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Cost-Effectiveness Analysis of Drotrecogin Alfa (activated) as a Treatment for Severe Sepsis in Hospitalised Patients

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REES : Réseau d 'Evaluation en Economie de la Santé
http://smbh7.smbh.univ-paris13.fr

Objectives of the Study

- To improve knowledge of the type of patients admitted to intensive care for severe sepsis;
- To predict the treatment costs of these patients;
- To identify patient profiles for which treatment would be liable to be more efficient.

Epidemiological Context

- Severe sepsis: approximately 54,000 cases per year, mortality rate at least 28.5% *(PMSI 99)*
- Cost of care in intensive care units and clinical departments: 26 449.90 € $_{96}$ *(CUB Réa)*
- A new treatment allows the absolute mortality rate in this indication to be reduced by 6.1%: recombinant human activated Protein C (Xigris®) *(Bernard G, NEJM 2001)*

METHODS

Treatment strategies

- Conventional treatment (Usual Care)
  - In intensive care unit
  - Procedures described by the Oméga field
- Xigris®
  - Continuous infusion for 96 hours
  - 24 µg/kg/h
  - In addition to normal intensive care practices

Analytical Context

- **Population**: All patients with severe sepsis (and with least one organ system failure, originating from an inflammatory problem with a documented infectious focus)
- **Strategies compared**: Usual Care and Xigris®
- **Perspective**: Public hospital administration
- **End points**: Survival (years of life) and Cost
- **Temporel Horizon**: From the start of treatment in intensive care to death (including outside hospital)

