Evidence and Decisions

Carl-Fredrik Burman, PhD, Assoc Prof
Chalmers University (/ AstraZeneca)

EMA, 29 March 2017

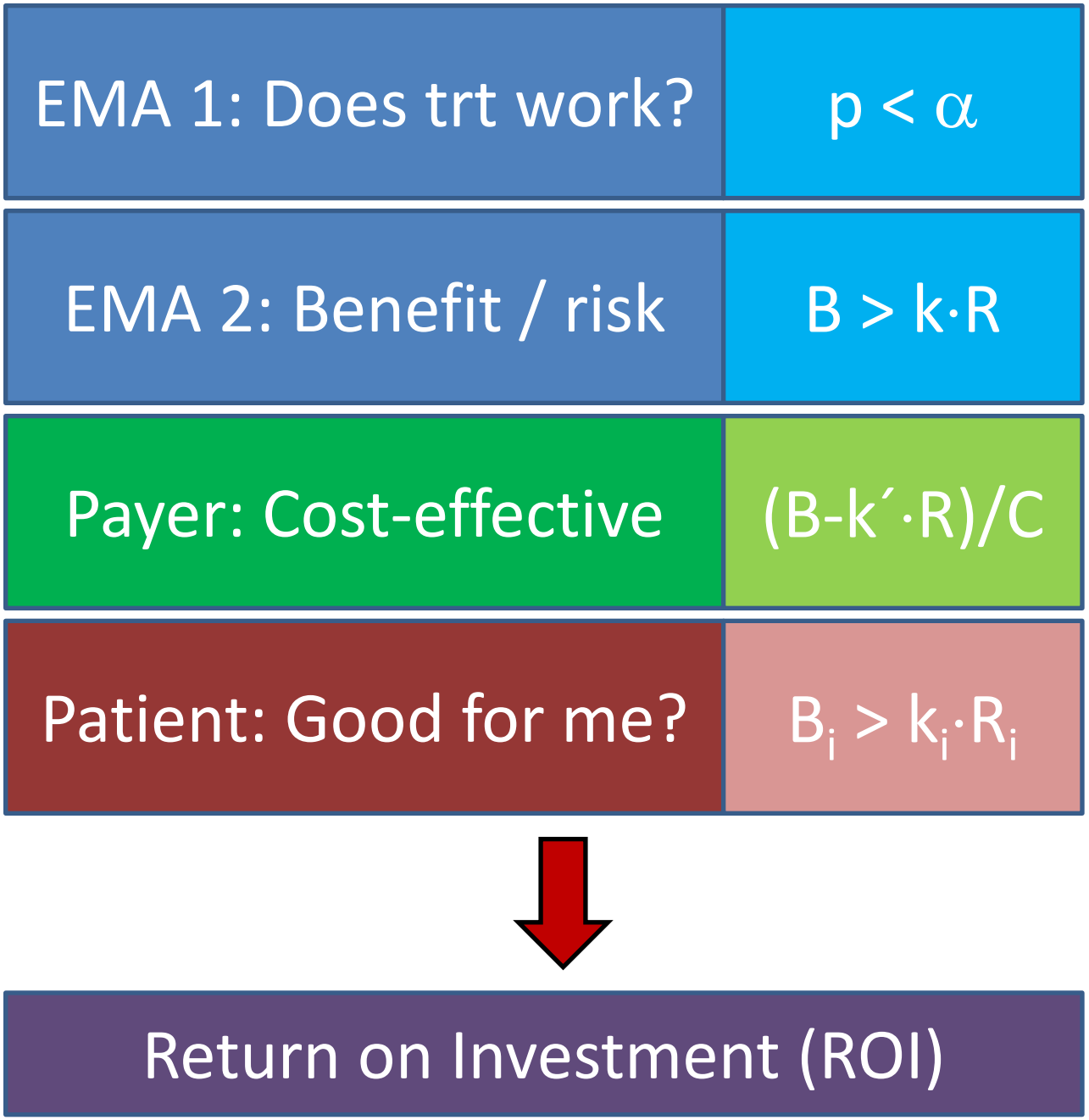
This project has received funding from the European Union's 7th Framework Programme for research, technological development and demonstration under the IDEAL Grant Agreement no 602552. The views expressed are the author's own and may not necessarily express those of IDEAL, AZ or Chalmers Univ.

