

Integrated Decision-theoretic Optimisation of Phase II/III Oncology Trials

---- PSI 2026

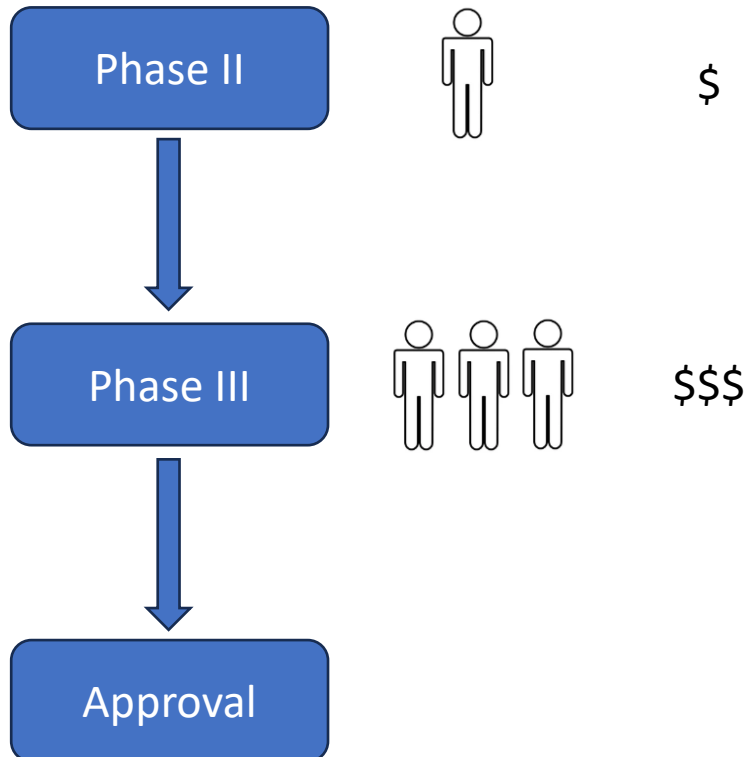
Presenter: Haotian Wang

Supervisors: Peter Kimani, Michael Grayling, Josephine Khan, Nigel Stallard



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Background & Motivation

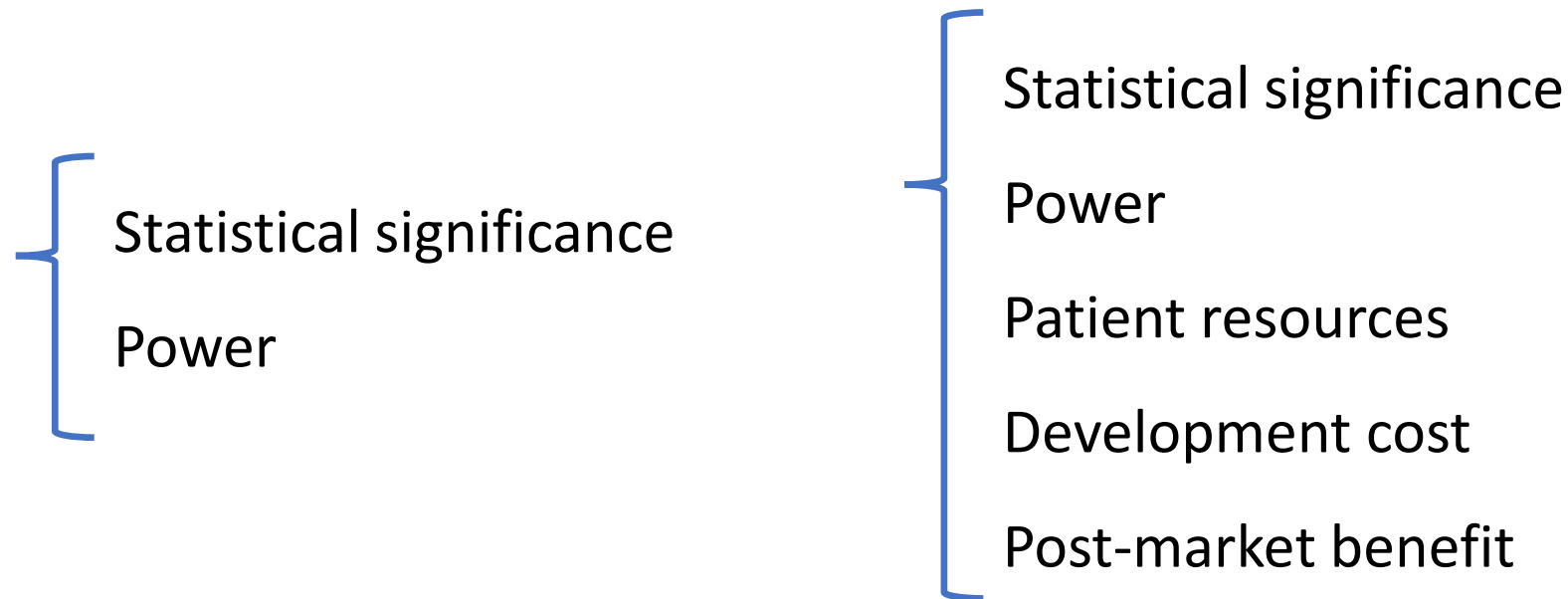


- ✓ Adaptive design methodology
- ✓ Phase II can inform later development
- ✗ Contribution of phase II information is unclear
- ✗ Programme-level decisions optimisation is lacking

Joint Optimisation Framework



Utility-focused instead of Success-focused



- An effective development programme should balance success, cost, and the value of information gained across trial phases.

