Cost-effectiveness and managing invasive candidiasis in the ICU

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CENTRE OF RESEARCH EXCELLENCE
REDUCING HEALTHCARE ASSOCIATED INFECTIONS

Background

Candidiasis is a problematic fungal infection

Treatment Costs $13,000

4/10 cases will die

Difficult to diagnose

- slow turnaround time
- symptoms hard to distinguish from other forms of sepsis

Incidence density rose 3.5 times in 10 years to 2008

Background

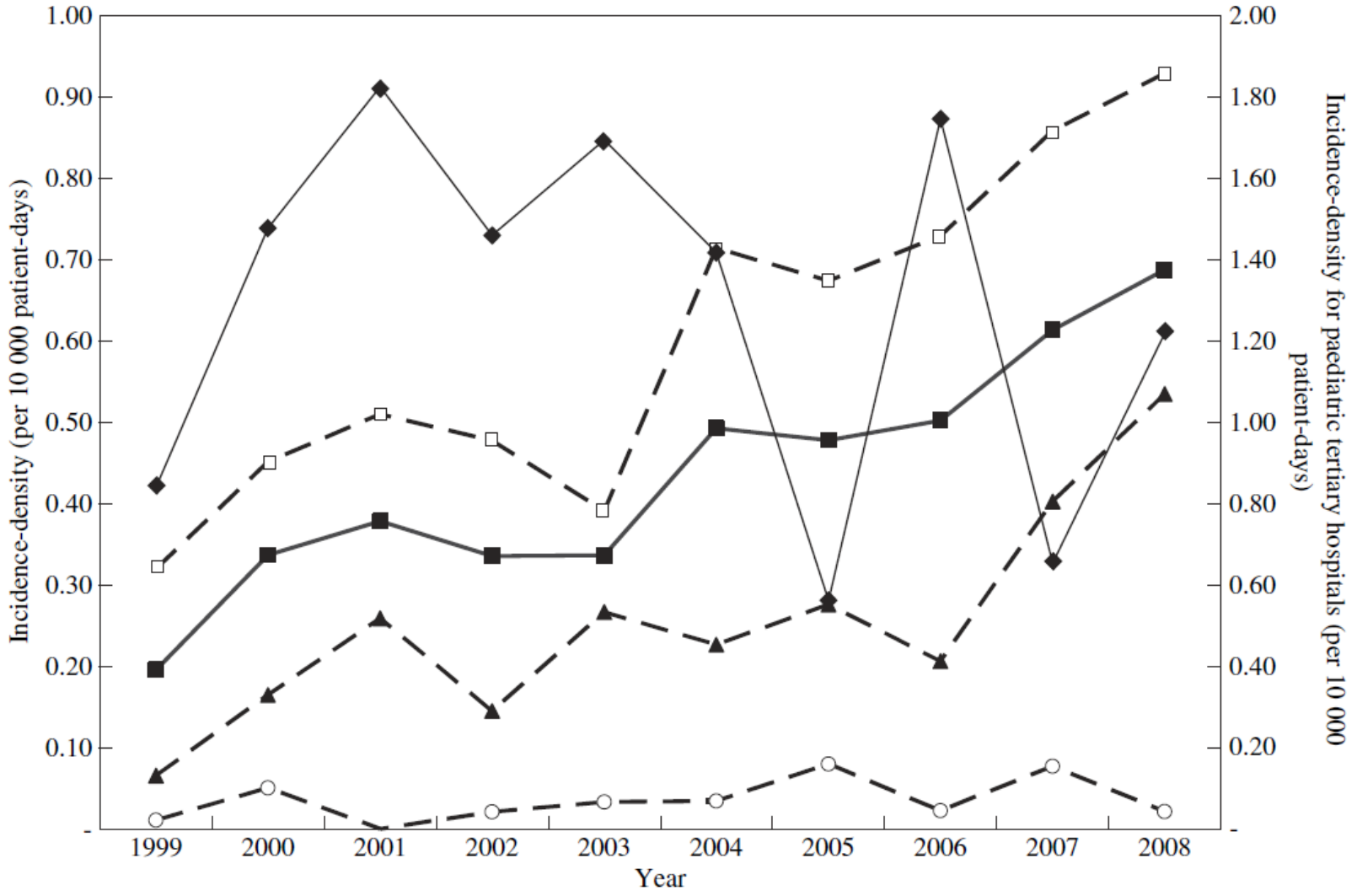


Figure 1. Secular trends in incidence-density of candidaemia, Queensland 1999–2008. ■, all hospitals; □, adult tertiary hospitals; ▲, secondary hospitals; ○, community hospitals; ◆, paediatric tertiary hospitals.