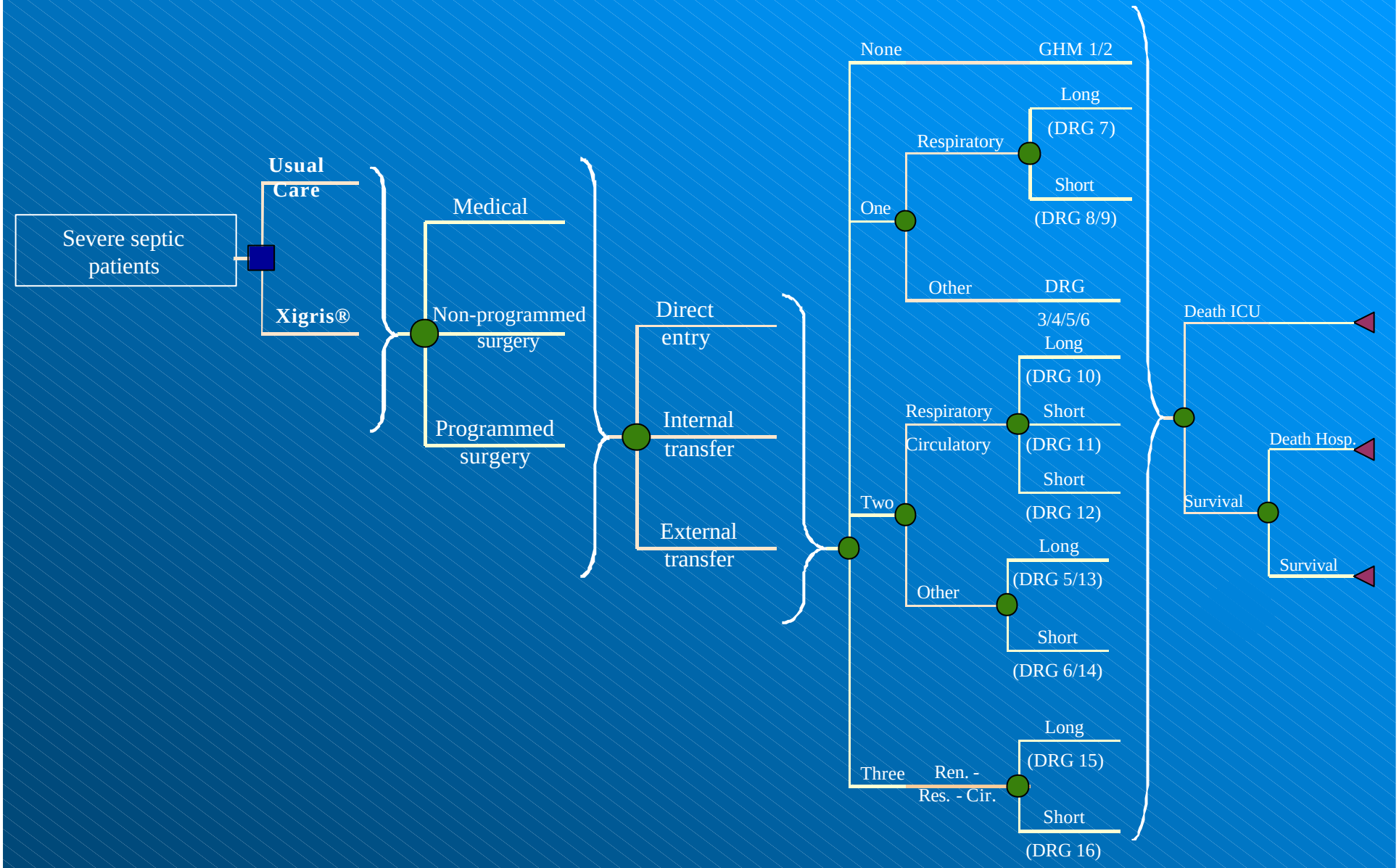
Choice of a Classical Decision Tree

- **Transparency**:
  - Simple understandable tree
  - Directly legible parameter values
- **Exhaustivity**: Integration of various sources of data
  - CUB Réa
  - PROWESS
  - Literature
- **Adaptability**: Ability to introduce new data

