# Staffing And Cost-effectiveness Of Antimicrobial Stewardship Programmes

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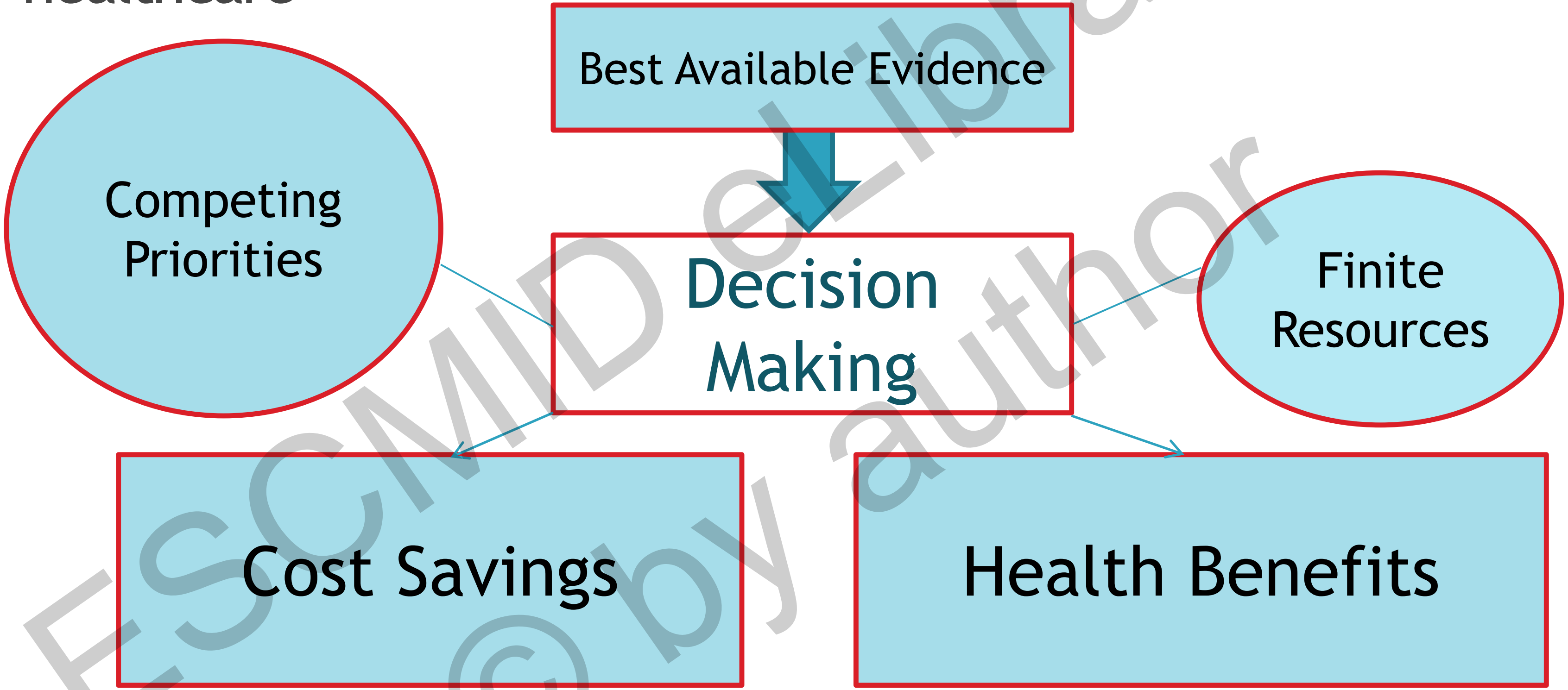
(I have no conflicts of interest to declare)

# Cost-effectiveness analysis as a tool for decision making in healthcare



# Overview

North Stradbroke Island, Queensland, Australia

- Cost Effectiveness Analysis (CEA)
- Current evidence on CEA of AMS interventions
- Importance of Staffing and AMS
- CEA of AMS intervention in Brisbane, Australia
- Conclusions & Recommendations

# Cost-effectiveness analysis (CEA)

Compares the relative **costs** and outcomes of different courses of action

Example outcomes: Life years gained (LYG), cases detected

**Cost utility analysis (CUA)** uses QALYs as an outcome measure

- QALY the quality and the quantity of life associated with a disease process
- One QALY equals one year in perfect health
- Allows for the comparison of different interventions with one measure