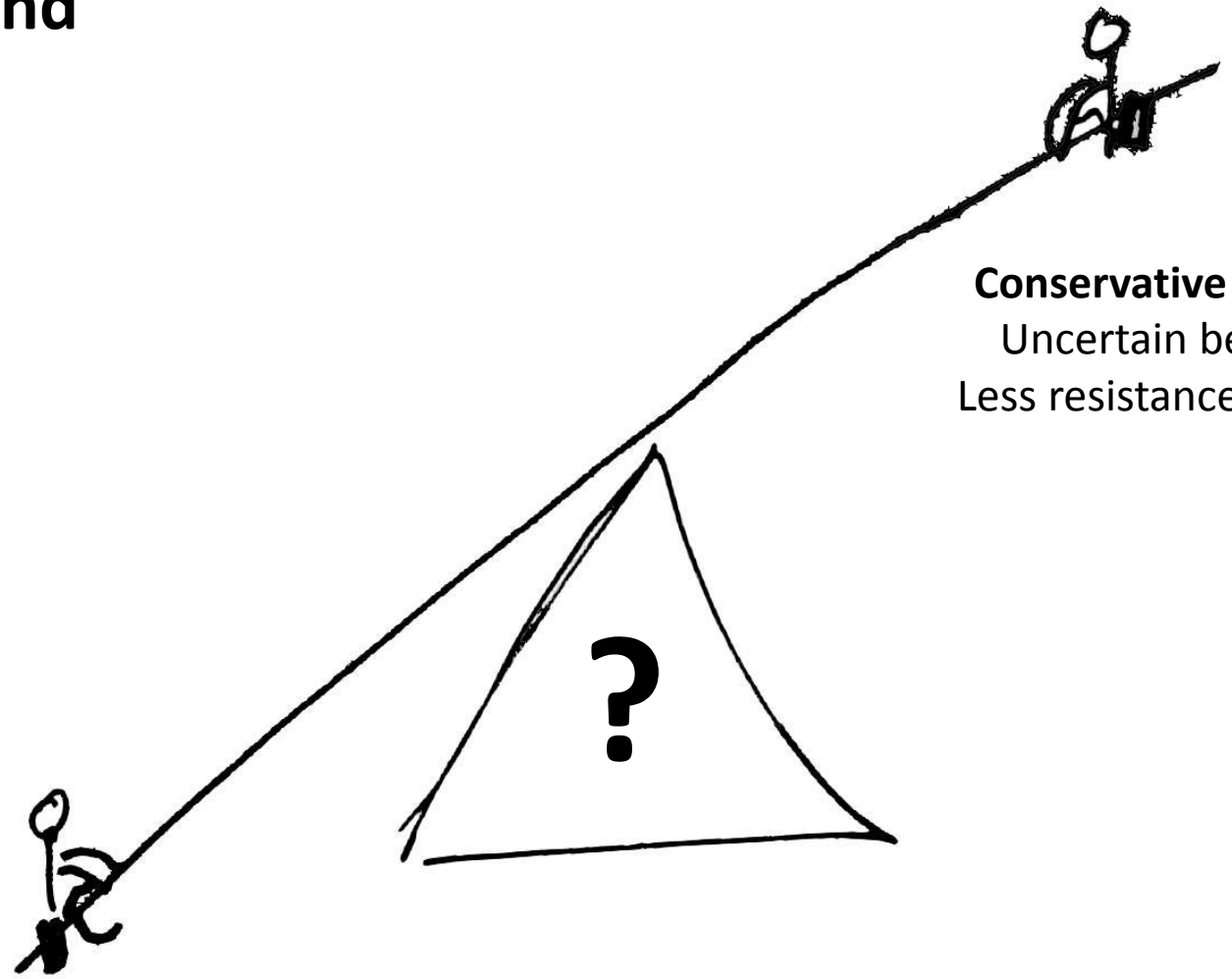
Background

Better outcomes arise from early initiation of anti-fungal therapy

- Fluconazole
- Caspofungin (for strains resistant to Fluconazole)

