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Pharmacoeconomy and Antifungal Prescriptions

Educational Workshop EFISG AFST-EUCAST
20th ECCMID 2010 in Vienna

April 10, 2010 | Pharmacoeconomics | **Oliver A. Cornely, MD, FIDSA**

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Outline

Pharmacoeconomics

- Definitions
- Challenges
- Types of analyses
  - QALYs
- Perspectives
- Sensitivity Analysis
- Examples
- Markov Modelling
- Monte Carlo Simulation

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Pharmacoeconomics – Wikipedia

- Compares the value of one pharmaceutical drug or drug therapy to another.
- A pharmacoeconomic study evaluates the cost (expressed in monetary terms) and effects (expressed in terms of monetary value, efficacy or enhanced quality of life) of a pharmaceutical product.
- One important consideration in a pharmacoeconomic evaluation is to decide the perspective from which the analysis should be conducted (such as institutional or societal).
- A complete compilation of cost-utility analyses in the peer reviewed medical literature is available at
  - "The CEA Registry"
  - http://www.tufts-nemc.org/CEARegistry

Wikipedia *(accessed 2010-03-21).*

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Challenges of Pharmacoeconomics

1. The wide variety of IFIs and affected populations make it difficult to apply the results of one study to all populations;

2. Small patient populations, often from a single medical facility, limit the power and ability to generalize study results;

3. Variability in geographical, environmental, patient and therapeutic factors that result in regional/hospital differences in IFI incidence;

4. Changing patterns in standards of care and development of newer therapies make it difficult to predict future trends based on historical data;

Johnson MD et al. *Expert Opin. Pharmacother. (2005) 6(15): 2617-2632.*

Challenges of Pharmacoeconomics

5. Changing treatment patterns influence how and where patients are treated (e.g., in-patient versus out-patient);

6. Separating costs of IFI and antifungal drug toxicities from costs associated with comorbidity (e.g., diabetes, cancer, sepsis) is difficult;

7. Newer, more effective therapies may be associated with a longer survival time and, therefore, longer, more expensive courses of treatment.

8. If market acquisition costs of antifungals are incorporated, the result is highly country specific.

Johnson MD et al. *Expert Opin. Pharmacother. (2005) 6(15): 2617-2632.*

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Types of Economic Analyses

The most common include

1. cost-minimization,
2. cost-benefit,
3. cost-effectiveness,
4. cost-utility, and
5. quality of life.

The differences between these methods include differences in how outcomes are valued.

Johnson MD et al. *Expert Opin. Pharmacother. (2005) 6(15): 2617-2632.*

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Cost-Minimization Analysis

- Is the simplest of the pharmacoeconomics tools
- Comparing two drugs of equal efficacy and equal tolerability
- No denominator necessary, e.g. no "cost/cure" or "cost/year of life gained“
- Measure all costs inherent to the delivery of the therapeutic intervention

Wikipedia *(accessed 2010-03-21)*.

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Cost-Benefit Analysis

- A technique designed to determine the feasibility of a project or plan by quantifying its cost and benefits.
- Monetary value spent to avoid certain health hazards, OR
- Monetary value spent to achieve certain health effects.

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Cost-Effectiveness Analysis (CEA)

- Compares the relative costs and outcomes (effects) of two or more courses of action.
- Used where it may be inappropriate to monetize health effect.
- Typically the CEA is expressed in terms of a ratio where the denominator is a gain in health from a measure (years of life, premature births averted, sight-years gained)
- The numerator is the cost associated with the health gain.
- The most commonly used outcome measure is quality-adjusted life years (QALY).

Wikipedia *(accessed 2010-03-21).*

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CEA in Pharmacoeconomics

- Ratio of the cost of the intervention to a relevant measure of its effect.
- Cost refers to the resource expended for the intervention, usually measured in monetary terms.
- The measure of effects depends on the intervention being considered. Examples include the number of people cured of a disease, the mm Hg reduction in diastolic blood pressure and the number of symptom-free days experienced by a patient.
- The selection of the appropriate effect measure should be based on clinical judgement in the context of the intervention being considered.
- A special case of CEA is cost-utility analysis.