Joint Optimisation Framework



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Notation

p_e : response rate in treatment group

$\beta_r, \beta_e, \beta_{re}$: coefficient parameters

n_2 : sample size in phase II

P_{go} : probability of a go decision in phase II

$E[n_3]$: expected number of events in phase III

P_{sp} : probability of a successful programme

p_c : response rate in control group

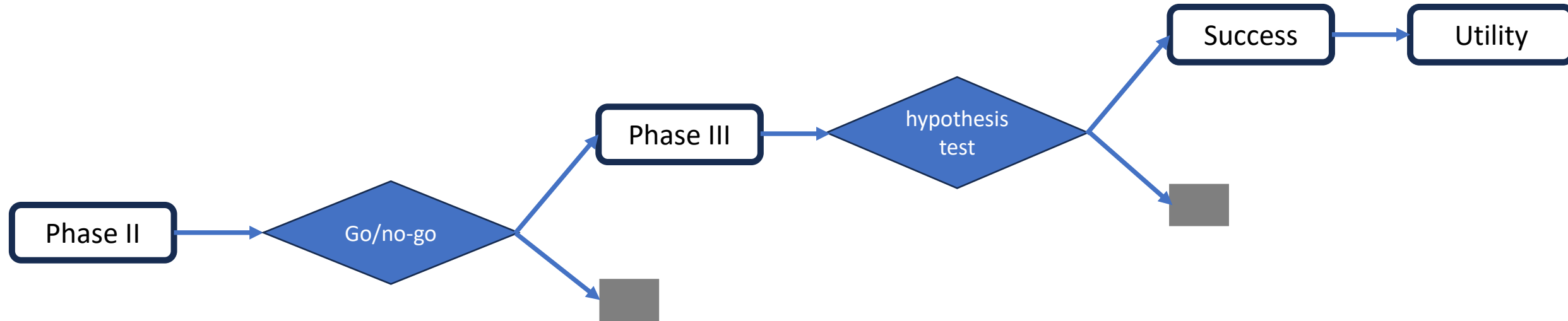
κ : threshold for a go/no-go decision

n_3 : sample size in phase III

c_{02}, c_{03} : fixed cost in phase II, III

c_2, c_3 : variable cost in phase II, III

Joint Optimisation Framework

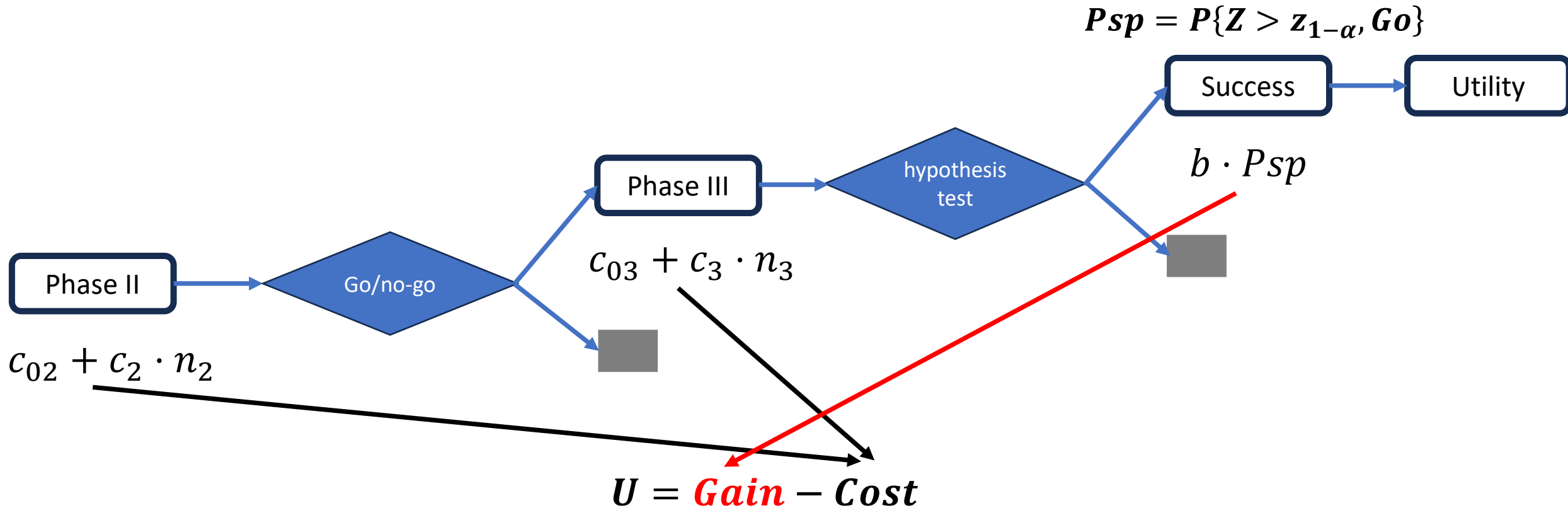


$$U = \textit{Gain} - \textit{Cost}$$

Choose the design that maximises expected utility depending on

- phase II sample size n_2
- phase II decision rule κ
- phase III sample size n_3