Problems with accurate diagnosis means prophylaxis might be attractive

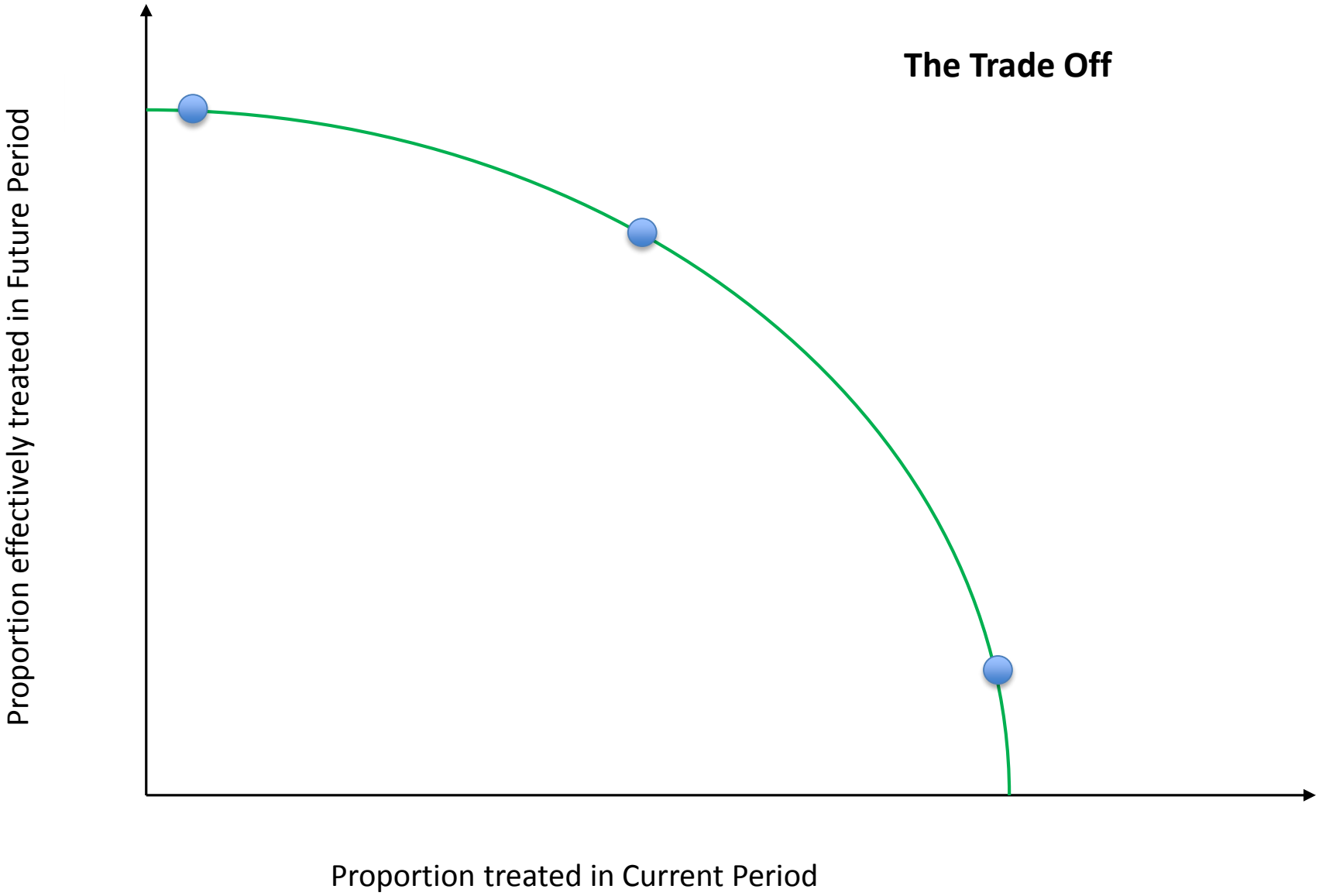
Background



Conservative use of drugs
Uncertain benefits now
Less resistance in the future

Prophylaxis
Certain benefits now
Unknown future resistance costs

Background


The Trade Off
Proportion effectively treated in Future Period
Proportion treated in Current Period

Background

Antifungal treatment options prior to diagnosis of IC

Empirical therapy	(based on clinical features)
Pre-emptive therapy	(risk factors/candida colonisation)
Prophylaxis	(all pts on admission to ICU)

Putting patients into high risk & low risk groups can aid with treatment choices

Classification rules exist…..

Background

Six Classification Rules for high risk vs. Current standard of care (Baseline, 0.)

0. **Baseline:** No patients are in the high-risk group. Only empiric therapy is given to any patient not diagnosed with invasive candidiasis. .
A. **Clinical rule 1:** either systemic antibiotic receipt on days 1-3 of ICU admission or central venous catheter on days 1-3, together with **two** additional risk factors described below. [25].
B. **Clinical rule 2:** either systemic antibiotic receipt on days 1-3 of ICU admission or central venous catheter on days 1-3, together with **one** other risk factor described below. [26]
C. **Candida score:** Candida score . > 2.5. Candida score is: surgery (1 point); total parenteral nutrition (1 point); multi-focal Candida colonisation (1 point); severe sepsis (2 points). [27]
D. **Colonisation index:** $\geq 50\%$ of sampled superficial body sites are positive for Candida. [28].
E. **Corrected Colonisation index:** $\geq 40\%$ of sampled superficial body sites are positive (with 3+ growth) for Candida.) [28].
1. **Universal:** All patients are in the high-risk group so all patients receive antifungal prophylaxis.