Wikipedia *(accessed 2010-03-21)*.

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Cost-Utility Analysis

- CEA with effects measured in terms of
  - years of full health lived
  - quality-adjusted life years (QALY).
- Cost-effectiveness is typically expressed as an incremental cost-effectiveness ratio (ICER), the ratio of change in costs to the change in effects.
- A 1995 study of the cost-effectiveness of over 500 life-saving medical interventions found that the median cost per intervention was $42,000 per life-year saved.
- A 2006 systematic review found that industry-funded studies reported lower costs, as did studies with lower methodological quality and those from outside the U.S. and Europe.

Wikipedia *(accessed 2010-03-21)*.

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Quality-Adjusted Life Year (QALY)

- A measure of disease burden, including both the quality and the quantity of life lived.
- Used in assessing the value for money of a medical intervention.
- The QALY is based on the number of years of life that would be added by the intervention. Each year in perfect health is assigned the value of 1.0 down to a value of 0.0 for death.
- If the extra years would not be lived in full health, for example if the patient would lose a limb, or be blind or have to use a wheelchair, then the extra life-years are given a value between 0 and 1 to account for this.

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QALY – Challenges to the Concept

- Perfect health is hard, if not impossible, to define
- Some argue that there are health states worse than death
- Determining the level of health depends on measures that some argue place disproportionate importance on physical pain or disability over mental health.
- The effects of a patient's health on the quality of life of others (e.g. caregivers or family) do not figure into these calculations.

Wikipedia *(accessed 2010-03-21)*.

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Common Paradigms in PE analyses

Type of Analysis	Description	Outcome Measure, e.g.	Limitations
Cost-minimisation analysis	Requires equal alternatives	€, total drug therapy Costs	Requires therapeutic equality
Cost-benefit analysis	Costs and benefits of alternatives	€, benefit : cost ratio (€ saved in dialysis costs for € spent on L-AmB instead of cAmB)	Difficult to convert all inputs into monetary costs
Cost-effectiveness analysis	Outcomes measured in uniform non-monetary units and expressed as cost per unit of success/effect	€, natural units (e.g., mmHg of blood pressure) or total costs per episode of therapy (i.e., costs per IA)	Cost-effective is not necessarily less expensive
Cost-utility analysis	Includes measures of patient satisfaction or QoL, as well as monetary costs	€, costs per quality-adjusted life year	No standard criteria for measuring utilities
Quality-of-life analysis	Measure of health of an individual	Quality-of-life scale	Need for more standardised tools