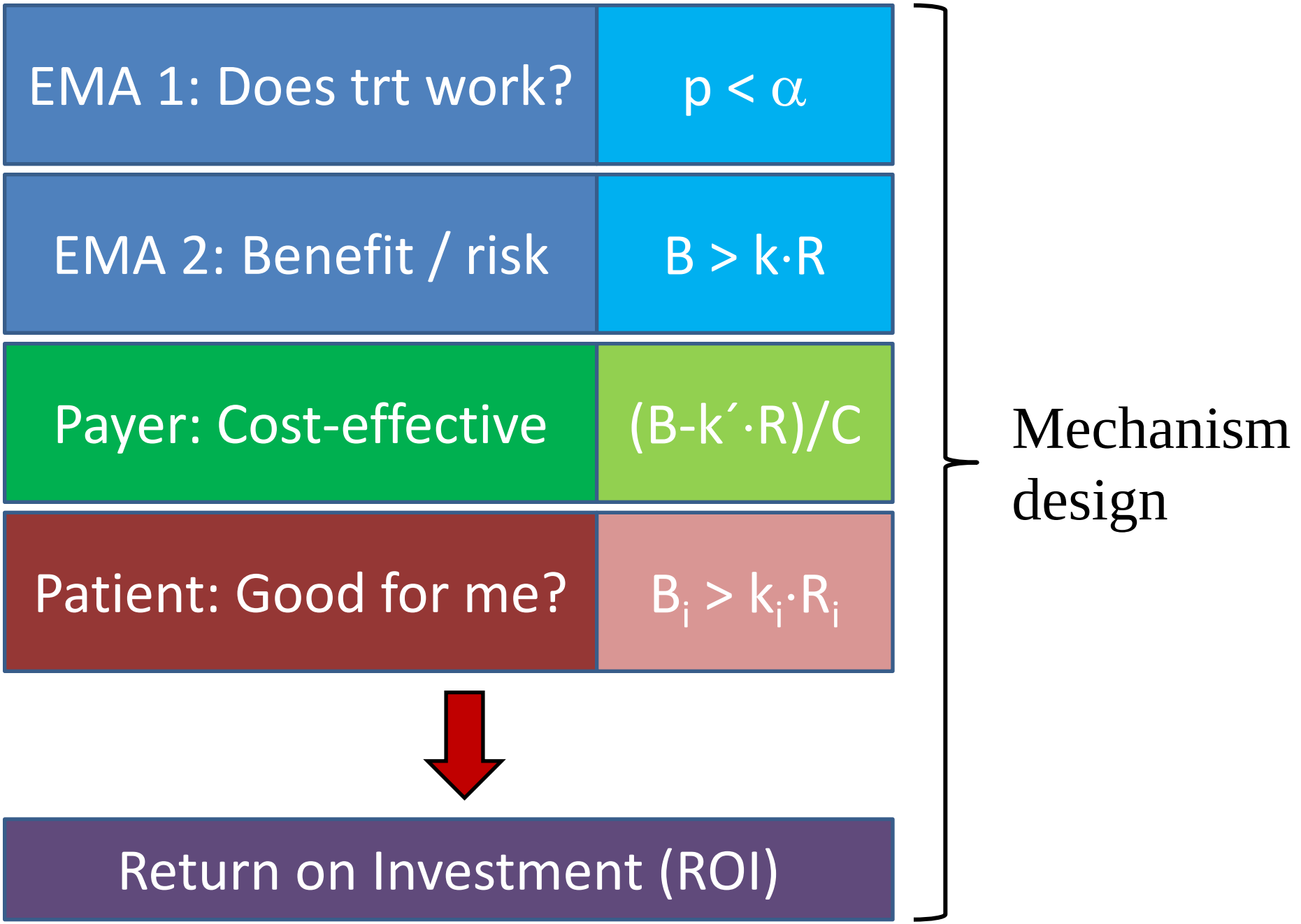
EMA 1: Does trt work?	$p < \alpha$

EMA 1: Does trt work?	$p < \alpha$
EMA 2: Benefit / risk	$B > k \cdot R$

EMA 1: Does trt work?	$p < \alpha$
EMA 2: Benefit / risk	$B > k \cdot R$
Payer: Cost-effective	$(B-k' \cdot R)/C$

EMA 1: Does trt work?	$p < \alpha$