RISK FACTORS

TPN

Dialysis

Major surgery

Pancreatitis

Corticosteroids

Other immunosuppressive agent

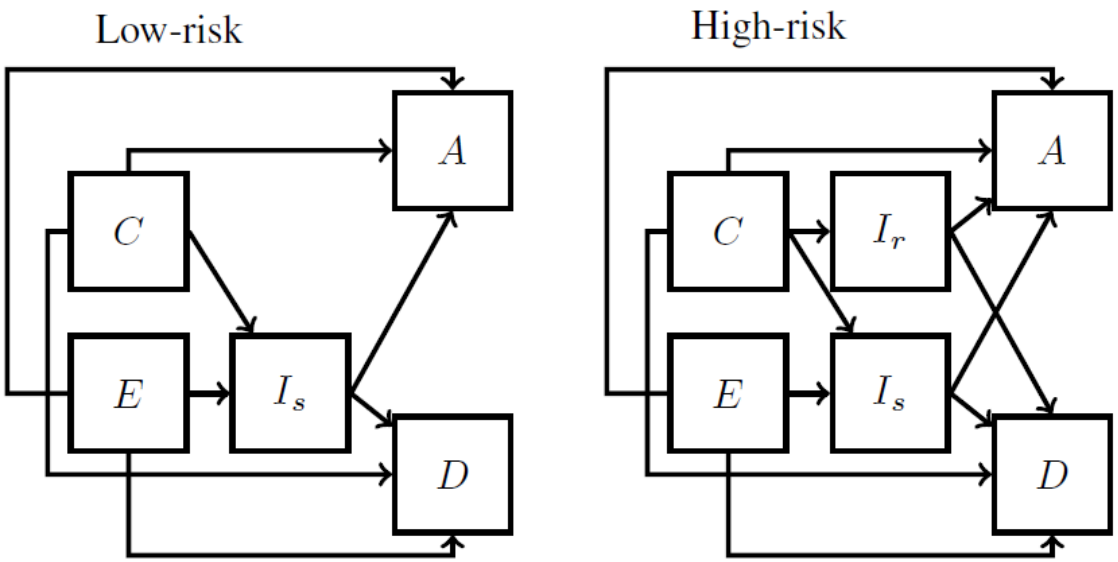
Aim

To evaluate the change to costs and health benefits of using different classification rules (A – E & 1) to identify high risk patients.

Where Fluconazole prophylaxis treatment given to all patients in a high risk group.

This is a cost-effectiveness analysis

Method



C = colonised

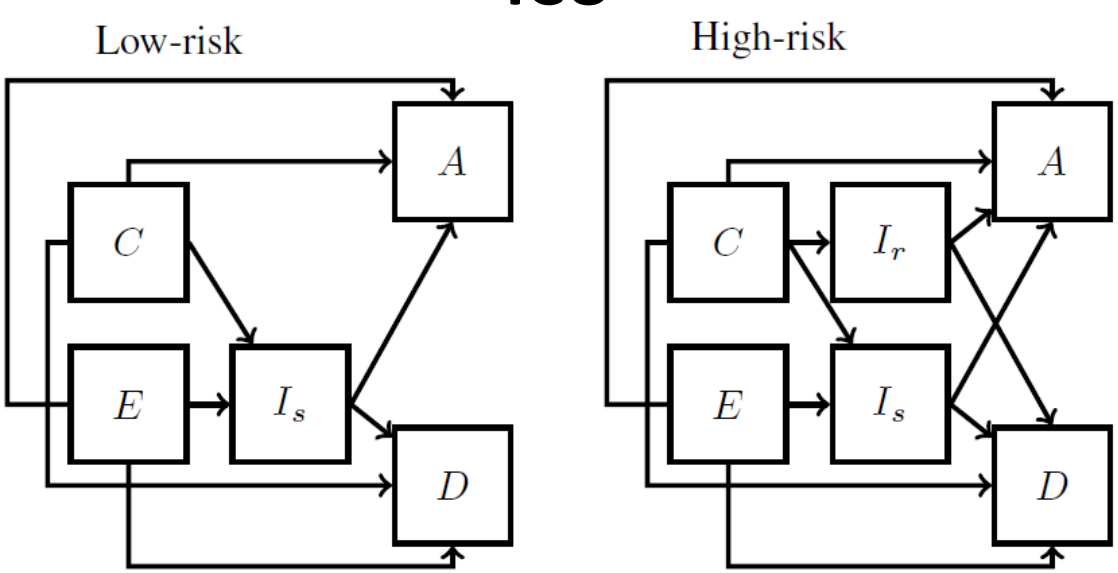
E = patients already receiving empirical Caspofungin treatment

I = Invasive Candidiasis (resistant and sensitive to Fluconazole)

