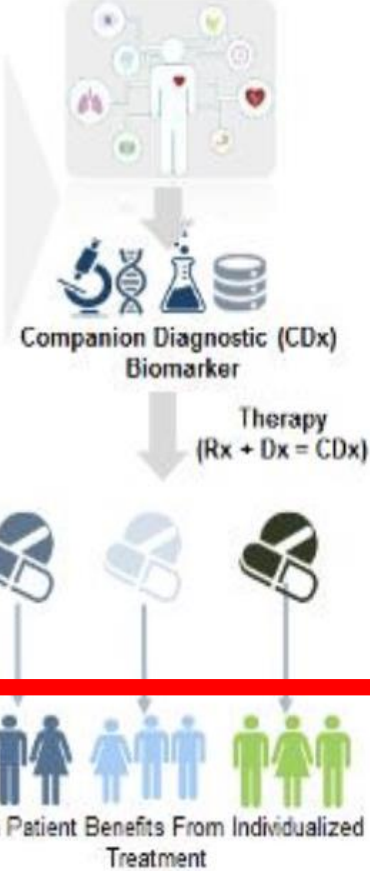


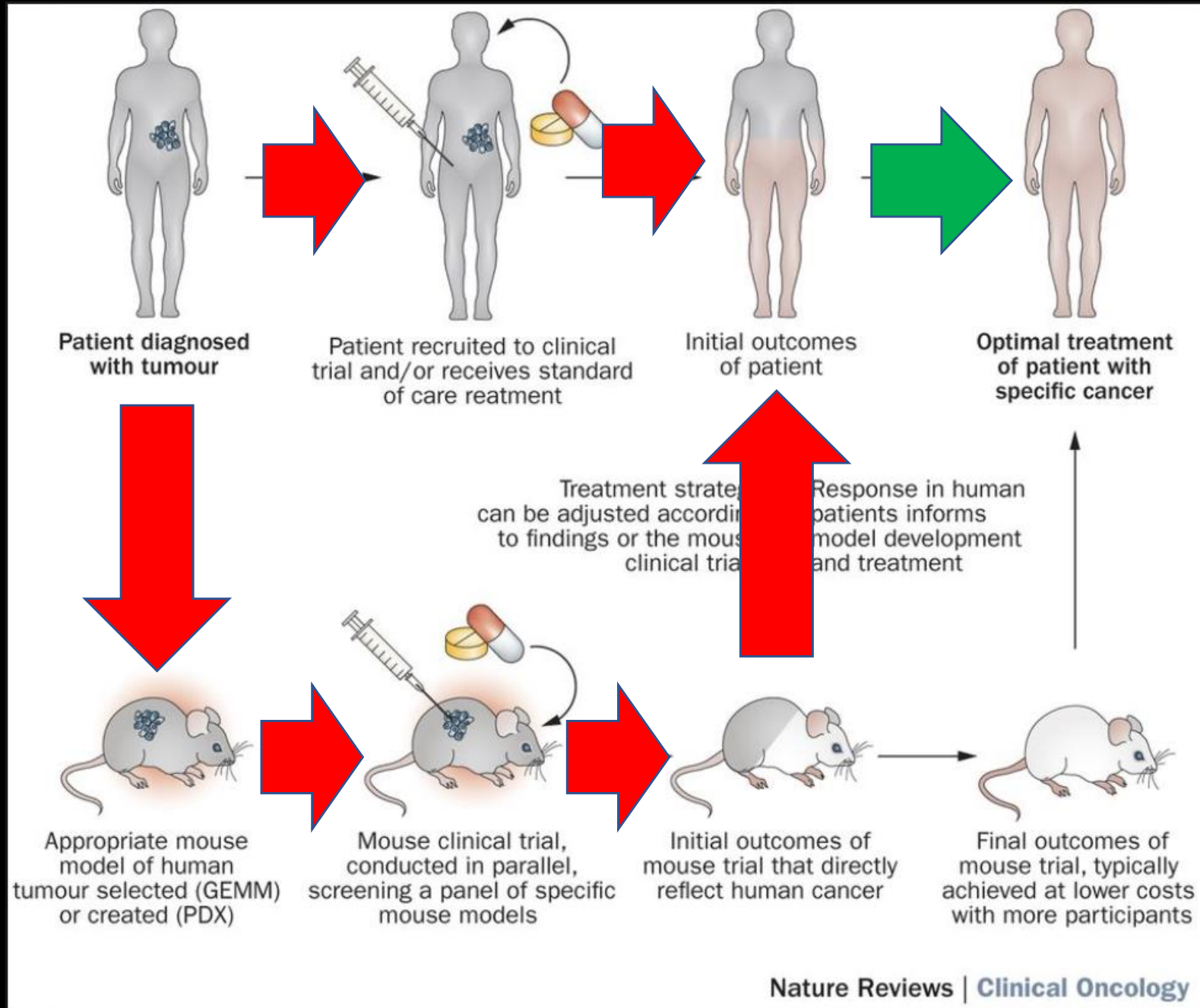
2

Individual patient level:

- Genomics and Omics
- Lifestyle
- Preferences
- Health History
- Medical Records
- Compliance
- Exogenous Factors

Precision medicine ensures delivery of the right intervention to the right patient at the right time.