EMA 2: Benefit / risk	$B > k \cdot R$
Payer: Cost-effective	$(B-k' \cdot R)/C$
Patient: Good for me?	$B_i > k_i \cdot R_i$


EMA 1: Does trt work?
$p < \alpha$
EMA 2: Benefit / risk
$B > k \cdot R$
Payer: Cost-effective
$(B-k' \cdot R)/C$
Patient: Good for me?
$B_i > k_i \cdot R_i$
Return on Investment (ROI)


EMA 1: Does trt work?
$p < \alpha$
EMA 2: Benefit / risk
$B > k \cdot R$
Payer: Cost-effective
$(B-k' \cdot R)/C$
Patient: Good for me?
$B_i > k_i \cdot R_i$
Return on Investment (ROI)
Mechanism design

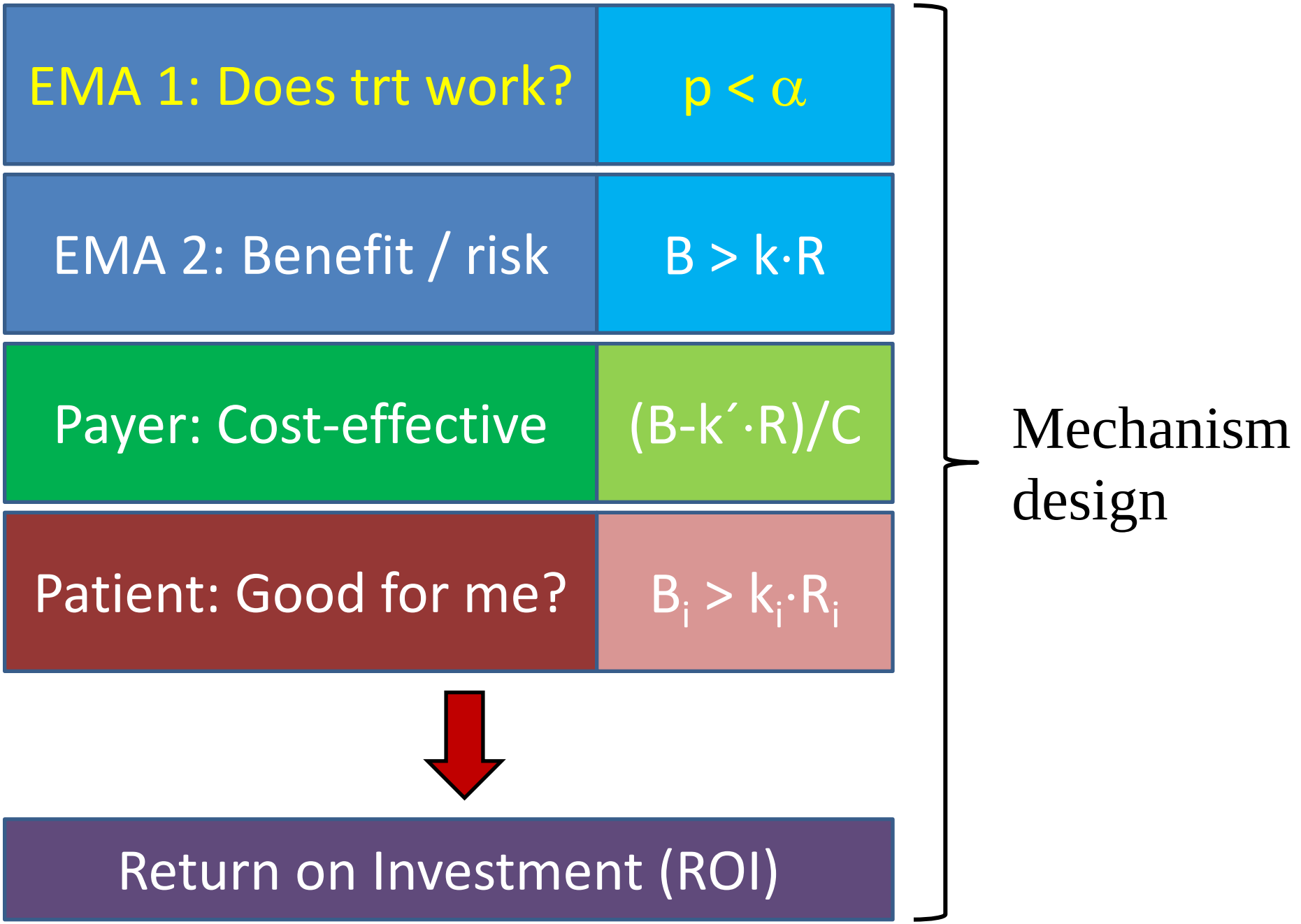
What's important?