A = discharged alive

D = died in ICU

Method



Simulate with a Bayesian method

- number of cases in ICU
- total costs
- deaths & years of life lost

Classification rules (A to E, 1) used to populate low risk & high risk

Prophylaxis antifungal treatment given to patients in the high risk group

Data & Parameters

n = 6,750 non-neutropenic patients, June 2007 to Jan 2012

PAH, RBWH, Westmead, St Vincent's Hospital, Concord Hospital, Nepean, RMH

Linked to 30,000 records on treatments with antibiotics and antifungal medicines

Assumed 10% of fluconazole patients developed resistance (Comert et al. Mycoses; 2006)

Swab data was also collected showing presence of Candidiasis on any of three sites (throat, perineum and urine)

Costing data synthesized from hospitals, PBS & expert opinion

Meta analysis used for treatment effectiveness & mortality relative risk

Data & Parameters

Eur J Clin Microbiol Infect Dis (2006) 25:549–561
DOI 10.1007/s10096-006-0182-3

REVIEW

Systematic review and meta-analysis of antifungal agents for preventing fungal infections in liver transplant recipients

E. G. Playford · A. C. Webster · T. C. Sorrell · J. C. Craig

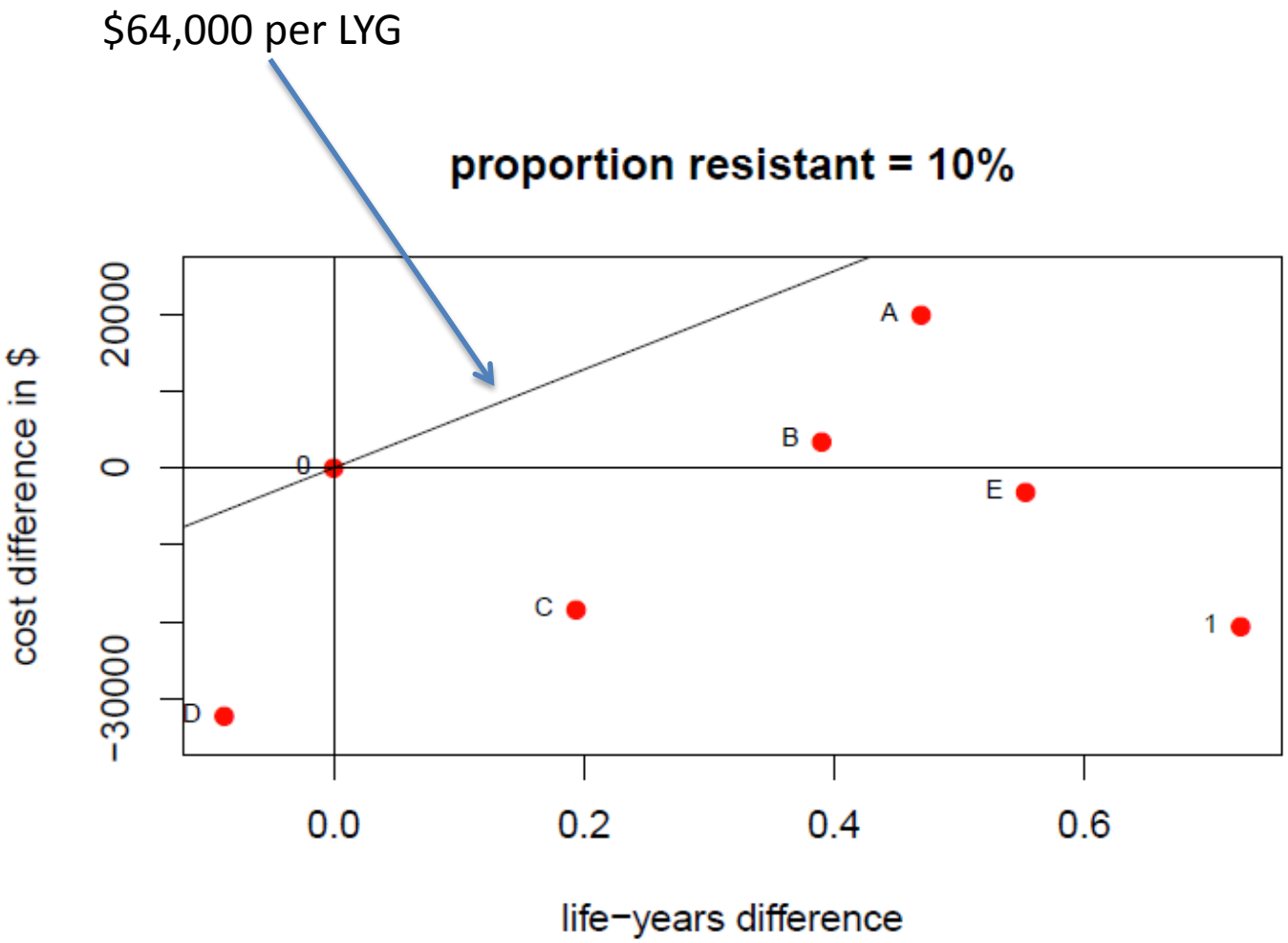
Results

110/6750 with IC	rate of 1.75%	
18/110 deaths	rate of 15.25%	IC cases
687/6750 deaths	rate of 10.2%	All patients