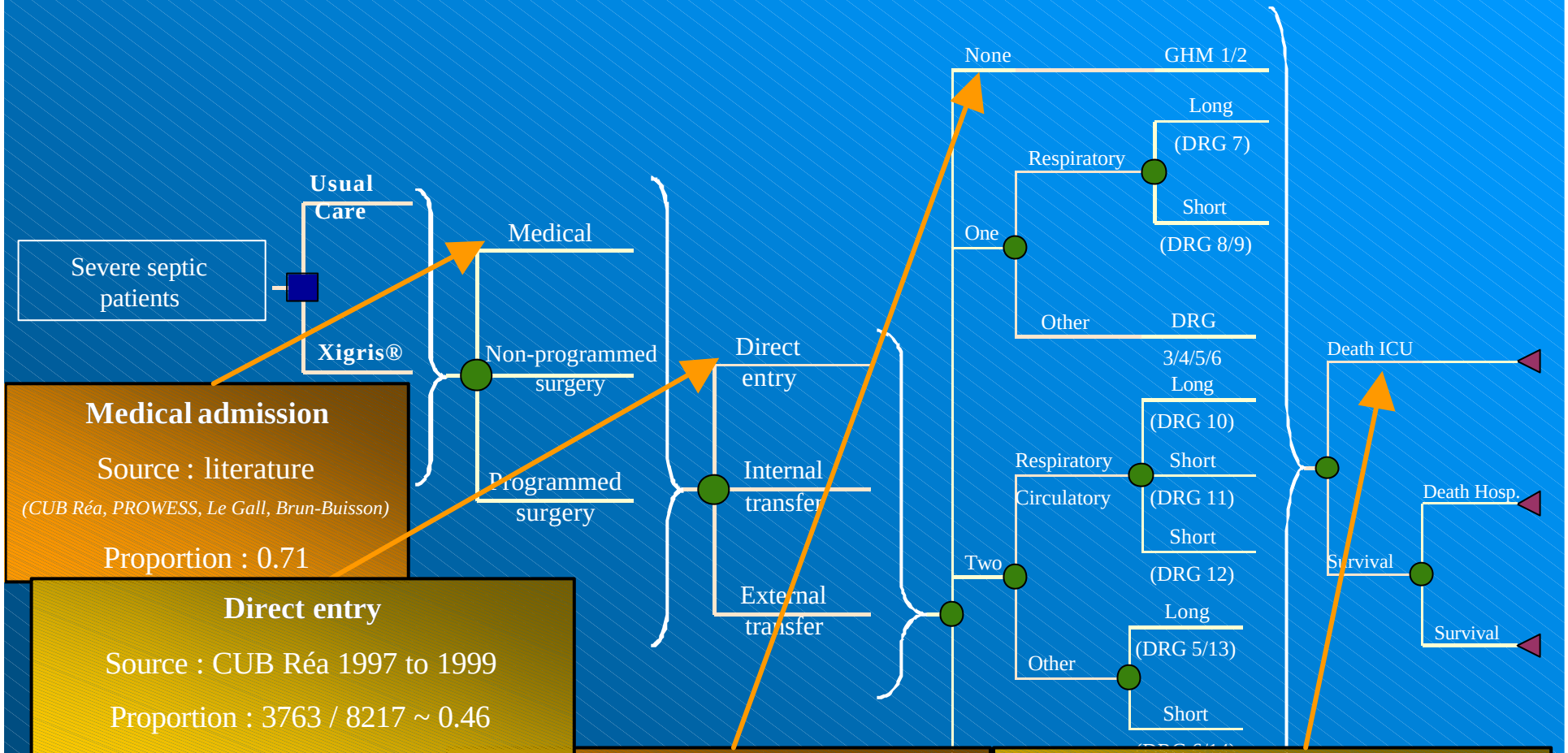
List of Variables

- Admission category: surgical, medical
- Method of admission: direct, transfer
- Type of support: renal, respiratory, circulatory
- Number of supports: None, 1, 2, 3
- Duration of support (Ω score)
- Risk to life (IGS2 score)

Reduced Form of Model



Allocation of Probabilities



Medical admission

Source : literature

(CUB Réa, PROWESS, Le Gall, Brun-Buisson)

Proportion : 0.71

Direct entry

Source : CUB Réa 1997 to 1999

Proportion : 3763 / 8217 ~ 0.46

Cumulative Proportion : 0.71*0.46 ~ 0.33

No organ support

Source : CUB Réa (97 to 99)

Proportion : 620 / 3763 ~ 0.16

Cumulative Proportion : 0.33*0.16 ~ 0.05

Death in Intensive Care

Source : CUB Réa (97 to 99)

Proportion : 12/620 ~ 0,02

Cumulative Proportion : 0.02*0.05 ~ 0.001

Medical End Point

Life expectancy of patients receiving care

- Death
  - Estimated from the Xigris® RR based on the patient's MHS (mean hospital stay)
  - Death in intensive care and in subsequent departments
- Life expectancy of survivors
  - Estimated from the McCabe score, sex, mean patient age and INSEE 1997 life expectancy tables.

Budget End Point

- Individual complete cost estimated by linear regression: from the Ω, score, length of stay, IGSII score and status (alive or dead) *(CUB Réa)*
- Different costs between survivors and those who die
- No difference in cost between death in intensive care and death in a conventional department
- Drug costs: 7 881.16 €