"Salus aegroti"

(The well-being of the patient)

Not all rare diseases are equal

Rare disease ≠ neglected disease


EMA 1: Does trt work?
$p < \alpha$
EMA 2: Benefit / risk
$B > k \cdot R$
Payer: Cost-effective
$(B-k' \cdot R)/C$
Patient: Good for me?
$B_i > k_i \cdot R_i$
Return on Investment (ROI)
Mechanism design

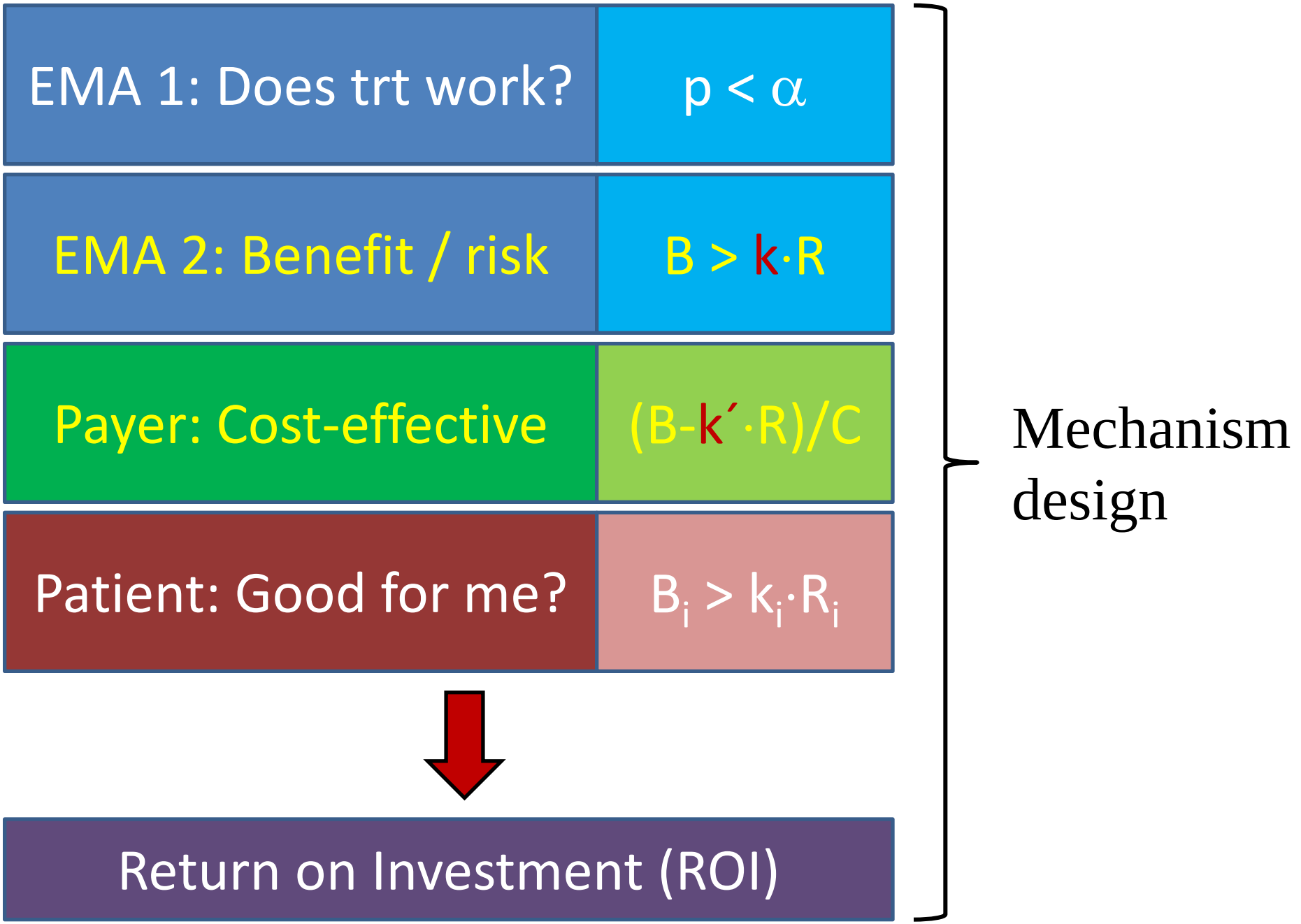
"Level of evidence", α, should depend on disease population size etc.