Joint Optimisation Framework



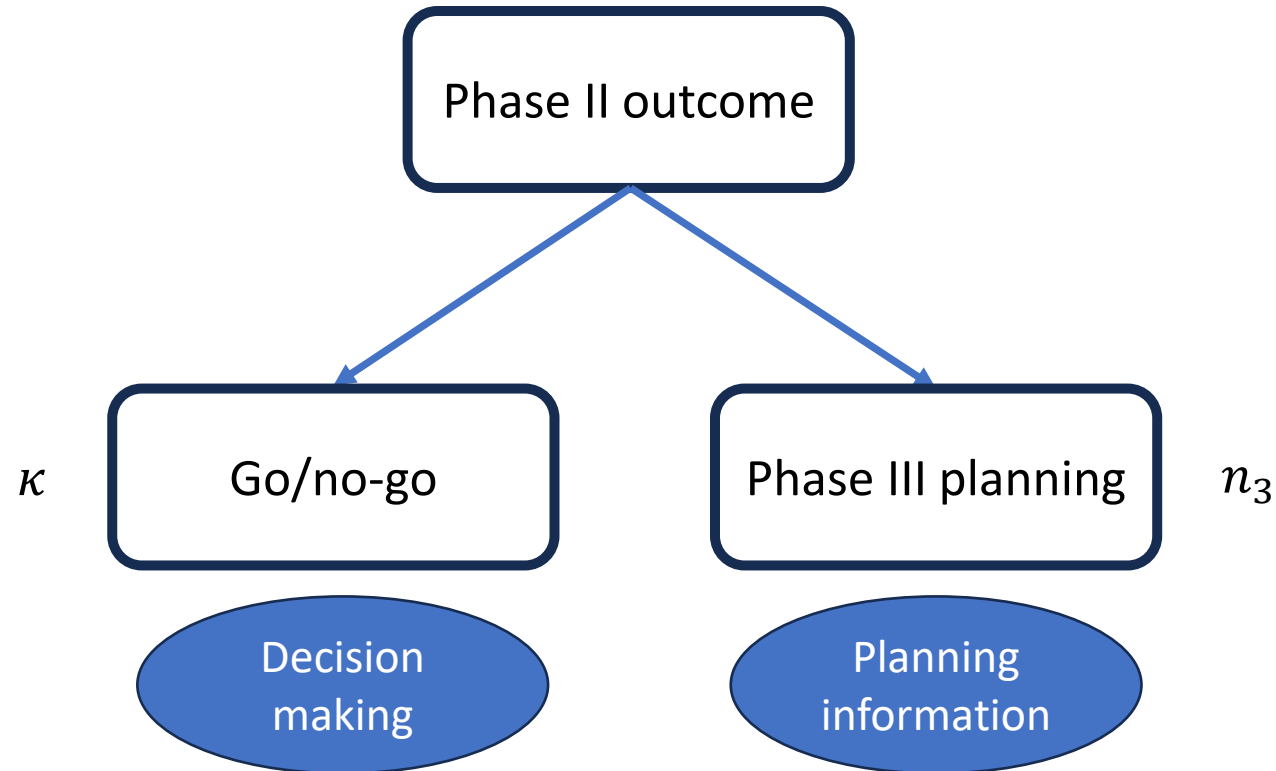
Choose the design that maximises expected utility depending on

- phase II sample size n_2
- phase II decision rule κ
- phase III sample size n_3

Joint Optimisation Framework



Using phase II information in phase III planning



Phase II contributes both decision support and planning information

Joint Optimisation Framework



Comparison of development strategies

Conventional Design

- Separate phase II & III
- Fixed target HR
- Fixed n_3

Phase II informed Design

- Integrated phase II/III
- Phase II informs target HR
- n_3 adapts to maintain power