Johnson MD et al. *Expert Opin. Pharmacother. (2005) 6(15): 2617-2632.*

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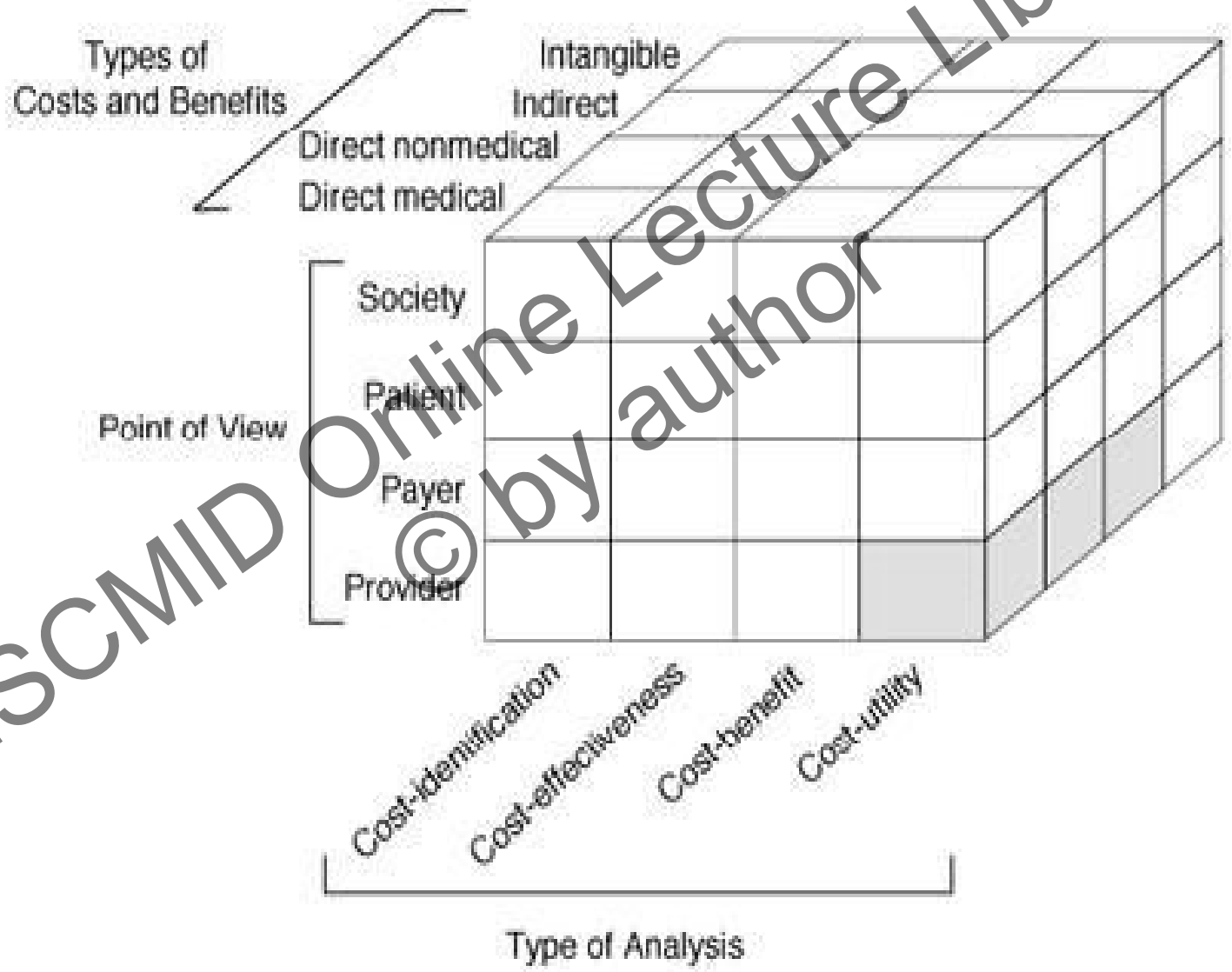
Common paradigms in PE analyses



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Perspectives

- Pharmacoeconomic analyses can be performed from any number of perspectives, including those of the
  - Patient
  - Payer
  - Institution
  - Department
  - Hospital
  - Society

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Sensitivity Analysis

Variations in the values of key variables and assumptions, related to deterministic and probabilistic data analysed to assess the robustness of the study conclusion.

- can reveal when the study results might be sensitive to a particular study parameter:

✓if a small change in one input causes a large change in the study findings.

Johnson MD et al. *Expert Opin. Pharmacother. (2005) 6(15): 2617-2632.*
Al-Badriyeh D et al. *J Antimicrob Chemother* 2010 Mar 17. [Epub ahead of print].

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Invasive Aspergillosis

Herbrecht R et al. NEJM 2002	Wenzel R et al. JAC 2005	Lewis JS et al. Pharmacother 2005	Jansen JP et al. Value in Health 2006
Methods, Type of Analysis	• Incremental cost-effectiveness analysis • Compared overall costs for a total of 12 weeks		• Incremental cost-effectiveness analysis • … in Germany. • Lifetime Markov model, focusing on the long-term survival of patients treated for invasive aspergillosis. • Long-term survival extrapolated from survival after 12 weeks • Medical resource consumption and treatment pathways from the study and an expert committee. • € per life-weeks gained.