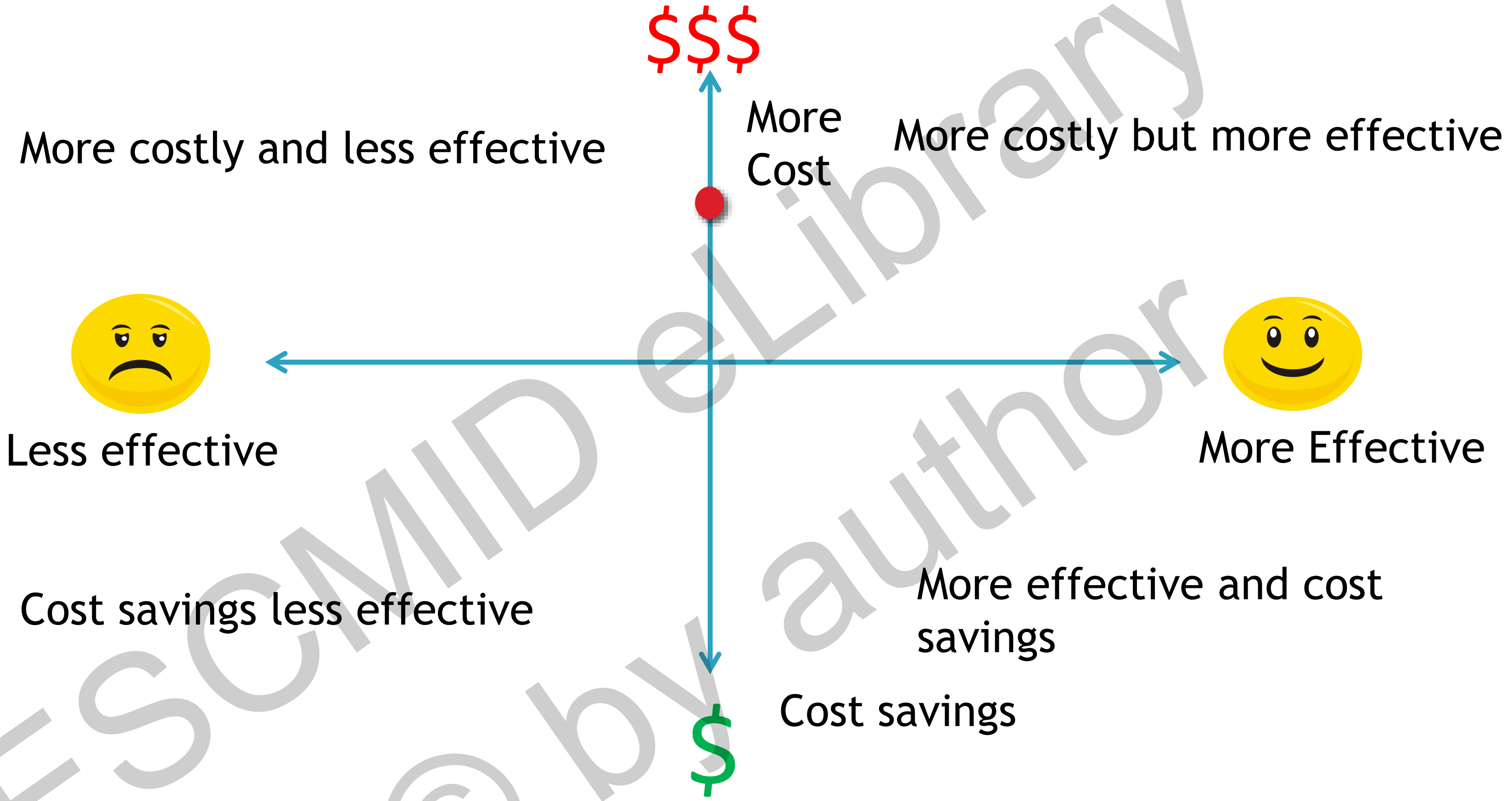
# Cost-effectiveness Analysis- CUA

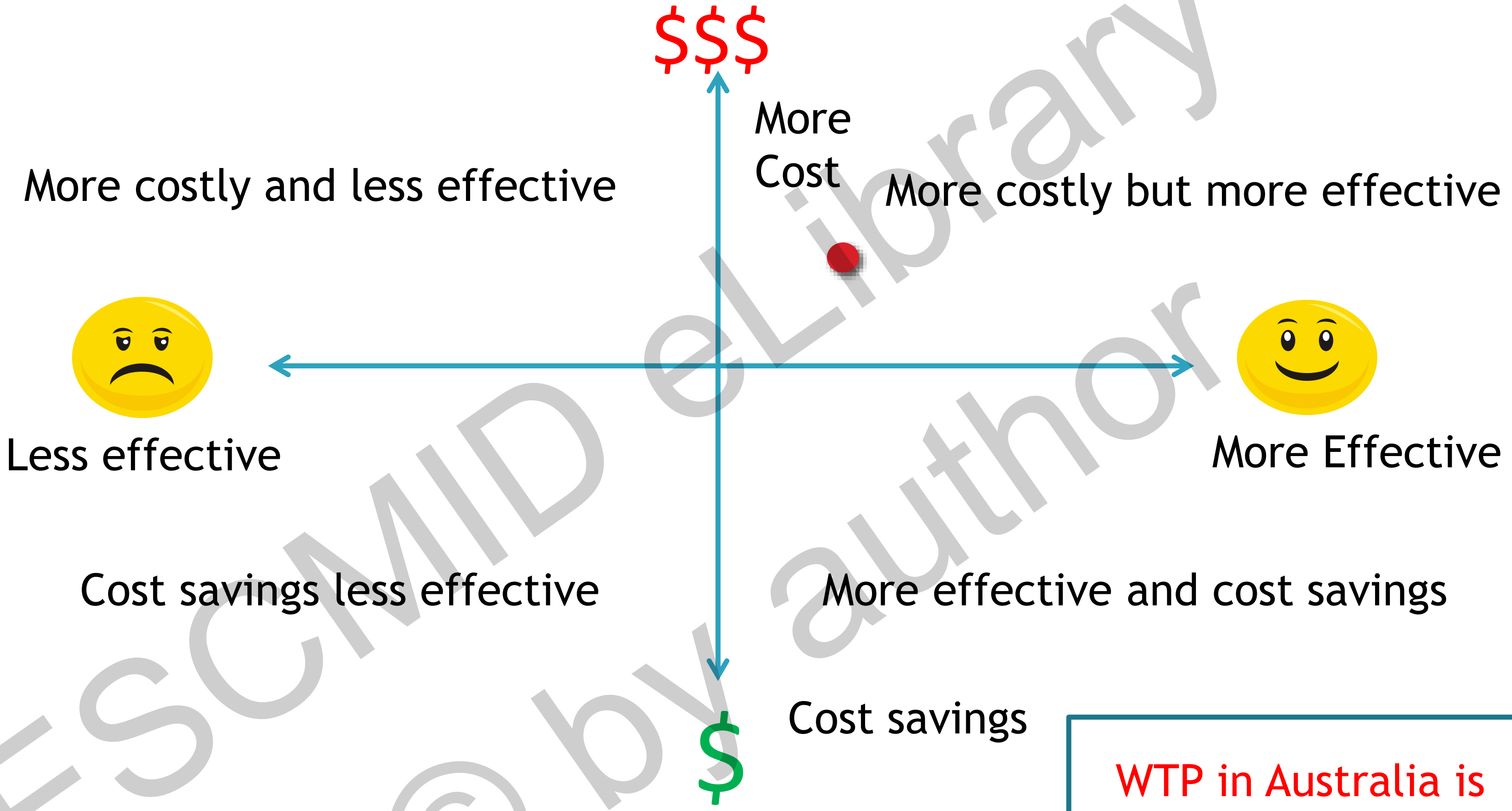
- Change in costs and change in health benefits due to an intervention

- Incremental Cost Effectiveness Ratio(ICER)

$$= \frac{\Delta \text{ cost}}{\Delta \text{ effectiveness}}$$

$$= \text{cost per QALY}$$


$$$
More Cost
More costly and less effective
More costly but more effective
Less effective
More Effective
Cost savings less effective
More effective and cost savings
$
Cost savings




WTP in Australia is less than $64,000

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Review

**The need for cost-effectiveness analyses of antimicrobial stewardship programmes: A structured review**

Sonali Coulter[a,*], Katharina Merollini[a], Jason A. Roberts[b], Nicholas Graves[a], Kate Halton[a]

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[b] Faculty of Medicine and Biomedical Sciences, University of Queensland, Royal Brisbane and Women's Hospital, Herston, Brisbane, QLD, 4029, Australia

- Review of literature up to June 2014
- 36 studies; OECD countries; Adult inpatients
- Majority reported cost savings due the reduction in antimicrobial utilisation and length of stay in hospital
- $22k-$4.3million per year
- Single study performed a CEA of an AMS program in the USA (Scheetz et al 2009) – AMS intervention at their hospital was found to be Cost-effective

# More recent review

J Pharm Pharm Sci (www.cspsCanada.org) 20, 397 - 406, 2017

**Economic Evaluations on Antimicrobial Stewardship Programme: A Systematic Review**

Nor Haizan Ibrahim[1], Khalidah Maruan[1], Hasryn Azzuar Mohd Khairy[1], Yet Hoi Hong[2], Ahmad Fauzi Dali[1], Chin Fen Neoh[1,3]

[1]Department of Pharmacy Practice, Faculty of Pharmacy, Universiti Teknologi MARA (UiTM), 42300 Bandar Puncak Alam, Selangor Darul Ehsan, Malaysia. [2]Department of Physiology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia. [3]Collaborative Drug Discovery Research (CDDR) Group, Pharmaceutical and Life Sciences Community of Research, UiTM, Selangor Darul Ehsan, Malaysia.