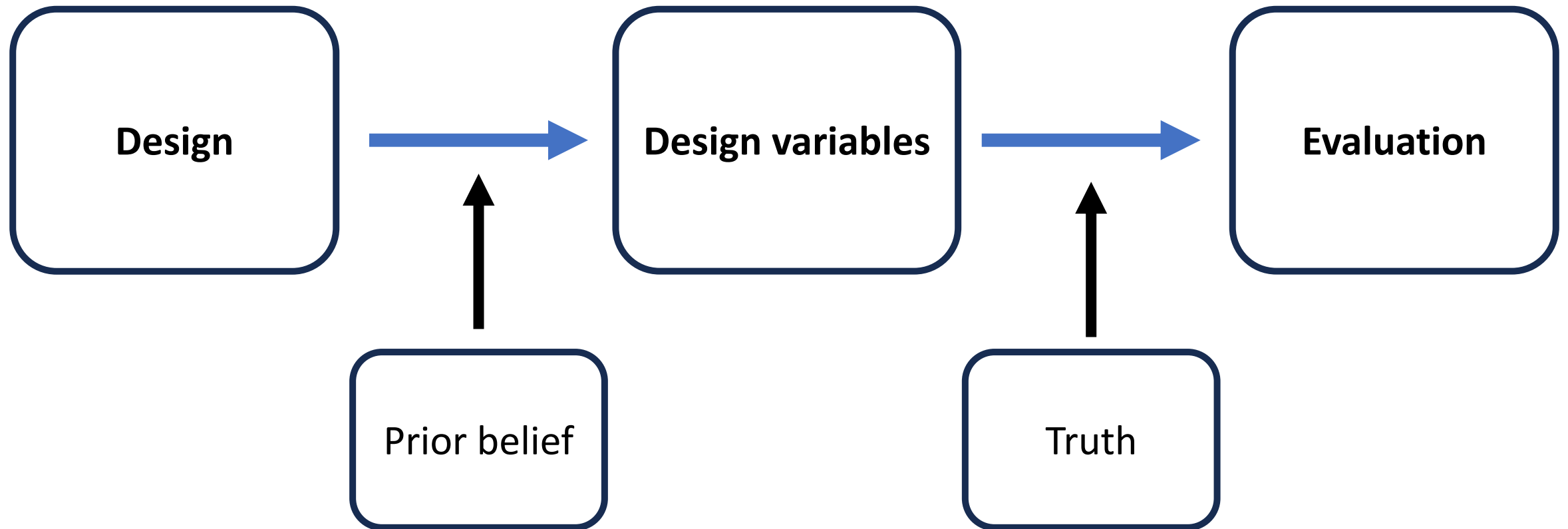
Fully optimal Design

- Integrated phase II/III
- Phase II informs target HR
- n_3 chosen by optimisation



Increasing use of phase II information in programme-level decision-making

Evaluation Results



Evaluation Results



$$p_e \sim \text{Beta}(1.2, 3.8), \beta_e \sim N(0.4851, 0.1^2), \beta_r \sim N(1.1395, 0.1^2)$$

$$p_e^{(t)} = 0.2418, \beta_e^{(t)} = 0.4851, \beta_r^{(t)} = 1.1395$$

Design Strategies	n_2	κ	P_{go}	$E[n_3]$	P_{sp}	$Utility$
Conventional	46	0.1739	0.8978	97.4493	0.8080	1863.039
Phase II informed	35	0	1	100.4322	0.8904	2060.145
Fully optimal	28	0	1	134.2477	0.9576	2154.239