Relative risk of death with IC was 50% larger

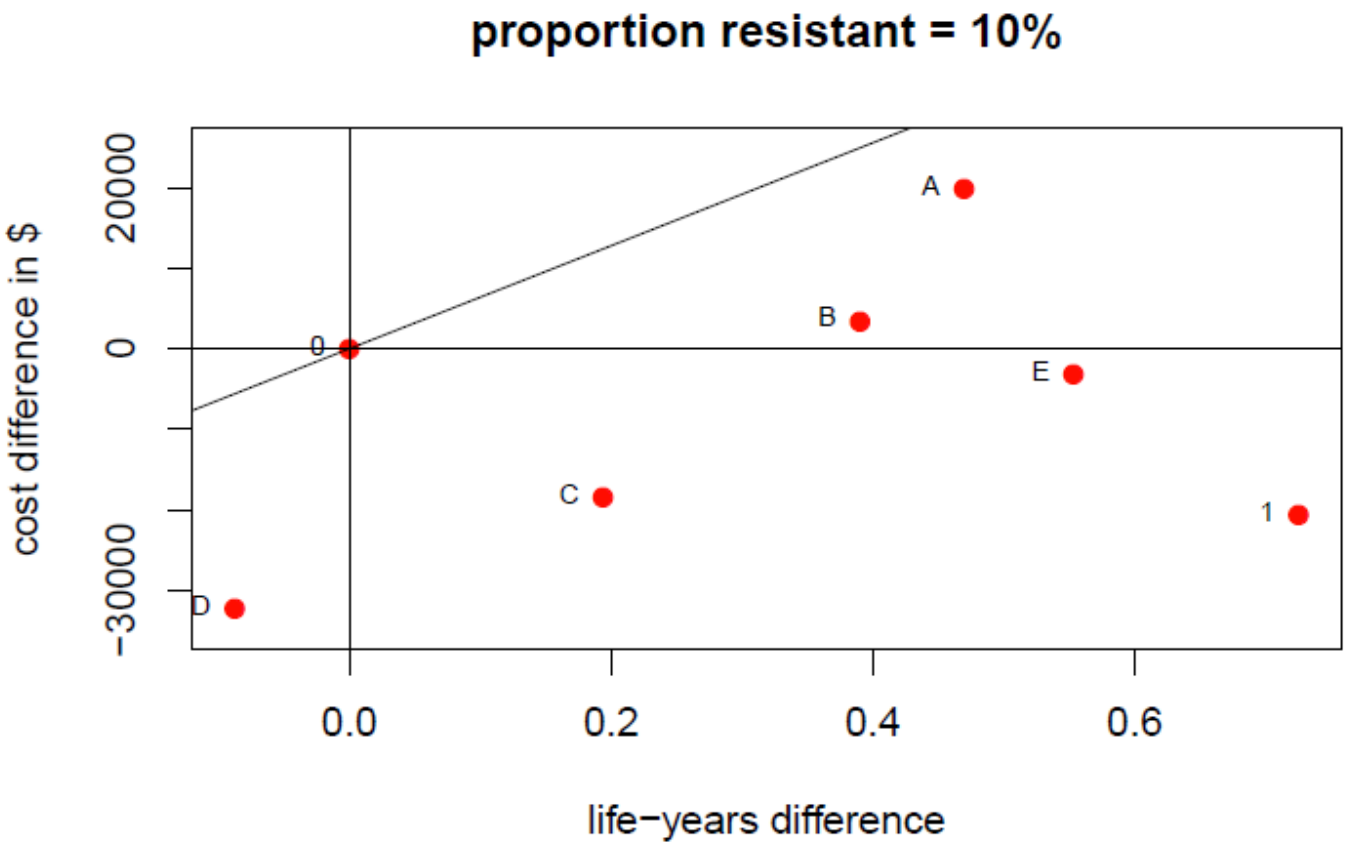
816/6750 received empiric therapy under baseline (0)

Results



Need to show uncertainty……

Results (as a linear measure)



Life years difference * Willingness to pay – cost difference = Net Monetary Benefits

Results (as a linear measure)