- 5 studies:
  - 1 Cost Utility Analysis (USA)
  - 1 Cost Benefit Analysis (Netherlands)
  - 3 Cost Effectiveness Analysis (Brazil, Spain, Netherlands)

| | Comparison | Outcome | Result |
|---|---|---|---|
| Sheetz et. al. (2009)<br>USA<br>**CUA** | AMS & CDSS vs standard care Patients with BSI<br>**Cost of AMS USD 150,000/annum** | 30 day mortality<br>LOS<br>Ab use | ICER<br>USD 2,367 per QALY |
| Dik et. al. (2015)<br>Netherlands<br>**CBA** | AMS to standard care (day 2 review) **Urology**<br>**Cost of HR €17,732** | LOS<br>Ab use | **€60,000 saved per 114 patients per annum** |
| Okumura et. al. (2016)<br>Brazil<br>**CEA** | Bundled approach vs traditional AMS<br>**Cost$93 vs $45 per patient** | 30 day mortality<br>LOS<br>Ab use | **ICER**<br>**USD 19,287.54 per averted death in 30 days** |
| Ruiz-Ramos et. al. (2017) Spain<br>**CEA** | AMS & CDSS vs standard care<br>**Critical care patients with BSI, CAP, VAP or UTI**<br>**Cost €107,569** | per avoided resistance | **ICER**<br>**9,788€ per LYG** |
| Van Daalen et. al. (2017)<br>Netherlands<br>**CEA** | ASP with checklist vs standard<br>**9 Dutch hospitals**<br>**Cost €11,048** | LOS<br>Ab use | ICERs<br>**€54.01 per extra patient**<br>**€51.43 per day reduction in LOS** |

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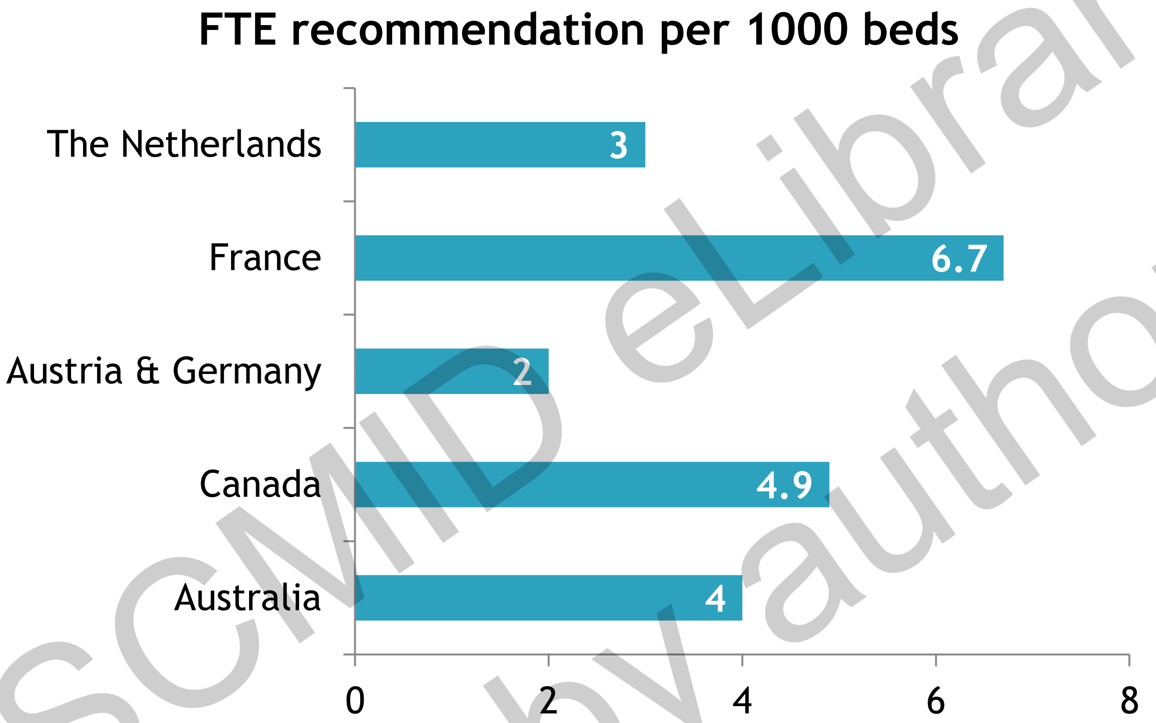
# Dedicated team in AMS

- Co-ordinated approach to AMS takes planning and resources
  - AMS committee, Education, AMS ward rounds
- Right balance of people
  - Lab, Pharmacy, ID physician, Clinical Microbiologist, IT personnel nurses
- AMS must be sustainable in the long term
  - Champions, funding
- Must be funded as part of patient safety




Adapted from estimates in Pulcini et al. (2018) Clin Microbiol Infect. doi: 10.1016/j.cmi.2018.01.009

# Staffing and AMS

- The number of FTE needed may depend on structure of staffing in each country.

- Each healthcare facility differs in their need: Metropolitan hospitals, LTCF, regional and remote hospitals and the community

- We need to be able to convince decision makers that the investment in HR is cost-effective and essential for patient safety