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Invasive Aspergillosis

Herbrecht R et al. NEJM 2002	Wenzel R et al. JAC 2005	Lewis JS et al. Pharmacother 2005	Jansen JP et al. Value in Health 2006
Methods, Perspective, Costs Included	• All direct costs associated with the treatment of invasive aspergillosis • Both in-patient and out-patient	• Drug-acquisition costs	• The evaluation was performed from a limited societal perspective (both in-patient and out-patient costs) and hospital perspective (only in-patient costs).
Methods, Perspective, Costs Excluded		• Costs of hospitalisation, management of adverse events or overall costs of managing the invasive aspergillosis episode.	

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Invasive Aspergillosis

Herbrecht R et al. NEJM 2002	Wenzel R et al. JAC 2005	Lewis JS et al. Pharmacother 2005	Jansen JP et al. Value in Health 2006
Results, Costs		• 12 weeks of therapy with voriconazole associated with lower total drug treatment costs than cAmB followed by OLAT ($826,005 versus $783,184)	• Hospital costs were approximately 90% of the mean total costs.
Results, Costs per patient	• Costs per patient lower for voriconazole than cAmB/OLAT ($30,663 versus $34,144.		• With voriconazole, the mean total costs per patient were €30,026 (95% CI €23,118– 37,947) compared with €26,669 for cAmB B (95% CI €21,259–34,263)
Results, Cost per life-week gained			• The corresponding incremental cost-effectiveness ratio was €62 per life-week gained

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Invasive Aspergillosis

Herbrecht R et al. NEJM 2002	Wenzel R et al. JAC 2005	Lewis JS et al. Pharmacother 2005	Jansen JP et al. Value in Health 2006
Results, Costs per treatment success	• Total costs per successfully-treated patient lower for voriconazole than cAmB/OLAT ($58,100 versus $108,124).	• The total cost per successful treatment outcome was $10,317 for subjects receiving voriconazole and $20,278 for those receiving cAmB/OLAT.	
Results, Hospital Costs			• Hospital costs are comparable for both treatments.
Results, Sensitivity Analyses	• Toxicities accounted for the majority of cAmB-associated costs. • Lack of response and other reasons accounted for most of the costs among subjects receiving voriconazole. • Voriconazole was cost-effective than cAmB/OLAT.		• In the treatment of invasive aspergillosis, voriconazole is cost-effective in comparison to amphotericin B.

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Invasive Aspergillosis

Herbrecht R et al. NEJM 2002	Wenzel R et al. JAC 2005	Lewis JS et al. Pharmacother 2005	Jansen JP et al. Value in Health 2006
Results, Currency	• 2002 US dollars		
Remarks		• In the randomised trial, subjects receiving voriconazole had increased rates of overall response to therapy and accordingly, reduced rates of mortality, which could actually result in increased treatment costs overall.	• Average survival of patients treated with voriconazole was 174.4 life-weeks (95% confidence interval [CI] 159.4–191.3), compared with 119.4 life-weeks (95% CI 106.4–132.3) for amphotericin B.