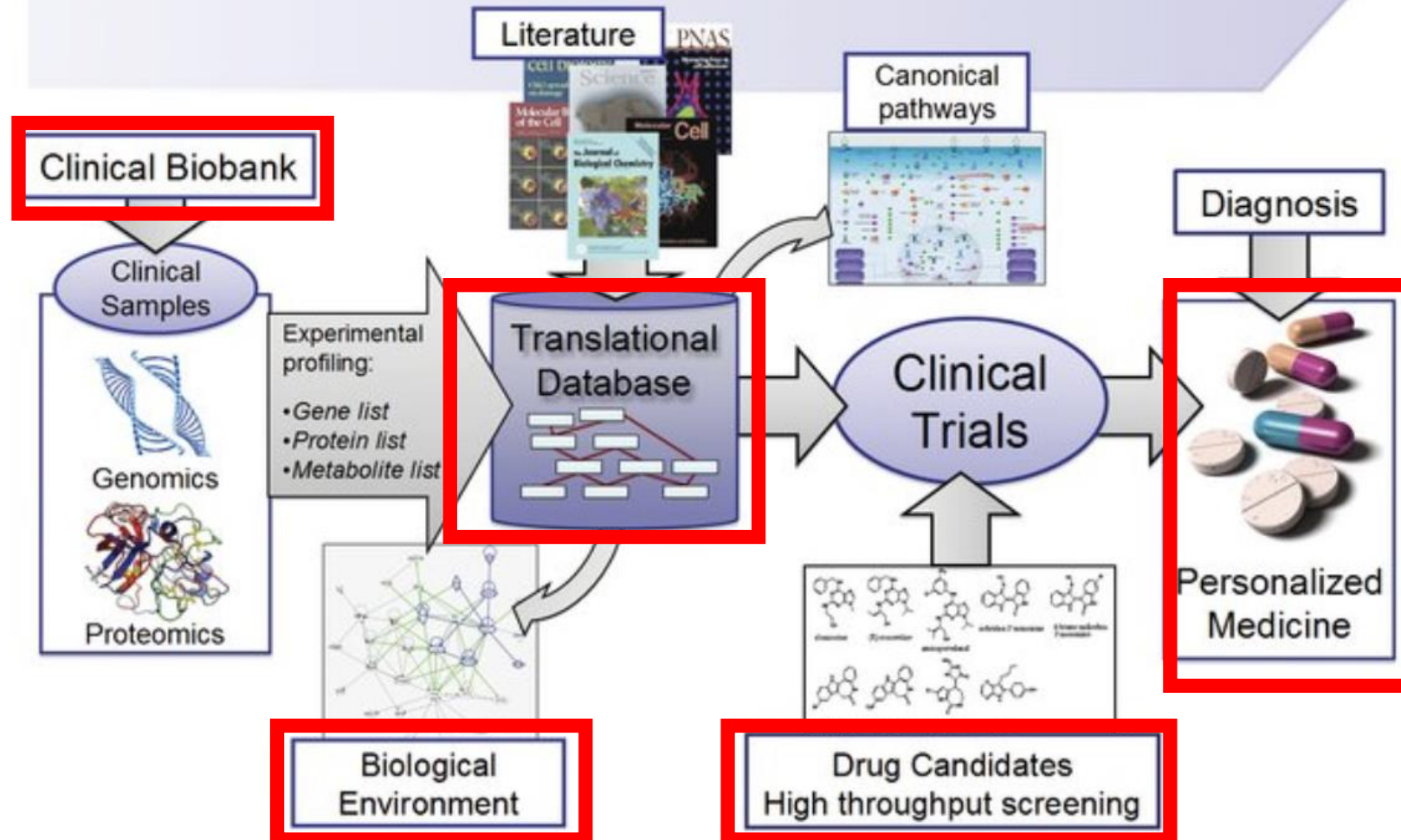


TRANSLATIONAL SCIENCE

Phase I

Phase II

Phase III



Future

Translation is key in Personalized Healthcare !

Adapted from:
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*"I'm afraid you're
suffering from an
increased IL-1 β and
an aberrant miR843
expression"*



Thank You
for Your
Time & Attention