Economic End Point

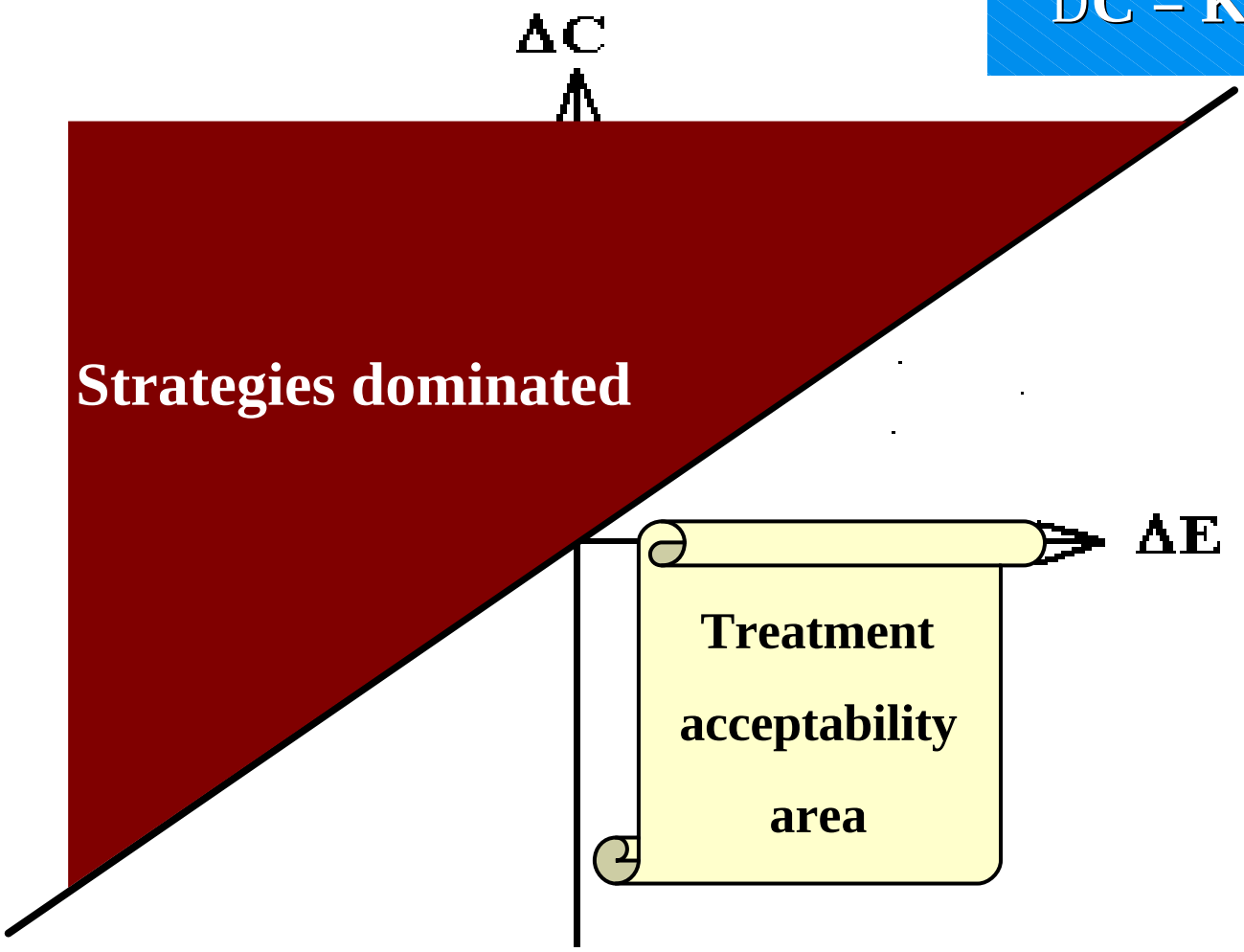
Classification of strategies as a function of efficiency

$$\frac{DC}{DE} = \frac{C_{UC} - C_{XG}}{E_{UC} - E_{XG}}$$

- C_{UC} : Usual cost of treatment of severe sepsis
- C_{XG} : Cost of treatment of severe sepsis by adding Xigris®
- E : Years of life
- D : Incremental cost or years of life gained

Field of Possibilities

DC = K*DE



Probabilist Sensitivity Analysis

- Allows all variables to be addressed simultaneously
- Allows the laws of distribution of variables to be defined and included
- Procedure: Third Order Monte Carlo Simulation

Treatment Acceptability Curve

- Acceptance of treatment depends on price (K) needed to be paid to obtain a gain in effectiveness of one year of life.
- For acceptance to pay a given (K) the treatment has a probability (p) of being acceptable, i.e. of being located in the dominance area of the cost-effectiveness quadrant.
- The acceptability curve for Xigris® produces the probability value (p) as a function of the agreement to pay K : p = f(K).