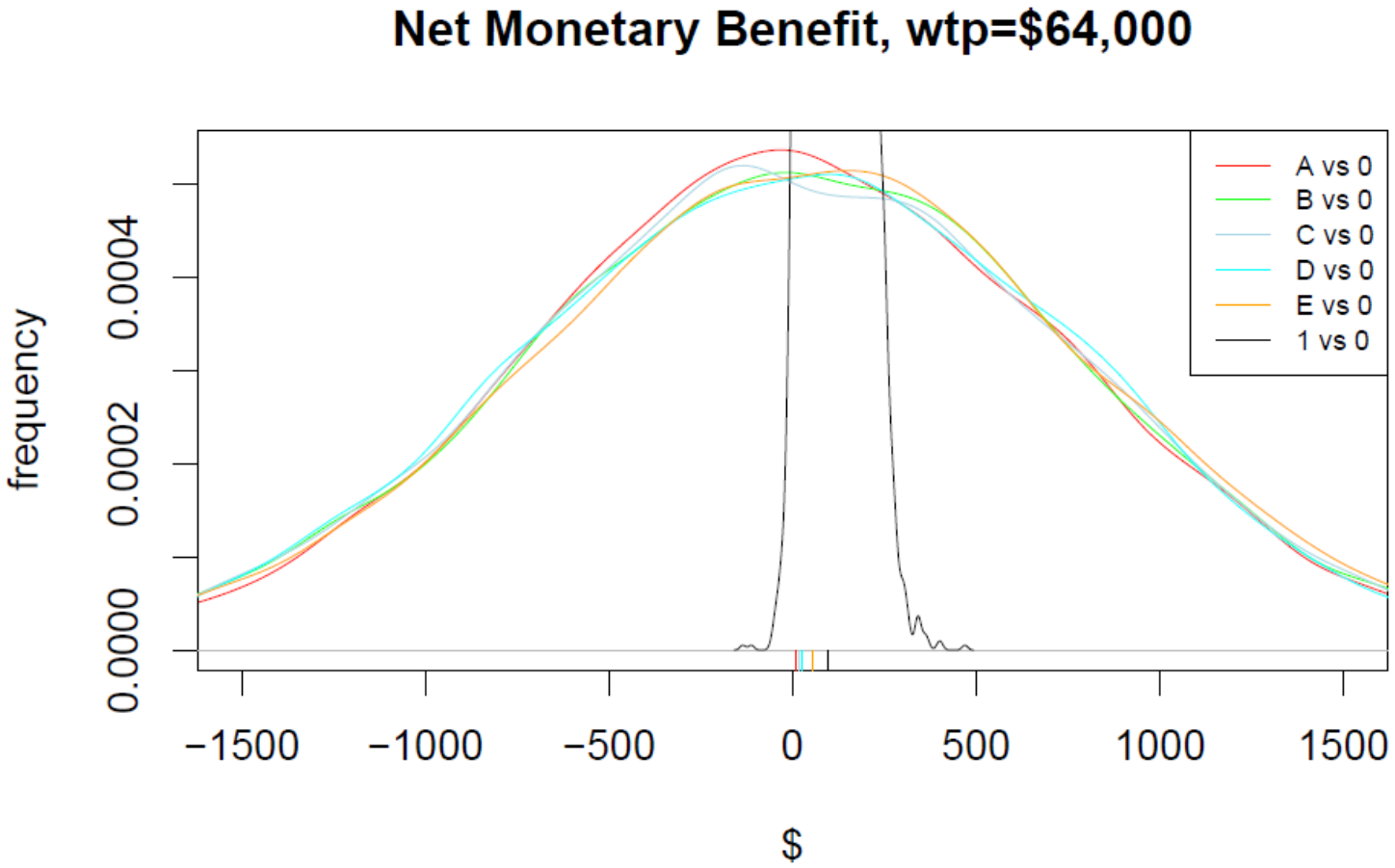
per 1,000 patients

	A vs 0	B vs 0	C vs 0	D vs 0	E vs 0	1 vs 0
cost difference ($1,000s)	19.91	3.54	-18.41	-32.28	-3.13	-20.57
life-years saved	0.47	0.39	0.19	-0.09	0.55	0.72
infections saved	2.57	2.60	2.68	0.16	2.45	7.12
deaths saved	0.32	0.23	0.22	-0.08	0.58	0.79
reduction in total ICU-days	7.18	10.42	10.91	8.94	6.68	23.01
reduction in infected ICU-days	63.50	61.76	39.47	5.11	35.08	103.34
NMB/patient $	10.14	21.45	30.81	26.68	38.54	66.97

Life years * Willingness to pay – cost difference = Net Monetary Benefits/pt.