Stallard et al. (2017)
Miller & Burman (2017, submitted)

Efficiency - bias tradeoff

- Pooling data over time points
- Dichotomous -> continuous endpoints
- Highly informative endpoints
- Borrowing data (historic, other populations)
- Cross-over
- Optimal sample size

Burman (2015)


EMA 1: Does trt work?
p < α
EMA 2: Benefit / risk
B > k·R
Payer: Cost-effective
(B-k´·R)/C
Patient: Good for me?
$B_i > k_i \cdot R_i$
Return on Investment (ROI)
Mechanism design

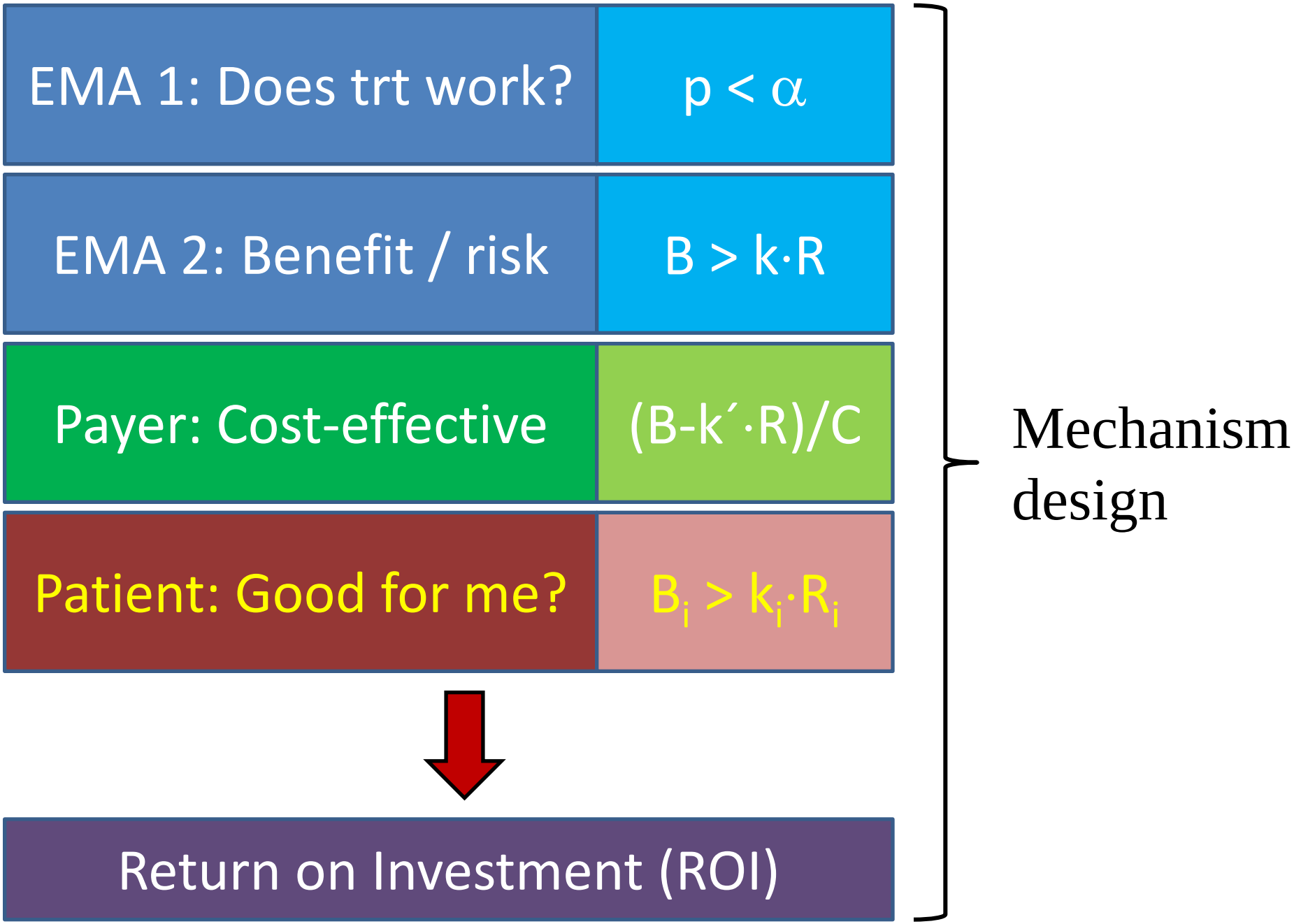
In-transparency in

- Benefit/risk assessment (k, k´) and/or
- Willingness to pay

lead to fewer drugs being developed and less value to patients

Jobjörnsson, Forster, Pertile, Burman (2016)
Jobjörnsson (2016; Section 3.3)

Lack of regulator-payer alignment lead to fewer drugs being developed and less value to patients


EMA 1: Does trt work?
p < α
EMA 2: Benefit / risk
B > k·R
Payer: Cost-effective
(B-k´·R)/C
Patient: Good for me?
$B_i > k_i \cdot R_i$
Return on Investment (ROI)
Mechanism design