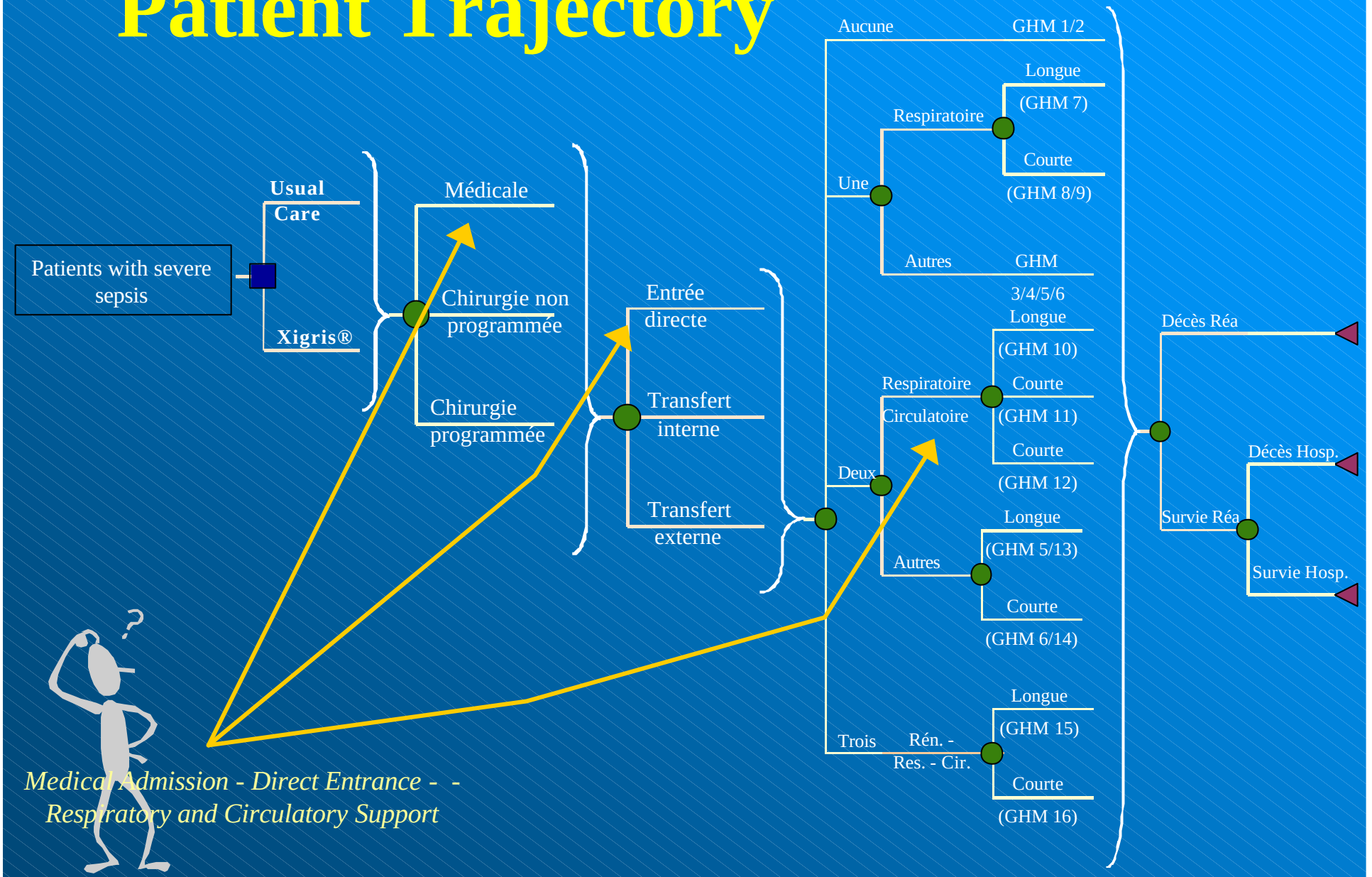
RESULTS

Clinical Case

50 year old man admitted directly by the emergency department for community acquired pneumonia. On admission the patient had two organ system failures (respiratory and circulatory) which were supported by mechanical ventilation and prescription of noradrenalin (Pa O_2/Fi O_2 < 200 mmHg). The patient had no co-morbidities.

Medical Admission - Direct Entrance - Respiratory and Circulatory Support

Patient Trajectory



Intensive Care Unit Stay

- 3 situations to consider:
  - (1) Support is of long duration
    - Case is represented in the database: 832
    - Corresponding probability: 0.595
- Support is of short duration
  - (2) With IGS II score < 51
    - Case is represented in the database: 257
    - Corresponding probability: 0.183
  - (3) With IGS II score > 51
    - Case is represented in the database: 310
    - Corresponding probability: 0.222

Effectiveness

> Man

> 50 years old

> McCabe score = 0

INSEE 97 life expectancy: 27.8 years