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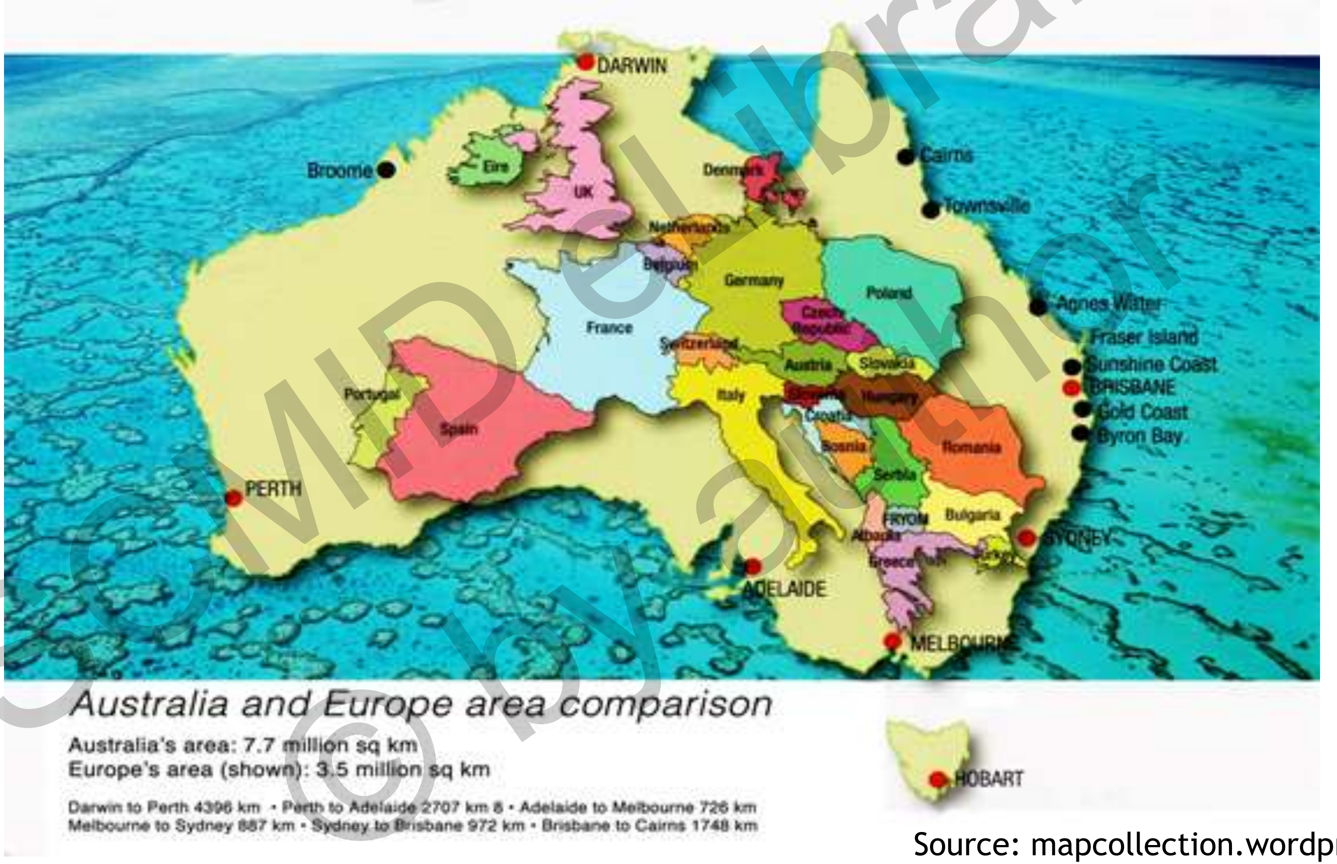
# Australian context




Source: mapcollection.wordpress.com

# Australia

- 8 states and territories

- 2011 AMS is mandatory in all Australian hospitals
- -part of hospital accreditation standards

- 2012 National surveillance program to monitor Antimicrobial Use and resistance in Australia (AURA)

- National guideline on antibiotic usage-
- Therapeutic guidelines
  - Established 1978 updated every 2 years
  - Great resource –but not mandatory

# Australian Setting

# AMS intervention at the Royal Brisbane and Women's Hospital

Setting:

RBWH 960 bed tertiary referral hospital


Population:

Adult inpatients in the non-ICU wards

Outcome measures for the evaluation:

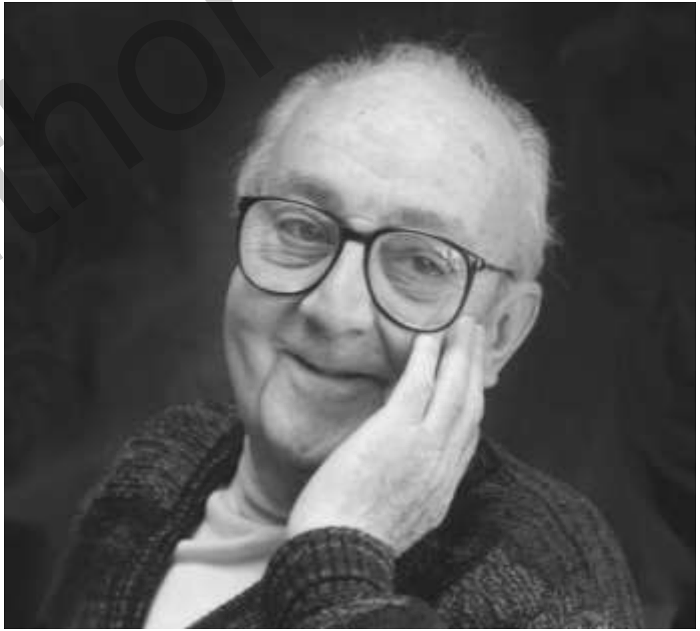
Costs associated with the intervention

Effectiveness of the intervention

# Model Development

*"All models are wrong but some are useful"*

George Box

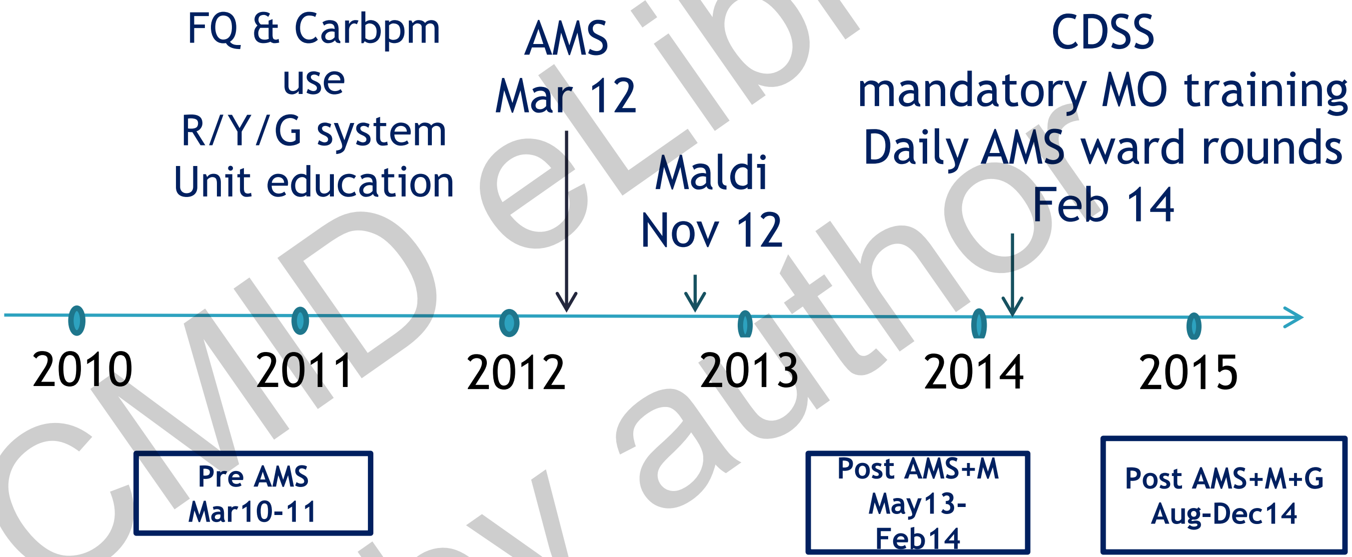


# Model Development

- Expert panel
  - expert advisory meeting at the RBWH on 9th October 2013 Infectious disease physicians, pharmacists and clinical microbiologists

- Expert opinion
  - Professor Marc Scheetz (Professor of Pharmacy, Mid-western University, Chicago USA)
  - Dr Jose Leal (Health economist Oxford University London U.K)
  - Dr Kate Halton (QUT), Professor Nicholas Graves (QUT) and Professor Jason Roberts (UQ).