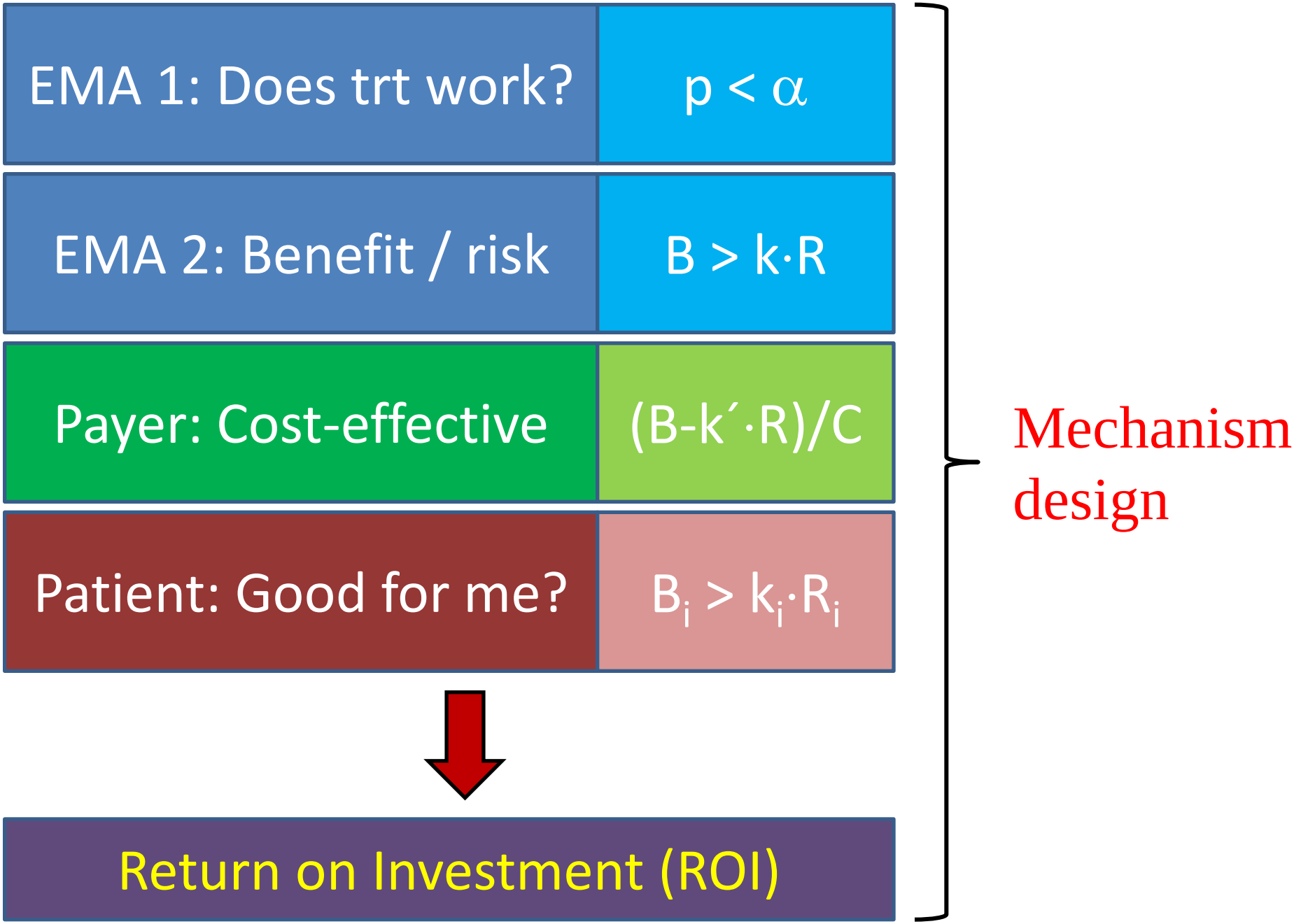
Individualised

- Benefit
- Risk
- Preferences

Biomarker-defined subpopulations

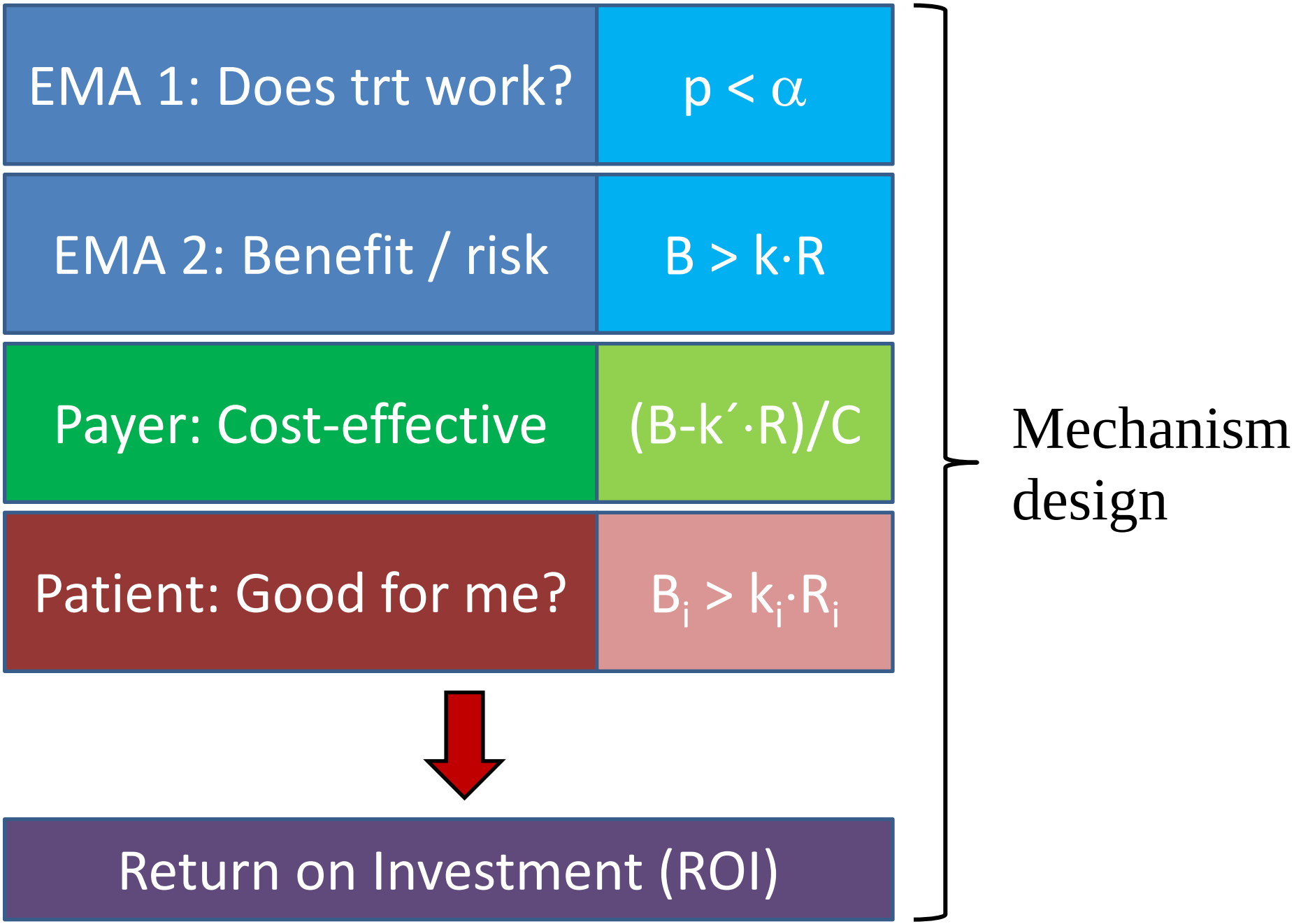
- Level of evidence in BM negatives
- Should we test a null hypothesis we know is wrong?

Ondra, Jobjörnsson, Beckman, Burman, König, Stallard, Posch (2016)


EMA 1: Does trt work?
$p < \alpha$
EMA 2: Benefit / risk
$B > k \cdot R$
Payer: Cost-effective
$(B-k' \cdot R)/C$
Patient: Good for me?
$B_i > k_i \cdot R_i$
Return on Investment (ROI)
Mechanism design

Incentivising mechanisms:

- Level of evidence needed to depend on context
- Progressive pay


EMA 1: Does trt work?
$p < \alpha$
EMA 2: Benefit / risk
$B > k \cdot R$
Payer: Cost-effective
$(B-k' \cdot R)/C$
Patient: Good for me?
$B_i > k_i \cdot R_i$
Return on Investment (ROI)
Mechanism design