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Treatment Costs of Invasive Fungal Infections in AML/MDS

Purpose	To determine the institutional cost of treating IFI
Methods	• retrospective chart review • German hospitals • non-randomized parallel group design • remission induction therapy for AML or MDS • cases: proven/probable IFI (EORTC/ MSG 2002) • controls matched by: duration of febrile neutropenia, age, type of chemotherapy • direct medical cost from hospital provider's perspective

Rieger CT et al. *unpublished.*

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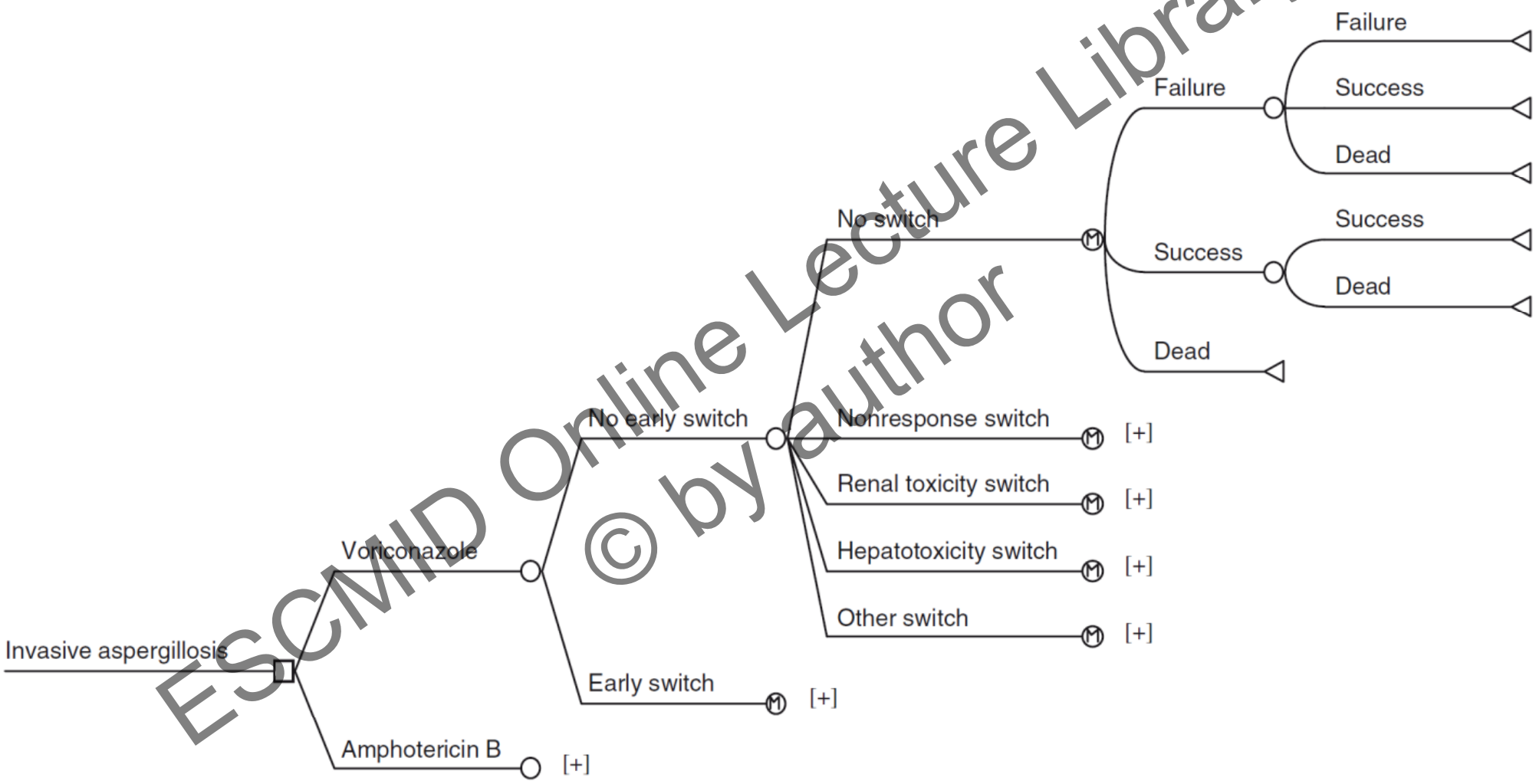
Treatment Costs of Invasive Fungal Infections in AML/MDS

Results	IFI	Controls
N= 108	N= 36	N= 72
Hospital stay	+12 days	
Received antifungals	100%	89%
Mean direct costs per patient	€51,517	€30,454
Incremental costs of €21,063 were dominated by cost for antifungal drugs (36%), hospital stay (32%) and blood products (23%).		

