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DPD deficiency: Medico-economic evaluation of pre-treatment screening of 5-FU toxicity

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Purpose

The objective of this study was to assess the cost-effectiveness of a screening test before treatment of the deficiency of DPD activity combining two approaches, genetic and phenotype (UH_2/U).

Introduction

If the efficacy of 5-FU is definitively accepted, it still remains very severe toxicities (or even death) in some patients. The frequency of treatment-related deaths in patients traited by the standard protocols of 5-FU is between **0.3%** and **1.2%** and frequency of WHO grade III-IV toxicities is between **25%** and **30%**. Furthermore, these toxicities mobilize significant resources. Deficiency of DPD activity is associated with severe toxicity or even death after the first two cycles 5-fluorouracil (5-FU) based of chemotherapy. A screening test of DPD deficiency has been developed (5-FU$^{\text{ODPM Tox}}$, ODPM, France). It is used to identify patients at risk of severe 5-FU related toxicity, with the aim of adapting doses of 5-FU according to the schema (5-FU$^{\text{ODPM Protocol}}$, ODPM, France). This test consists of a coupled approach **genetic** and **phenotyping** (UH_2/U). On the one hand, this screening helps prevent severe toxicities and costs of toxicities avoided. On the other hand, the test is an additional cost in the treatment.

Methods

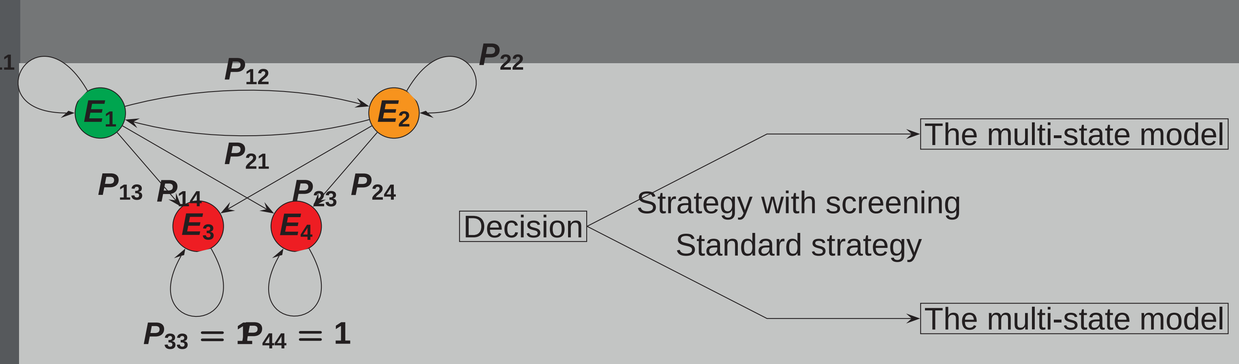
Patients and medico-economic design

- Retrospective data from a population of patients treated for colorectal cancer :
  1. Arm A standard protocol (2400 mg/m^2): no screening test n=886 patients
  2. Arm B 5-FU$^{\text{ODPM Protocol}}$: with screening 5-FU$^{\text{ODPM Tox}}$ test n=856 patients
- Cost-effectiveness study
- The main point of view was society perspective
- The time horizon was 2 cycles of chemotherapy

Model and outcomes

- A multi-state Markov-type model was used to estimate the mean cost and effectiveness for each of the two strategies.
- **Costs** :
  - Cost of the standard strategy $COST_{\text{Standard}} = COST_{\text{treatment of toxicities}}$
  - Cost of the screening strategy $COST_{\text{With Screening}} = COST_{\text{screening test}} + COST_{\text{treatment of toxicities}}$
- Effectiveness were cumulative prevalences of no toxicity : E_{Standard} and $E_{\text{With Screening}}$
- Incremental cost-effectiveness ratio (ICER) :

$$ICER = \frac{\left(COST_{\text{Standard}} - COST_{\text{With Screening}}\right)}{\left(E_{\text{Standard}} - E_{\text{With Screening}}\right)}$$



Statistc method and Probabilistic analysis

- Summary statistics for outcomes (costs, prevalences and ICER)
- Non-parametric bootstrap for outcomes : 5,000 iterations
- 95% Confidence Intervalle for costs, prevalences and ICER