# AMS interventions at the RBWH



# Matrix Assisted Laser Desorption Time of Flight Mass Spectrometry (MALDI-TOF)

- Revolutionised Microbiology in terms of TAT for organism identifications
- Implemented in a number of Australian hospitals
- AMS+MALDI-TOF
  - Reduction in 30 day mortality in patients with BSIs
    **21% versus 8.9%, P<0.01** (Perez et al 2014)
    **21% versus 12%, P < 0.01**(Patel et al 2017)
    Total hospital costs decreased by **$2439 per BSI**
  - Reduction in LOS in hospitalised patients

# Clinical Decision Support System: Guidance MS

- Recommendations in real time to assist with clinical decision making
- Guidance MS developed in Victoria and implemented at the RBWH and other hospitals in Australia
- Guidance MS implemented as a collaborative multisite ASP (NSW Australia)
  - associated with targeted antimicrobial use, decreased antimicrobial costs and HCA-CDI rates. (Bond et al *Journal of Antimicrobial Chemotherapy*, Volume 72, Issue 7, 1 July 2017, Pages 2110–2118)

# Potential Outcome Measures for Assessing AMS interventions

- Financial (antimicrobial usage reduction, LOS)
- Patient (mortality and morbidity)
  - **BSI**, VAP, SSI, UTIs, CAPs
- Microbiological (AMR, *C difficile*)

- Serious infection with a potential to costly complications
- BSI data collected in most hospital databases

# The use of bloodstream infection mortality to measure the impact of an AMS intervention

Infectious Disease Reports 2017; volume 9:6849

**The use of bloodstream infection mortality to measure the impact of antimicrobial stewardship interventions: assessing the evidence**

Sonali Coulter,[1] Jason A. Roberts,[2,3] Krispin Hajkowicz,[3] Kate Halton[4]

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**Abstract**

This review sets out to evaluate the current evidence on the impact of inappropriate therapy on bloodstream infections (BSI) and associated mortality. Based on the premise that better prescribing practices should result in better patient outcomes, BSI mortality may be a useful metric to evaluate antimicrobial stewardship (AMS)

... to GN BSI. The highest impact of inappropriate prescribing was seen in patients with GN BSI, which may be a useful metric to monitor the impact of AMS interventions.

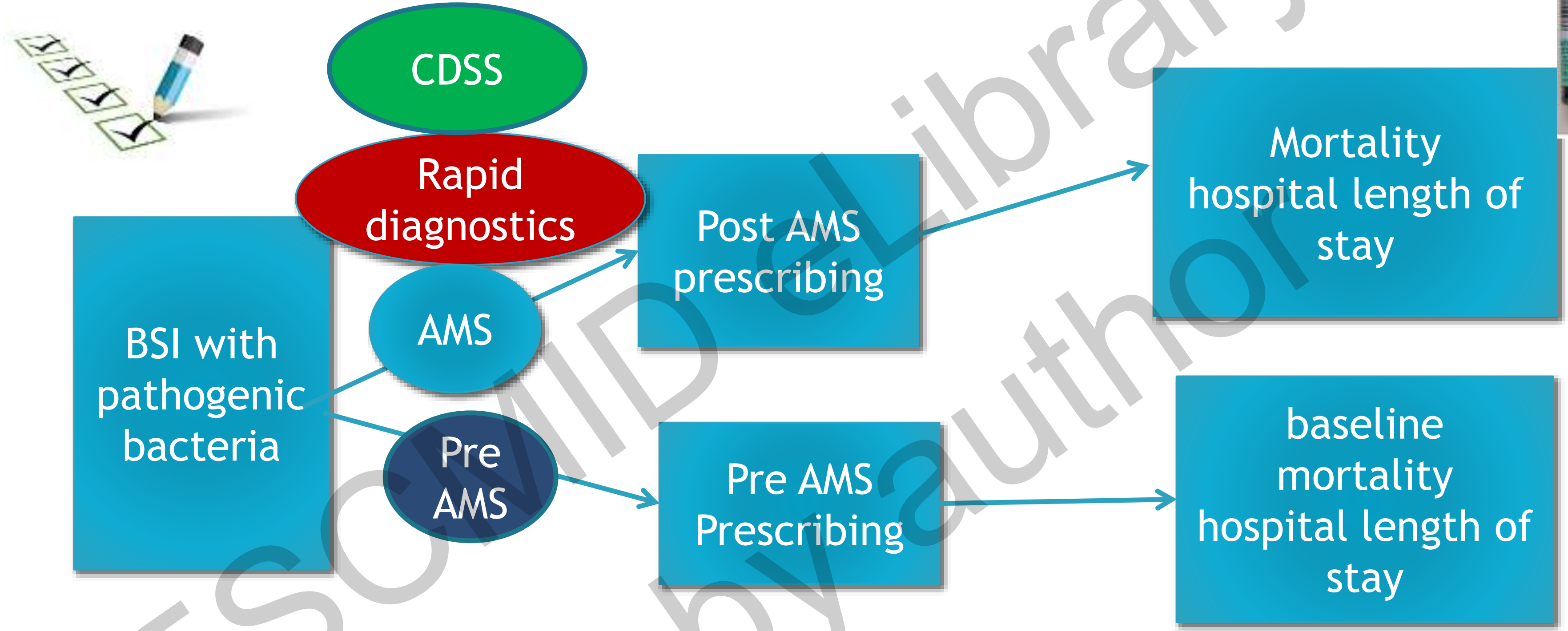
**Introduction**

One of the main goals of an antimicrobial stewardship (AMS) intervention is to ensure patients with infections receive the most appropriate antimicrobial agent at the optimal dose at the earliest time.[1] As AMS programs can take many forms there is a need to ensure that the intervention(s) selected can maximize the outcomes of the program. However, there is a lack of clarity around the outcome measures that provide the best indicators of a successful AMS program with most studies focusing on changes in antimicrobial utilization rates.[2] An update by Akpan *et al.* (2016) on current metrics to measure the impact of AMS programs in a recent review reported that only a handful of studies included patient outcomes.[3] The authors reported that only 13 of the 63 studies that met their inclusion criteria reported on mortality, length of stay and unplanned admissions related to post-AMS infection as an outcome measure. Okumura *et al.* (2015) focused on six studies that examined mortality and the non-significant impact was highlighted with only one study reporting an absolute risk reduction in 30-day mortality.[4]

## Findings

- 46 studies included (quality of the evidence was low)
- Inappropriate therapy was associated with an overall increase in mortality in BSI.
- Resistant organisms were associate with an increased mortality