0.47 $64,000 19,910 $10.14

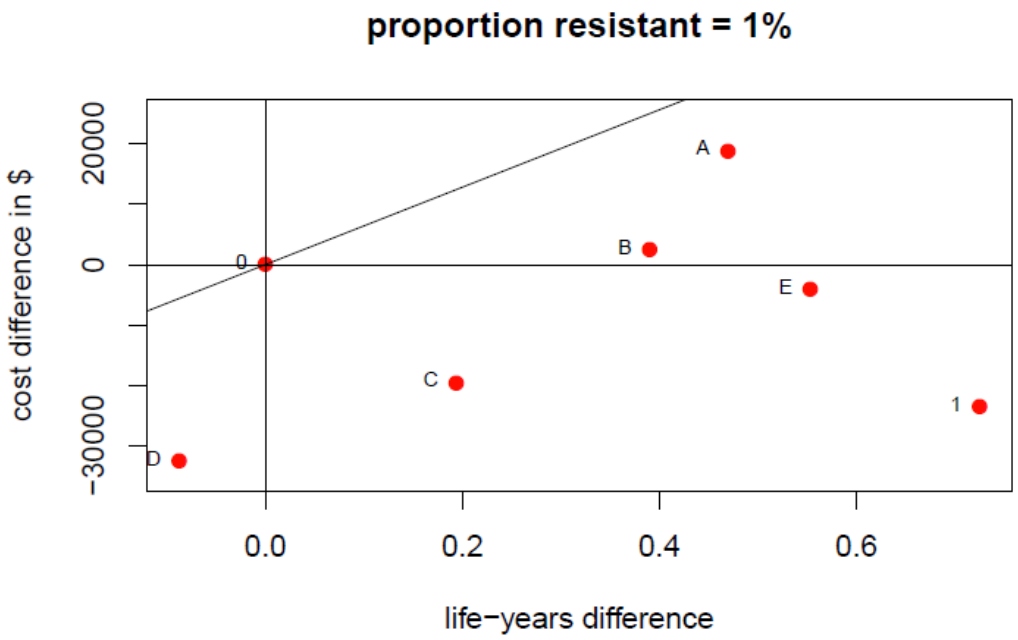
Results (with uncertainty)

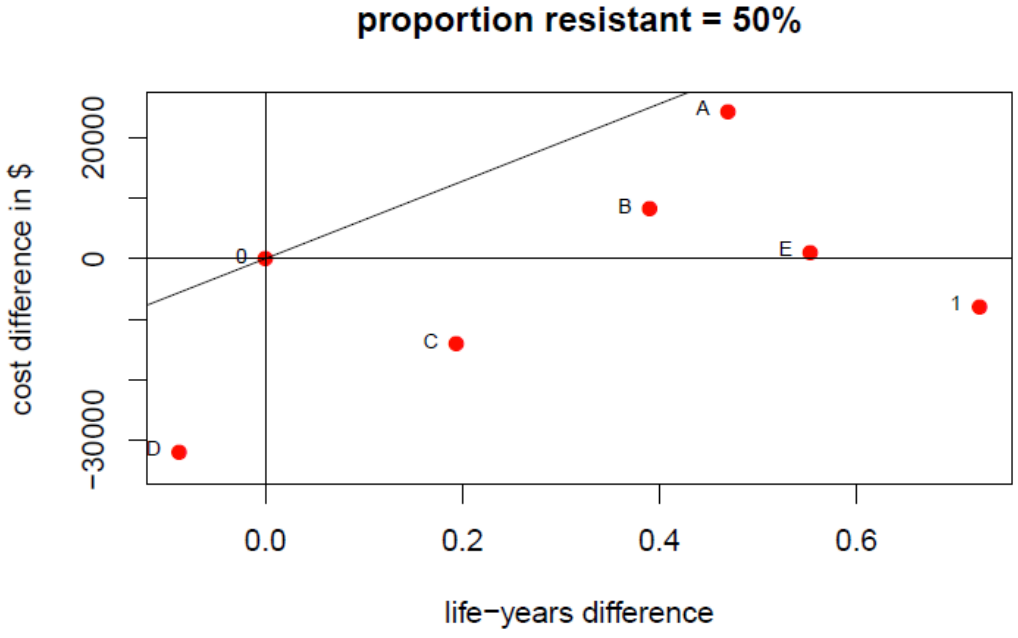


Results (scenarios)

Assumes that 1% & 50% of high risk patients receiving Fluconazole prophylaxis develop resistance.

Then treated by Caspofungin





Conclusions

Making every ICU admission high risk > universal Fluconazole prophylaxis (0) dominates all other approaches.

For 1000 admissions:

Saves 23 ICU-days, at $3,500 each

compensates the relatively low drug costs

Prevents most infections (7.12) and saves most life years (0.72)

This conclusion was robust to assumptions about resistance to Fluconazole emerging

A decision to treat all patients as high risk and so give all patients Fluconazole prophylaxis is cost-effective.