Model life expectancy: 13.9 years

Usual Care

> ICU Mortality: 0.411

> Post ICU mortality : 0.032

> Survival: 0.557

Effectiveness: 7.74 years

Xigris®

> ICU Mortality: 0.335

> Post ICU mortality: 0.029

> Survival: 0.636

Effectiveness: 8.85 years

DE = 1.11 years
DM = 0.080 avoidable deaths

Efficiency

Costs:

- Usual care: 33 378.71 €
- Xigris® : 40 637.72 €
- ΔC : 7 259.10 €

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1) End point: Avoidable death

→ ΔC/ΔM = 7 259.10 / 0.08 = 90 737.66 €/avoided death

2) End point « gainable » years of life:

→ ΔC/ΔE = 7 259.10 / 1.11 = 6 539.61 €/av

Incremental Cost-Effectiveness Ratio Depending on Individual Situations

Xigris Price 51 697 €

N Sup	C	DC	E	DE	DC/DE
0	7 241,48		7,0697		
	14 920,95	7 679,47	7,1970	0,1273	60 335,25
1	18 514,78		6,4454		
	26 135,85	7 621,07	6,6648	0,2194	34 735,96
2	32 433,99		3,7105		
	39 861,91	7 427,92	4,1982	0,4877	15 229,57
3	41 742,22		1,7034		
	50 024,62	8 282,40	2,5313	0,8279	10 004,23