# Economic model and data collection



# Data collection

1. Questionnaire
   - AMS lead infectious diseases(ID) physician
   - Director of Microbiology
   - Director of Pharmacy
2. BSI data linked with admission and discharge data

- Exclusions:
  - Duplicates, common skin contaminants, organisms other than listed below(Anaerobes, yeasts, fungi and mixed cultures)
- Inclusions: ESKAPE organisms
  - *Enterococcus faecalis & faecium*, *Staphylococcus aureus* including (MRSA), *K.pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Enterobacterieaceae*

# Data analysis: cost of AMS Intervention

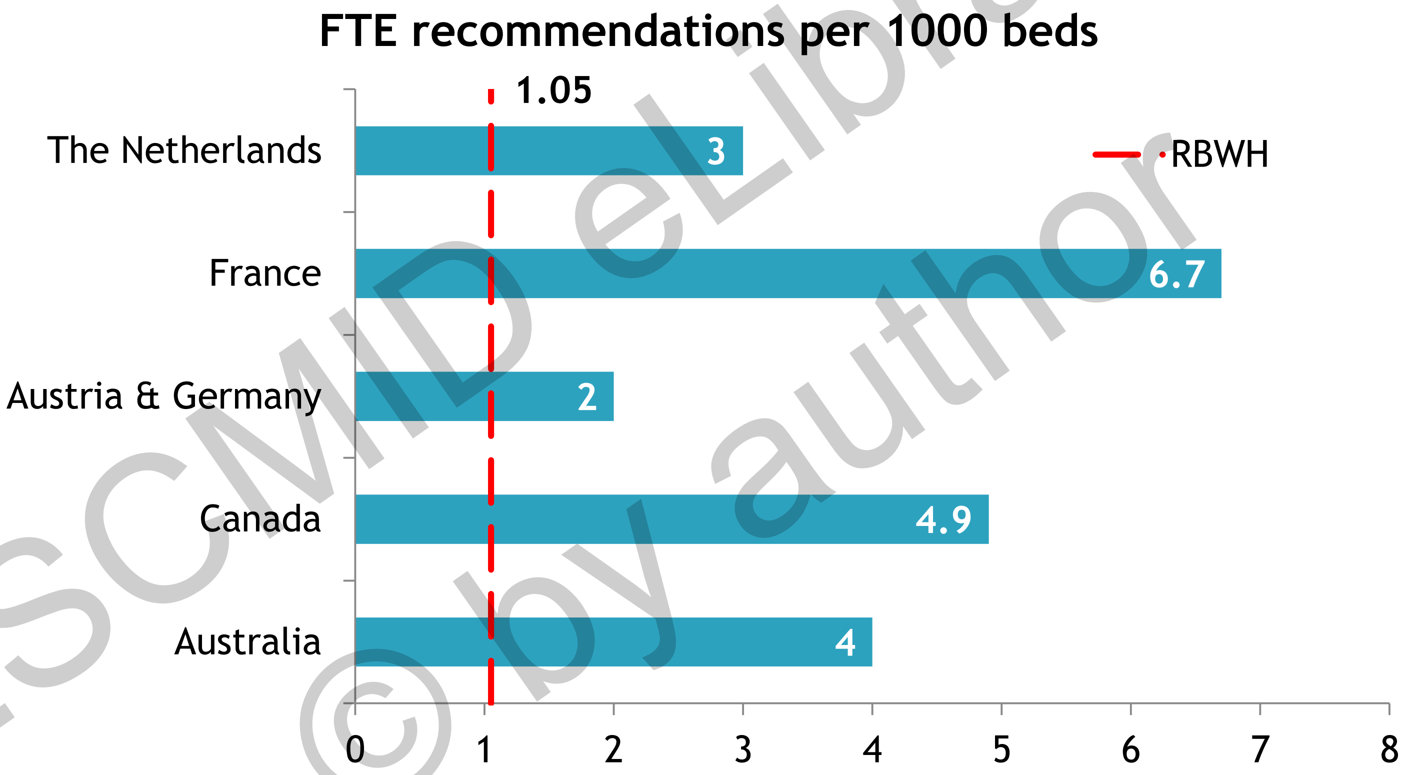
AMS team : ID Physician 0.3FTE; AMS Pharmacist 0.6FTE; Clinical Microbiologist (0.1FTE) =1.0FTE

AMS committee: 9 hrs per annum(Meeting frequency: every other month for 1.5hrs) = 0.0043FTE for each member on the committee = 0.05FTE

Total Full Time Equivalents (FTE) 1.05

CDSS: Cost of hardware, software, licence, annual support fee

# Our intervention



# Costing

| Cost per annum AUD | Pre AMS | AMS +M | AMS+M+G |
|---|---|---|---|
| **Antimicrobials** | $92,267 | $86,604 | $76,125 |
| **Laboratory** | $16,835 | $14,573 | $13,495 |
| **AMS intervention** | | $142,820 | $142,820 |
| **CDSS** | | | $26,298 |
| **Total** | $109,101 | $243,997 | $258,739 |
| **Difference in cost compared to Pre AMS** | | $134,896 | $149,637 |
| **Abbreviations: M: MALDI-TOF; G: Guidance MS.** | | | |

# ESKAPE organisms included in the analysis

| Intervention | Gram Positive | Gram Negative | Mortality | Total |
|---|---|---|---|---|
| **Pre AMS** | 98 | 227 | 40 (12.3%) | 325 |
| **AMS+M** | 111 | 126 | 21 (8.9%) | 237 |
| **AMS+M+G** | 41 | 75 | 10 (8.6%) | 116 |
| Total | 250 | 428 | 71 (10.5%) | 678 |
| Abbreviations: M: MALDI-TOF; G: Guidance | | | | |

# Costs per patient with BSI

| Cost per patient | Pre AMS | AMS+M | AMS+M+G |
|---|---|---|---|
| **Antimicrobials** | $99.00 | $92.92 | $81.68 |
| **AMS intervention** | | $153.24 | $153.24 |
| **CDSS** | | | $28.22 |
| **Laboratory** | $38.79 | $30.81 | $30.81 |
| **Total** | $137.79 | $276.97 | $293.95 |

# Changes in Mortality

| Intervention | | Probability of death estimate | Standard error |
|---|---|---|---|
| **Pre AMS** | Gram Positive | 0.156 | 0.037 |
| **AMS+M** | | 0.130 | 0.032 |
| **AMS+M+G** | | 0.144 | 0.055 |
| **Pre AMS** | Gram Negative | 0.097 | 0.020 |
| **AMS+M** | | 0.081 | 0.024 |
| **AMS+M+G** | | 0.090 | 0.033 |