Rieger CT et al. *unpublished.*

Markov Model – Life-Time Analysis



Jansen JP et al. *Value in Health.* 2006.

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Antifungal Prophylaxis in AML

Retrospective chart review AML induction 2003-2009 Australia Decision analytical model Cost-benefit analysis Sensitivity analyses	Voriconazole N=56	Posaconazole N=38	P
Cost of success per patient	AU$ 67617,00	AU$ 44074,00	
Overall deaths	5.4%	0	n.s.
Discontinuation due to possible IFI	14.3%	5.3%	n.s.
Discontinuation due to intolerance of administration	30.4	28.9	n.s.
Discontinuation due to proven IFI	0	5.3%	n.s.

Al-Badriyeh D et al. *J Antimicrob Chemother* 2010 Mar 17. [Epub ahead of print].

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Ressource Costs

Item	Unit	Unit Cost [AU$]
Voriconazole	200 mg iv vial	190.84
	200 mg oral tablet	45.62
Posaconazole	105 mL oral susp	669.50
L-AmB	50 mg iv vial	295.00
Caspofungin	50 mg iv vial	700.00
Fluconazole	200 mg oral capsule	2.61
	200 mg iv vial	19.90
Vancomycin	500 mg iv vial	5.45
Terbinafine	250 mg oral tablet	1.19
Chest X-ray scan	one test	35.35
CT scan	one test	295.00
Ultrasound scan	one test	111.30
MRI scan	one test	358.40
Non-blood culture	one or more tests (one culture)	34.00
Blood culture	one test (one culture)	30.95
Bronchoscopy	one test	207.70
PCR	one test	30.00
Microb. cult & sens	one test	49.00
Histology	one test	72.00
CBC	one test	17.20
Renal function test	one test	146.30
Liver function test	one test	17.80
Hospitalization	Inpatient per day	610.00

Al-Badriyeh D et al. *J Antimicrob Chemother* 2010 Mar 17.

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Sensitivity Analyses – Variation Range

Variable	Base Case	Low	High
Voriconazole cost/vial, AU$	190.64	0.00	381.68
Voriconazole cost/tablet, AU$	45.62	0.00	91.24
Posaconazole cost/vial, AU$	669.50	0.00	1339.00
L-AmB cost/vials, AU$	295.00	0.00	590.00
Caspofungin cost/vial, AU$	700.00	0.00	1400.00
Fluconazole cost/tablet, AU$	2.61	0.00	5.20
Fluconazole cost/vial, AU$	19.90	0.00	39.80
Terbinafine cost/tablet, AU$	1.19	0.00	4.00
Hospitalization cost/day, AU$	610.00	0.00	1220
Duration of therapy in VCZ group, days	46	31	46
Duration of therapy in POS group, days	45	45	66
Dosage form of VCZ given as oral:iv	1:1	0:1	1:0
Counting for the costs of monitoring, pathology and imaging tests	Yes	No	Yes

Al-Badriyeh D et al. *J Antimicrob Chemother* 2010 Mar 17.