Distribution of Individual Situations

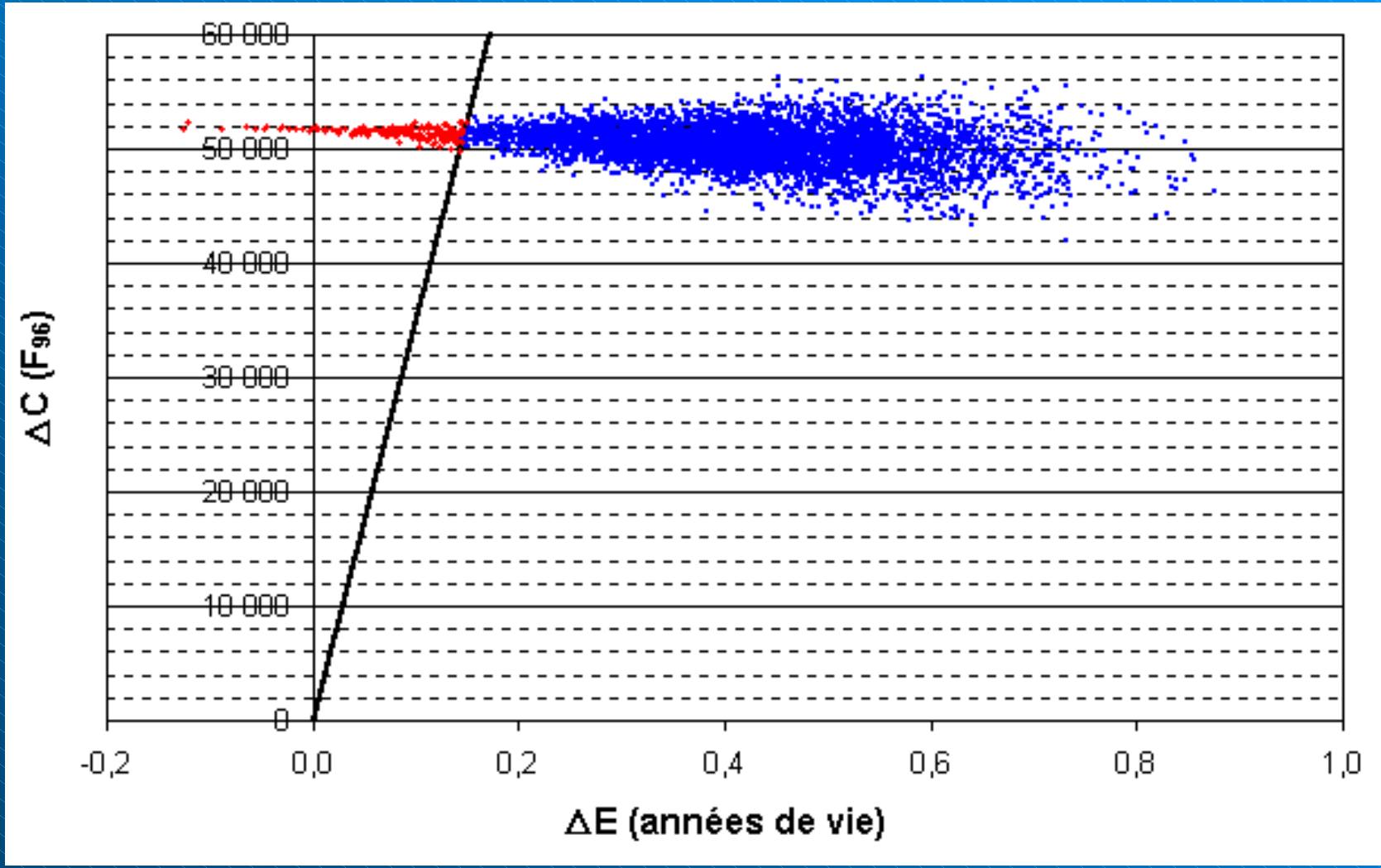
N Sup	CUB Réa	Model
0	11,47%	10,67%
1	30,82%	30,54%
2	42,06%	42,71%
3	15,65%	16,09%