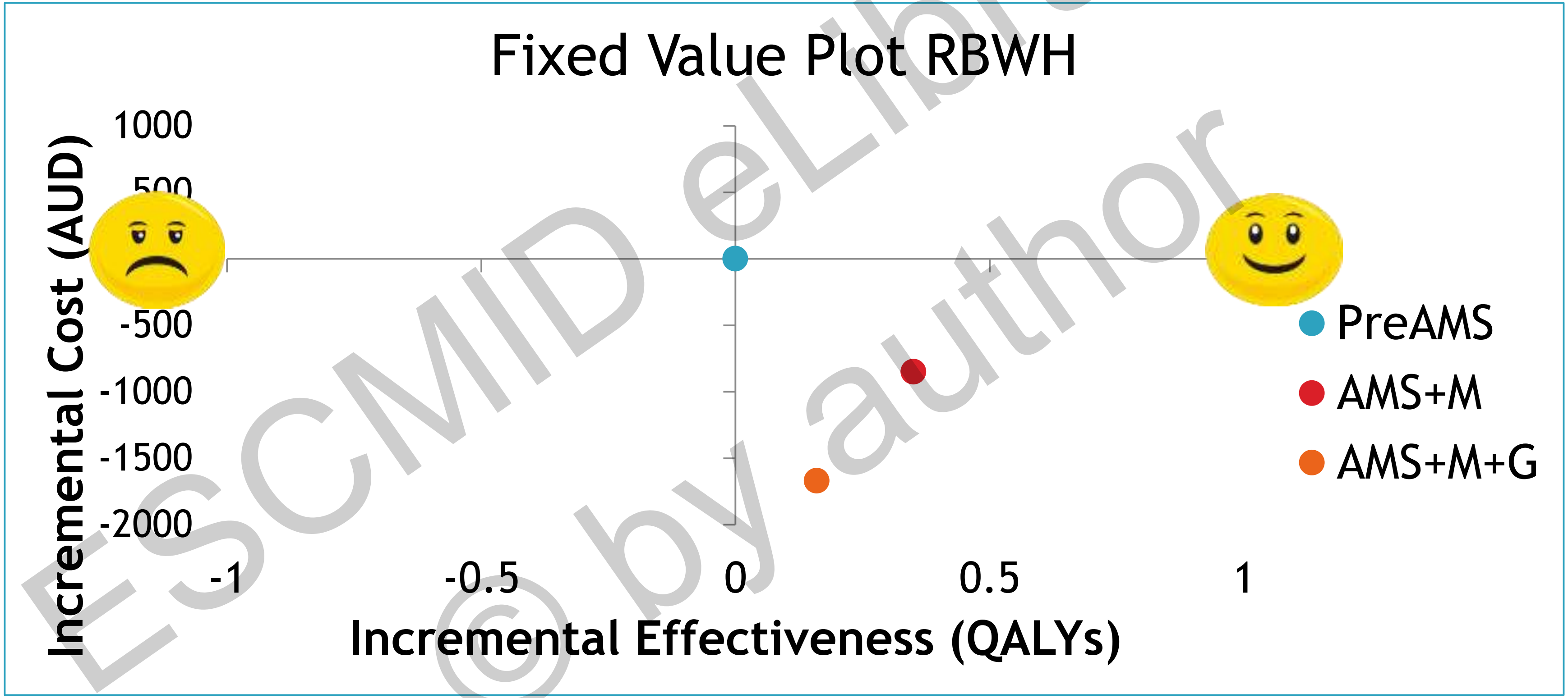
# Changes in average hospital LOS

| Intervention period | | LOS survivors(95% CI) | LOS deceased(95% CI) |
|---|---|---|---|
| Pre AMS | Gram Positive | 36.6 (30.1- 47.1) | 26.6 (8.3-44.9) |
| AMS+M | | 32.8 (25.1-40.6) | 19.3 (-1.1-39.7) |
| AMS+M+G | | 34.1 (21.5-46.7) | 30.1 (-3.6-63.8) |
| Pre AMS | Gram Negative | 31.6 (26.7-36.5) | 25.7 (10.9-40.6) |
| AMS+M | | 26.3 (19.9-32.7) | 39.6 (13.3-65.9) |
| AMS+M+G | | 20.4 (12.1-28.8) | 14.8 (-16.4-46.0) |

# Fixed Value Cost-effectiveness Analysis

| Strategy | Incremental Cost | Incremental QALY |
|---|---|---|
| AMS + M | -$851 | 0.35 |
| AMS+M+G | -$1,671 | 0.16 |
| Abbreviations: M: MALDI-TOF; G: Guidance MS; QALY: Quality Adjusted Life Year | | |