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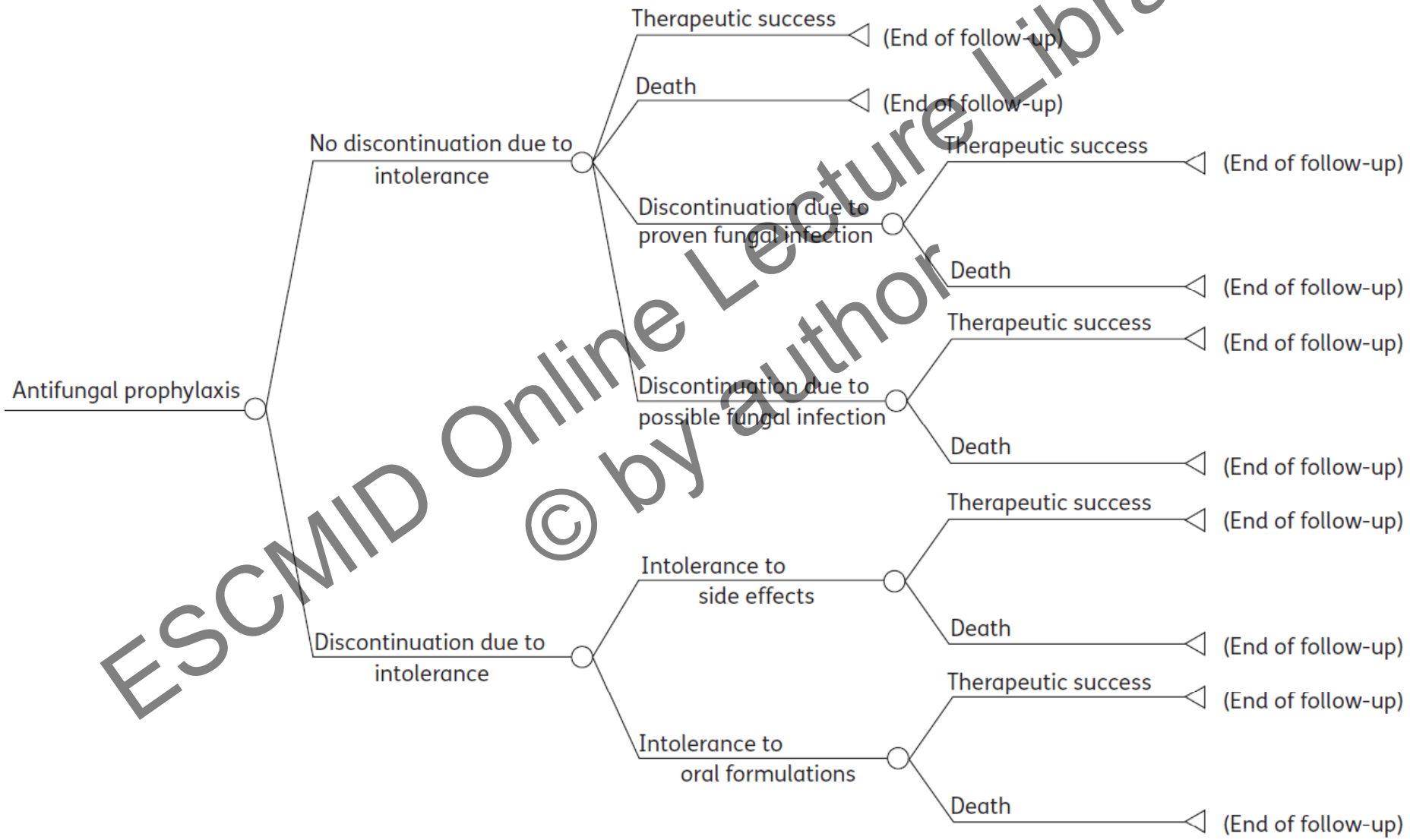
Antifungal Prophylaxis in AML Decision Analytical Model