Evaluation Results

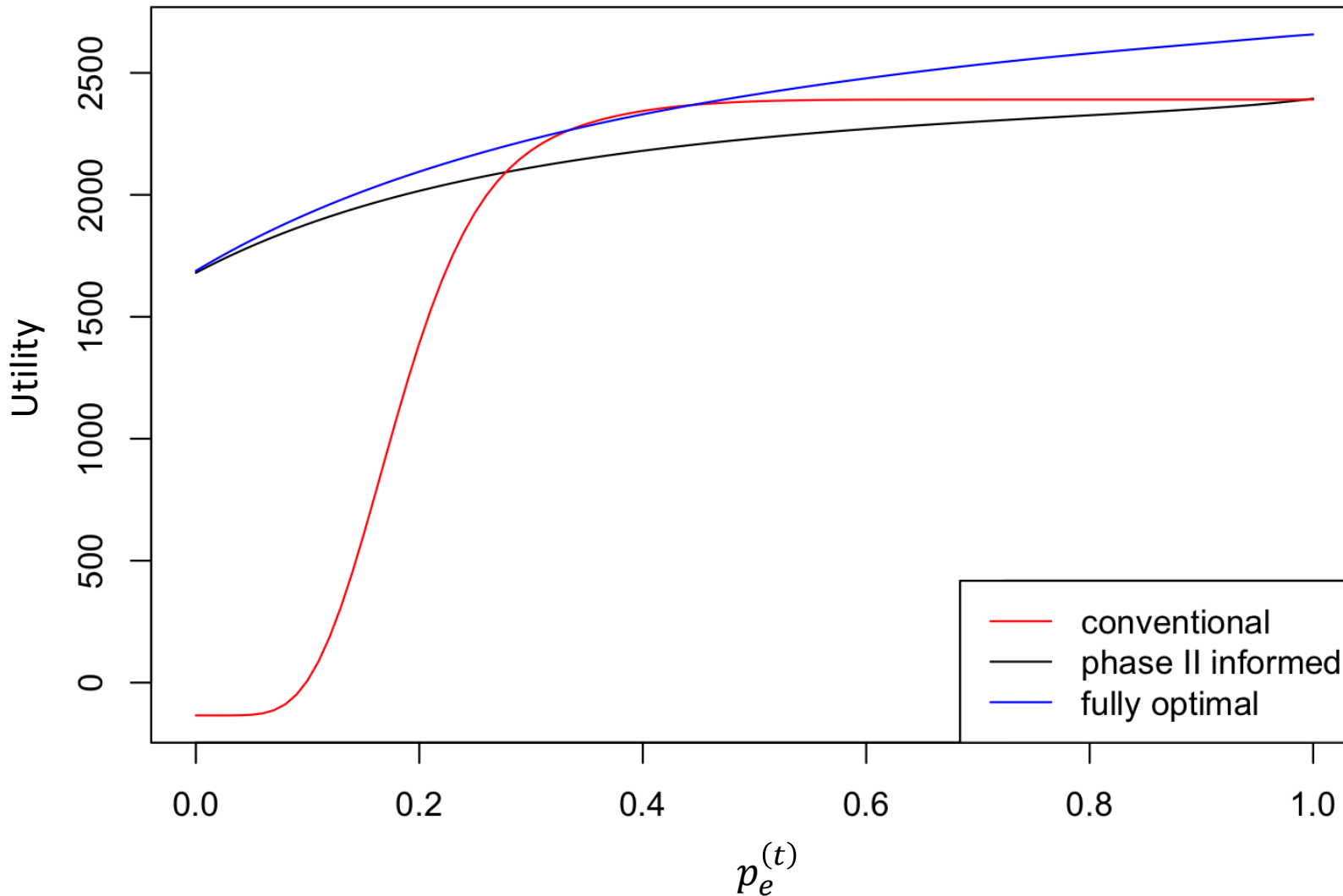


$$p_e \sim \text{Beta}(1.2, 3.8), \beta_e \sim N(0.4851, 0.1^2), \beta_r \sim N(1.1395, 0.1^2)$$

$$p_e^{(t)} = 0.1418, \beta_e^{(t)} = 0.4851, \beta_r^{(t)} = 1.1395$$

Design Strategies	n_2	κ	P_{go}	$E[n_3]$	P_{sp}	Utility
Conventional	46	0.1739	0.8978	97.4493	0.2556	478.194
Phase II informed	35	0	1	137.8916	0.8930	1943.096
Fully optimal	28	0	1	168.8405	0.9448	2000.744

Evaluation Results



- Optimal evaluation results are always positive because of strong survival belief
- Optimal design strategies are more robust under this favourable assumption