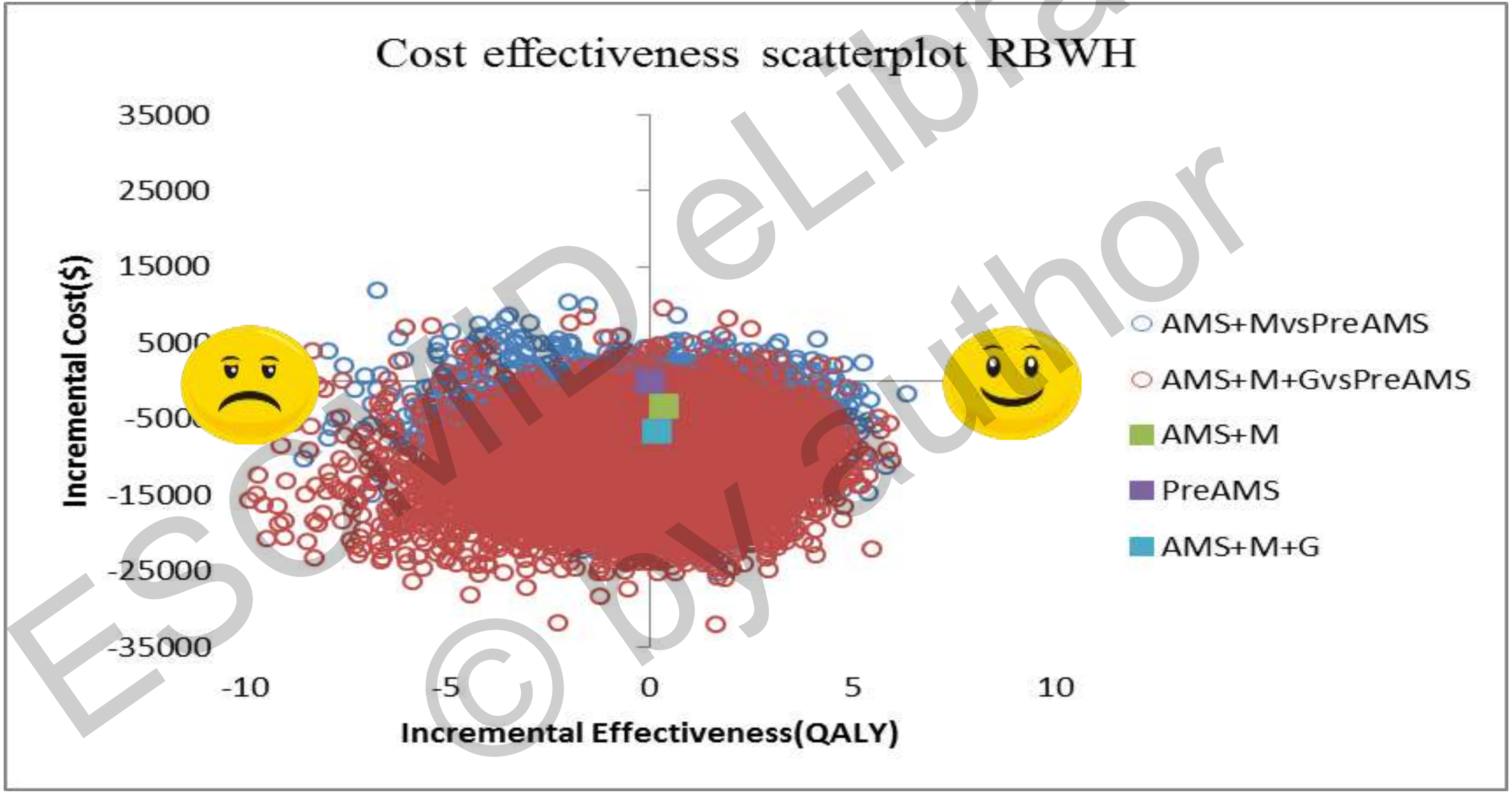
# Cost-effectiveness analysis RBWH



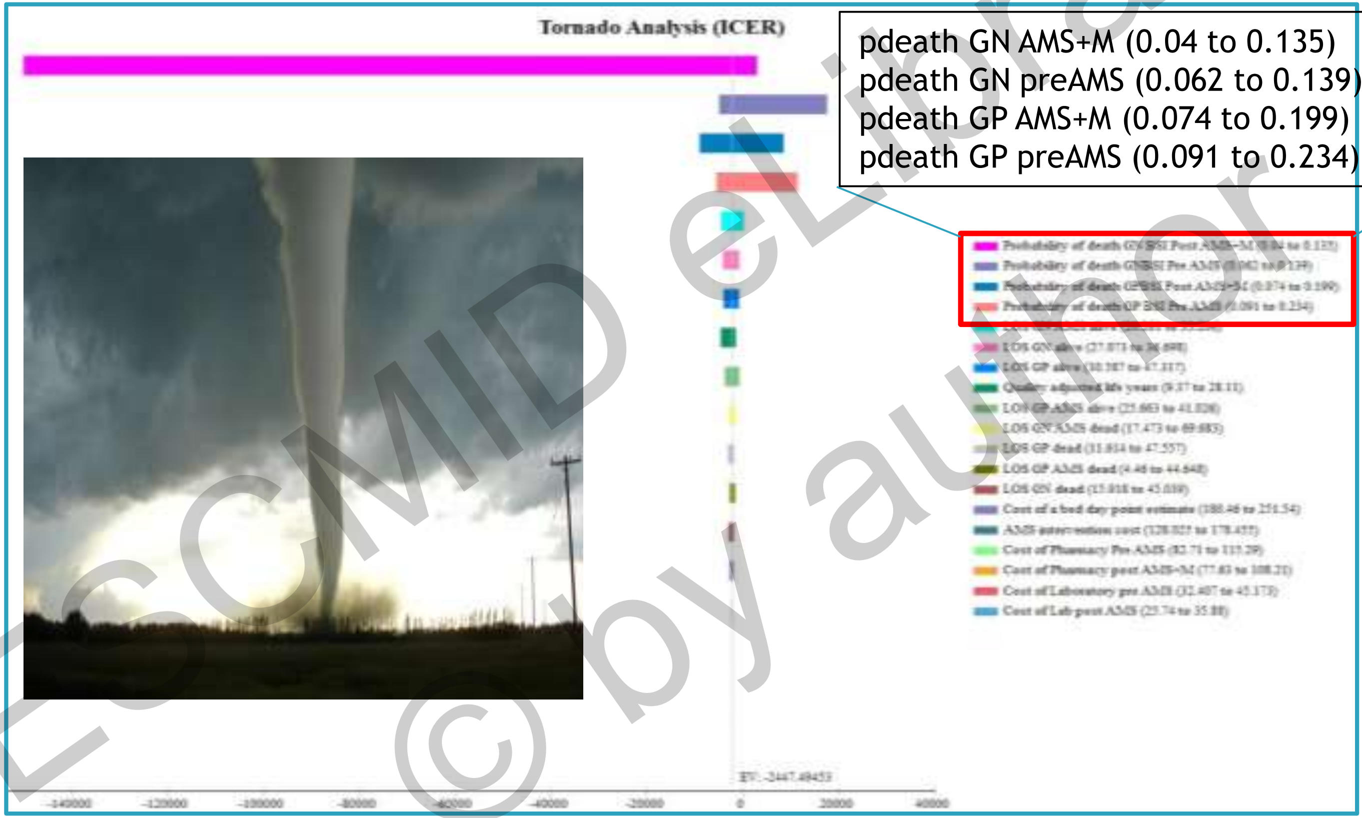
# Probabilistic sensitivity analysis (PSA)

- **PSA**
  - To measure the level of confidence of our results in view of the statistical uncertainty in our model parameter estimates
- **Monte Carlo simulation**
  - Joint distribution of the change to costs and changes to health benefits using different combinations of the variables
- Treeage software

# Probabilistic Sensitivity Analysis



# One way sensitivity analysis -Tornado diagrams




pdeath GN AMS+M (0.04 to 0.135)
pdeath GN preAMS (0.062 to 0.139)
pdeath GP AMS+M (0.074 to 0.199)
pdeath GP preAMS (0.091 to 0.234)

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# Conclusions

- The AMS intervention was cost saving at the RBWH
- The AMS intervention was cost-effective with a high level of uncertainty associated with the conclusion
- Choice of BSI mortality as a metric in a setting where overall baseline mortality and AMR is low contributed to the level of uncertainty

# Limitations

Short time frame for data collection and only 30 day mortality being included

Other factors not included in the analysis

- rates of AMR
- *C difficile infections and other HAIs*

(Difficulty accessing estimates in a setting of low rates of infection and confounders)

This led to an under estimation of the economic benefits of the AMS intervention

# Recommendations

- **Prior** to the implementation of healthcare interventions, a **data collection plan** including the type of costs and outcome data should be agreed to.
- Australia is in the process of introducing a digital hospital system and the EMR may provide us with more easy access to patient outcome data over a longer period of time to evaluate healthcare interventions

# Recommendations

- We need AMS interventions to be sustainable long term and to be well resourced
- While HR was the greatest cost, it is an essential part of an AMS intervention and needs to be accepted as part of the requirement for patient safety in hospitals
- A small investment in the laboratory and information technology such as CDSS may result in great benefits if teamed with an effective AMS program

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- Professor Jason Roberts (UQ)
- Dr Katharina Merollini (QUT)

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- www.cre-rhai.org.au

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- Data custodians and staff at the RBWH Brisbane

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