Results

Costs

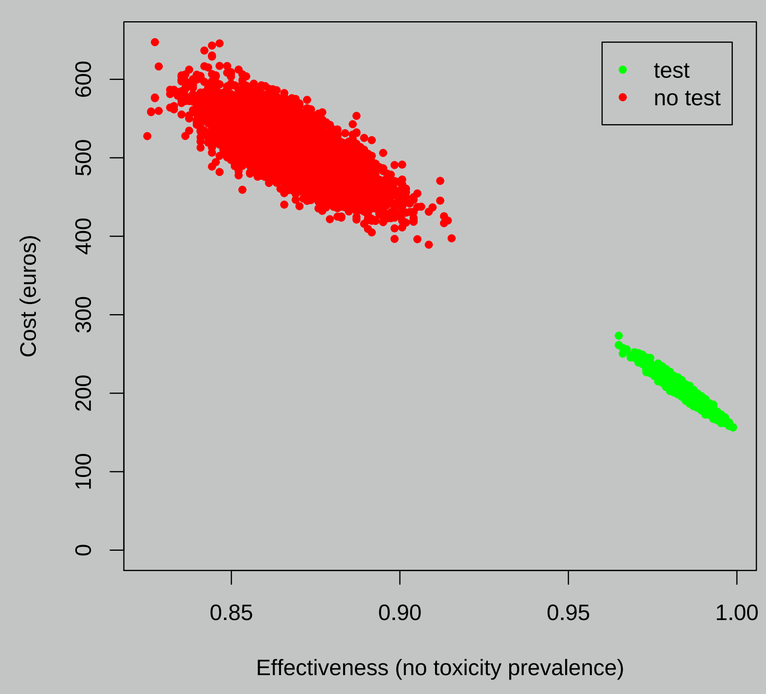
	Screening strategy	Standard strategy
Cost of screening test	153 €	0 €
Cost of treatment	X	X
Cost of toxicities TN	42€	508€
Total	195€	508 €

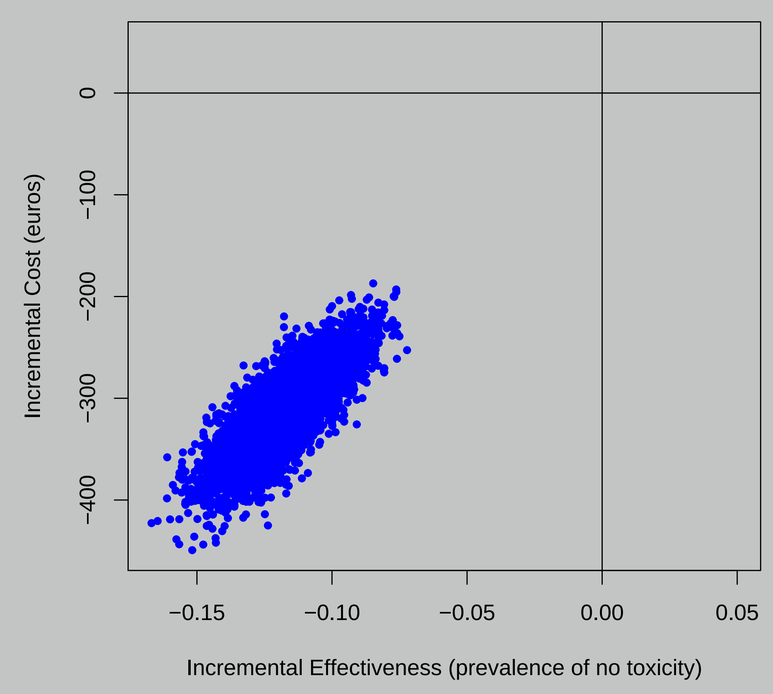
Effectiveness

Cycle 1	99.5%	94.2%
Cycle 2	99.1%	93.1%
Cumulative prevalences	98.6%	87.3%

ICER

Incremental Cost	-313€
Incremental Effectiveness	-11.30%
ICER	2770€/toxicity





	Cost(€)	Effectiveness (%)	Incremental Cost €	Incremental Effectiveness(%)	ICER (€/tox)
Standard strategy	509 (508;510)	13.08 (13.04;13.11)			
Screening strategy	196 (195.5;196.5)	1.38 (1.37;1.39)	-11.69 (-11.73;-11.65)	312.60 (311.52;313.67)	2680 (2674;2686)

Conclusions

Pre-treatment screening test combining genetic and phenotype reduced the incidence of toxicities associated with 5-FU, it avoided deaths due to 5-FU and its additional cost was less than the cost of care of toxicity that it avoided.

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