Evaluation Results

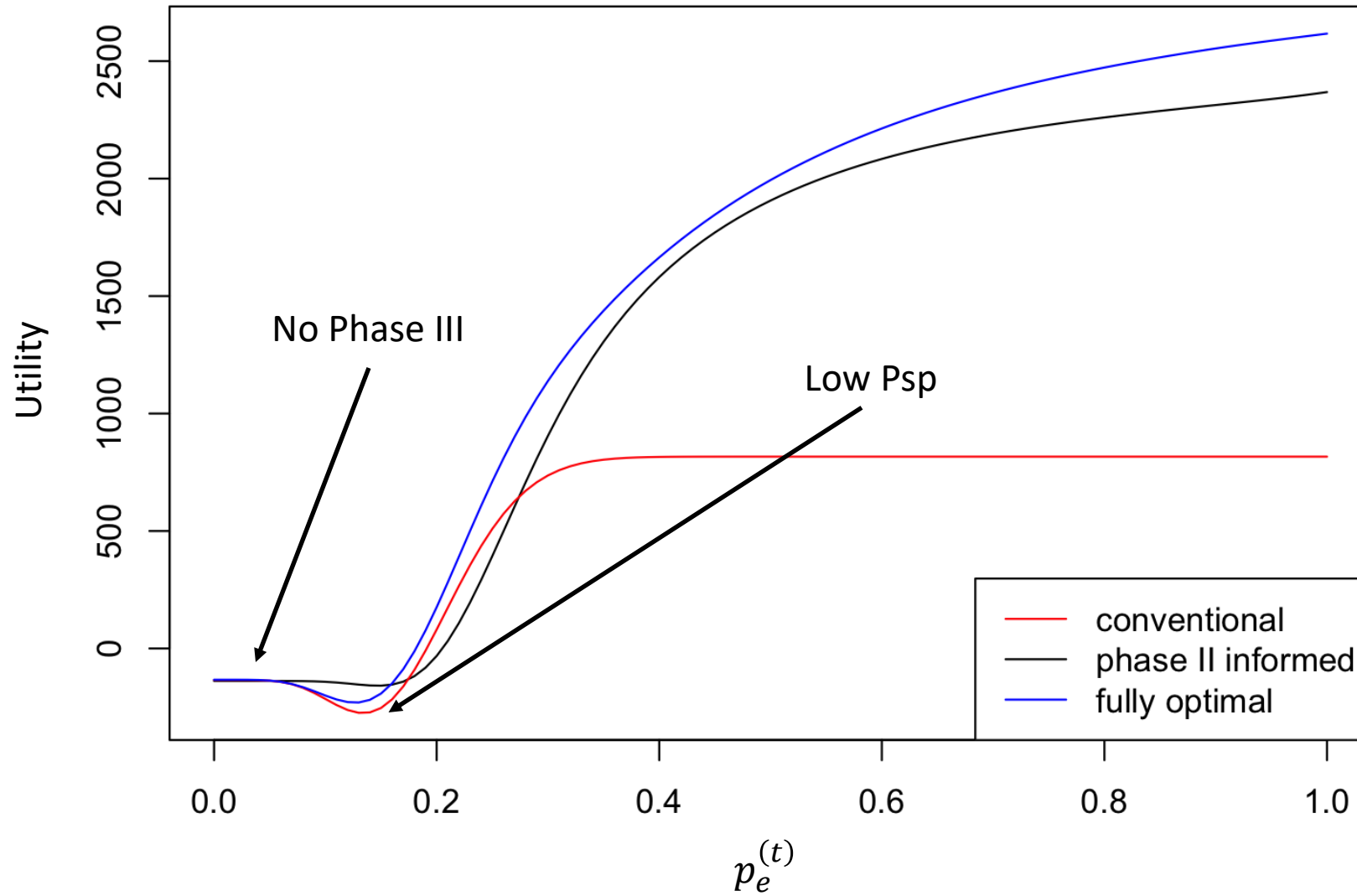


$$p_e \sim \text{Beta}(1.2, 3.8), \beta_e \sim N(\mathbf{0.1}, 0.1^2), \beta_r \sim N(1.1395, 0.1^2)$$

$$p_e^{(t)} = 0.2418, \beta_e^{(t)} = 0.1, \beta_r^{(t)} = 1.1395$$

Design Strategies	n_2	κ	Pgo	$E[n_3]$	Psp	Utility
Conventional	46	0.1739	0.8978	569.6284	0.8080	449.9484
Phase II informed	51	0.22	0.5968	450.7865	0.4780	309.6166
Fully optimal	44	0.14	0.9335	337.5289	0.6500	626.5782

Evaluation Results



Conclusions



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- Phase II outcomes inform both go/no-go decision and phase III planning
- Optimal strategies balance cost and information gain
- More efficient development may reduce unnecessary late-stage trials

Acknowledgement



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