Incremental Cost-Effectiveness Ratio
All Situations Combined

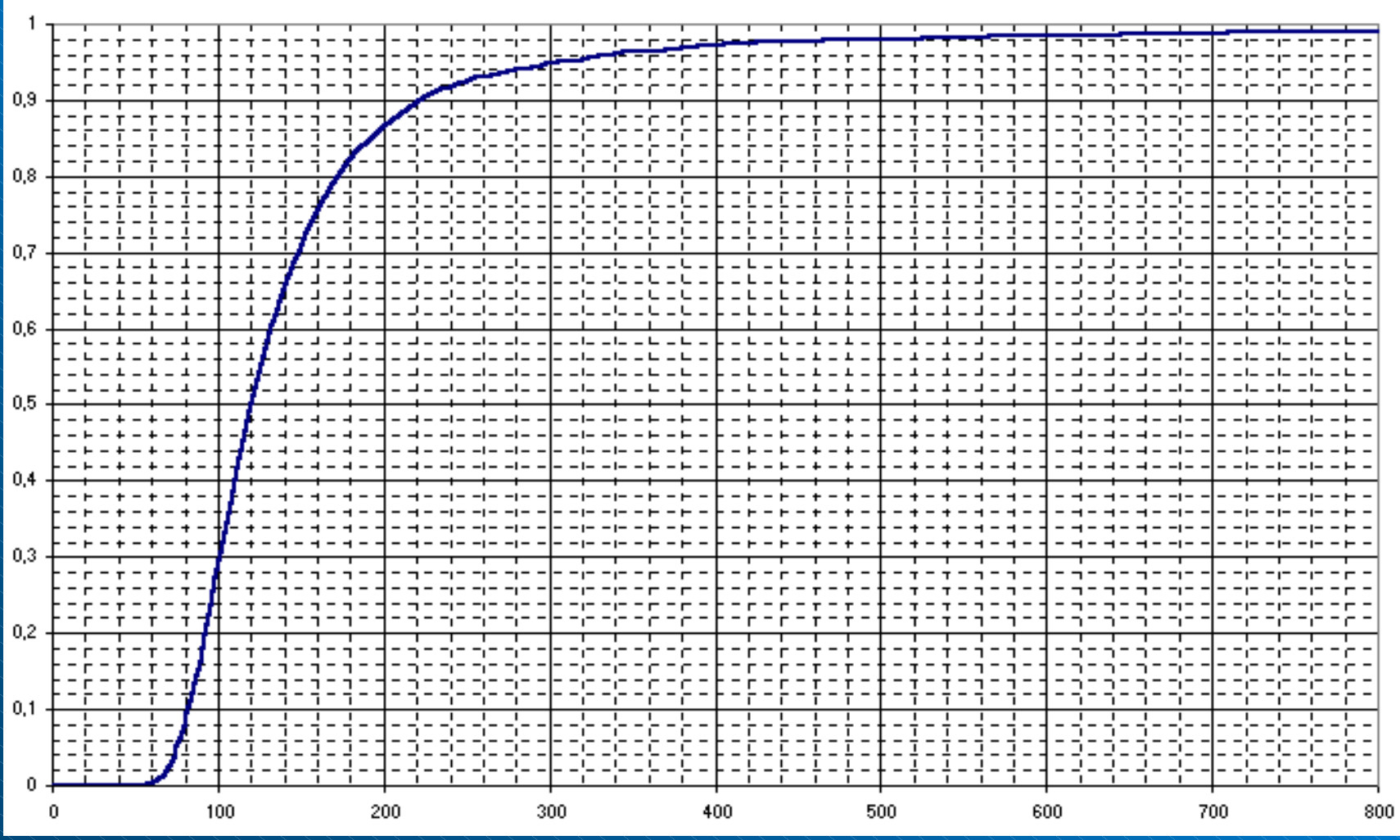
Strategy	**C** **(Euros €96)**	D**C**	**E** **(ans)**	D**E**	D**C**/D**E**
Usual Care	26 907.40		4.6042		
Xigris	34 586.41	7 679.10	5.0200	0.4158	18 467.98

Probabalist Sensitivity Analysis

Cost-Effectiveness Quadrant



Treatment Acceptability Curve, All Situations Combined, Depending on Will to Pay



Performance Scenarios

(Effectiveness: Median hypothesis)

Interventions	Cost tt be paid (K)	Probability of accepting Xigris
Beta-blocker treatment for survivors of myocardial infarction	971.86	0.00
Mammography every 3 years for women aged 50 to 65 years old	3 097.90	0.00
Intensive care for multiple injury victims	29 727.56	0.86
Renal dialysis for chronic renal failure in men aged 45-54 years old	53 738.28	0.96
Hormone replacement therapy for asymptomatic post-menopausal women between 55 and 70 years old	285 841.91	0.99

Conclusion

- Treatment with Xigris® is no more expensive than some interventions affecting patients of the same age.
- The value of this ratio is improved considerably by targeting patients with at least two organ system supports.
- Cost of care is not the most sensitive variable in defining the ratio.