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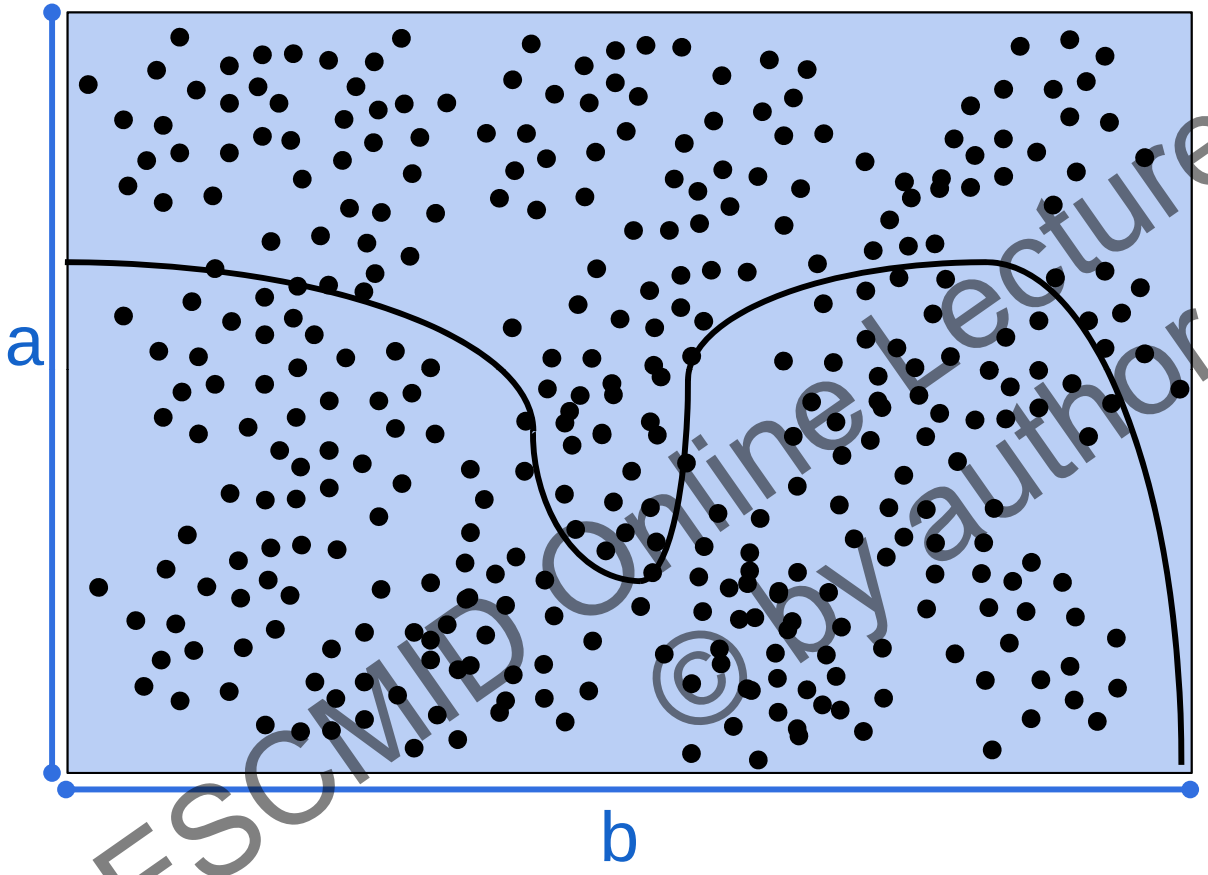
What is a Monte Carlo Approach?



- Imagine a graph
- a and b are known
- Determine the AUC
- ?
  - Print graph
  - Attach to wall
  - Load gun
  - Fire 1000 shots
  - Count the hits above and below the graph.
  - Questions?

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Points to Consider When Reading a Pharmacoeconomic Analysis

- How are outcomes valued?
  - Direct costs, e.g. diagnostic tests, drug acquisition costs
  - Indirect costs, e.g. loss of productivity or income (lost wages, family assistance, transportation costs).
  - Intangible costs, that cannot be directly associated with a monetary value, e.g. pain and suffering

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Points to Consider When Reading a Pharmacoeconomic Analysis

Are drug costs computed comparable to your setting?

- drug-acquisition contracts,
- local standards of care,
- local labor costs and,
- local demographics and
- rates of fungal infections.

Is the perspective clearly stated?

Has sensitivity analysis been performed?