

**Vannevar Bush,
U.S. Director of the Office of
Scientific Research & Development**

**“For a record to be useful to
Science it must be stored, it
must be maintained and
above all it must be
consulted.”**

Bush V As we may think. *Atlantic Monthly* June 1945

Building the data base of cancer control in developing countries.

Mark Lodge

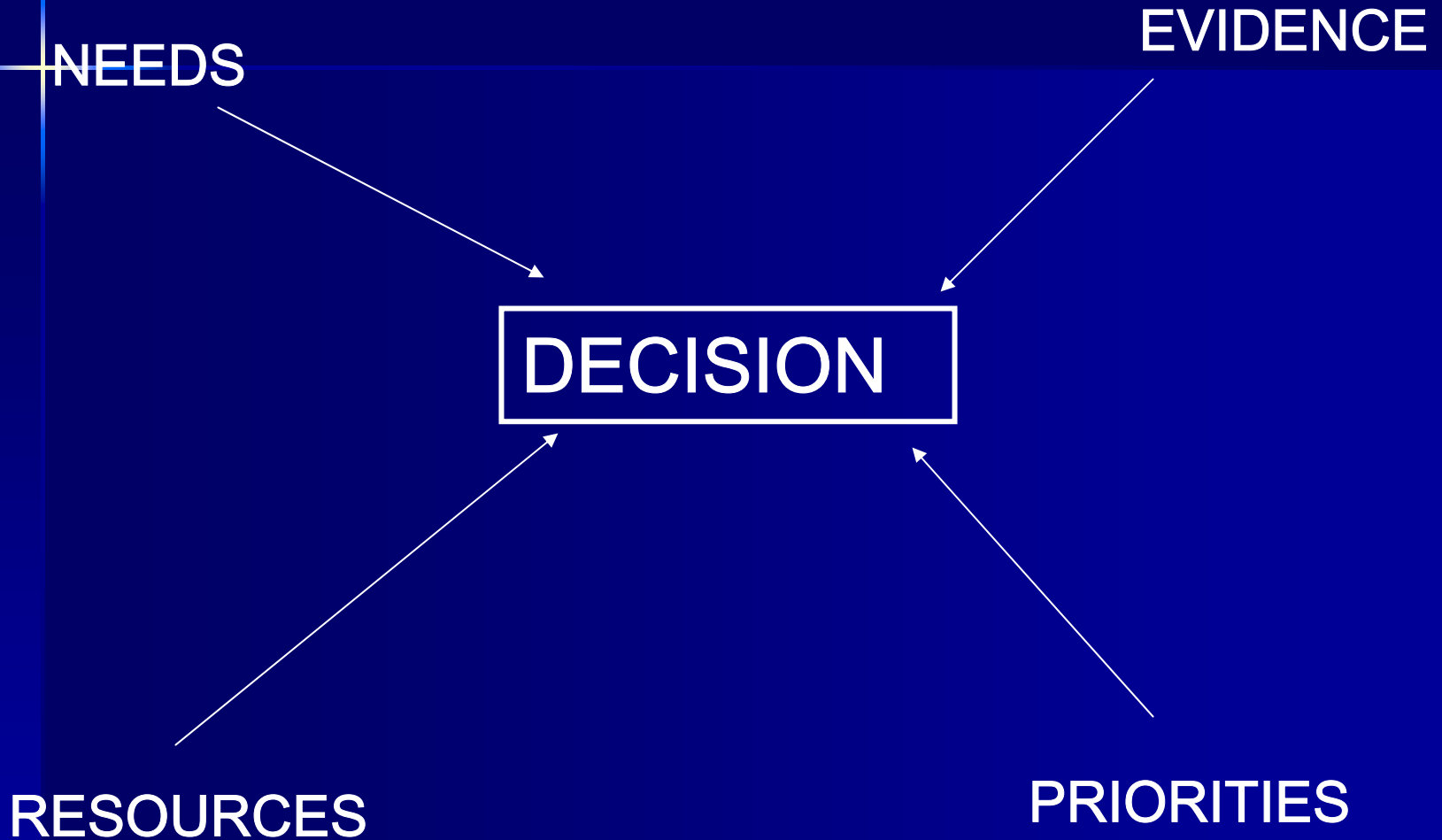
Cochrane Cancer Network

Oxford UK

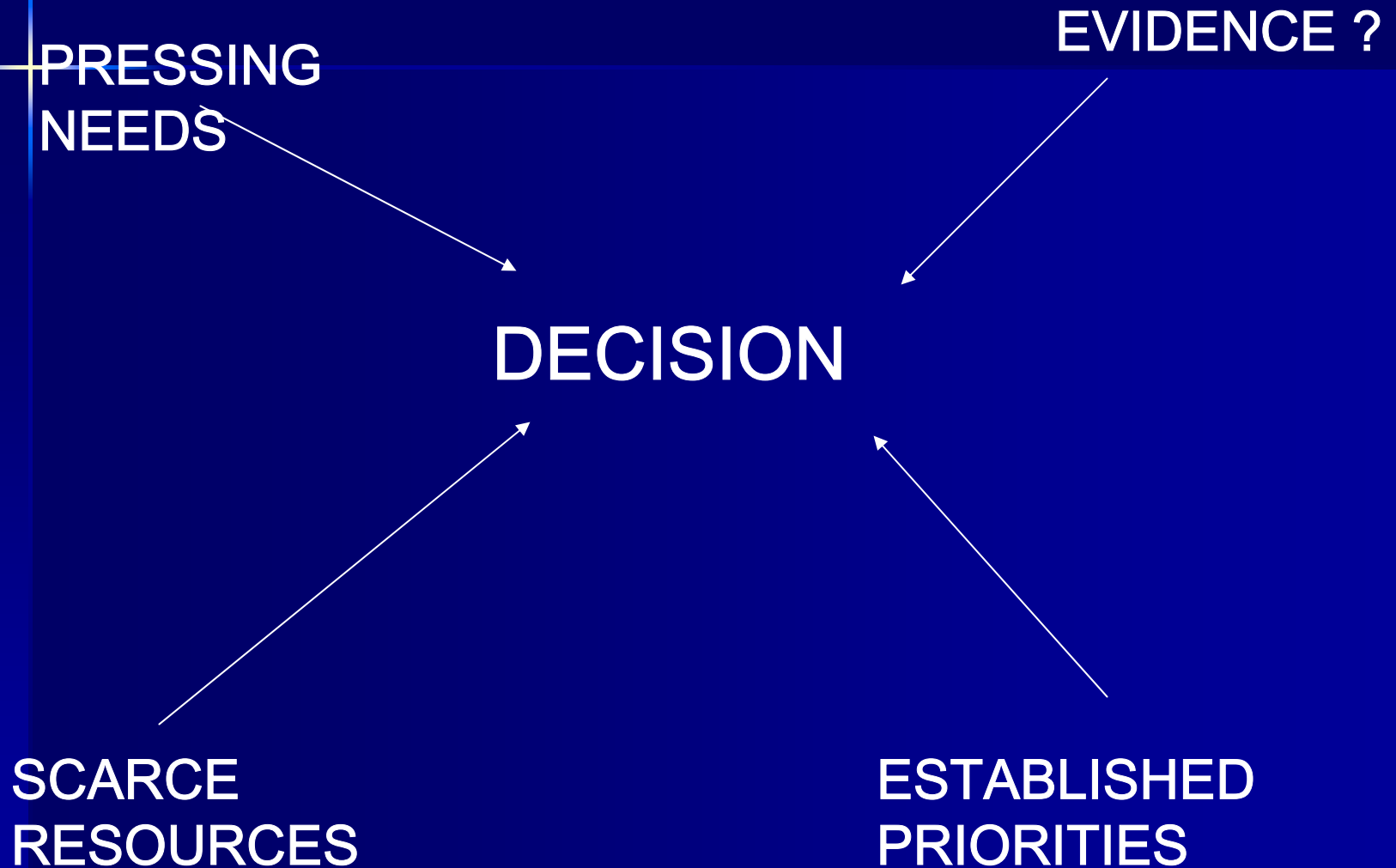
Presentation

- Cancer, Ignorance and Poverty
- Evidence based cancer control (includes tobacco control)
- Need for systematic reviews
- Identifying studies relevant to developing countries
- Building Database of relevant systematic reviews
- Conclusions

Decision table



Decision table



Describing the Evidence

- Robust

- Solid

- Equivocal

- Inadequate

- Non-existent

- Misleading

Assumptions of evidence-based decision-making

- Comprehensive knowledge of evidence
- Inclusion of all relevant studies
- Rigorous critical appraisal of evidence
- Systematic review methodology

Characteristics of Systematic reviews

- Include as many relevant studies as possible
- Systematic appraisal and summary
- Pre-determined inclusion & exclusion criteria
- Explicit methodology
- Designed to minimize bias
- Help decision-makers by providing reliable evidence about the effects and effectiveness of health care interventions

The medical review article: state of the science

Mulrow CD *Ann Intern Med* 1987 106(3):485-8

- Reviews published June 1985 -June 1986 (n= 50)
- *Ann Intern Med*, *Arch Intern Med*, *JAMA*, *New England J Med*
- Assessed on 8 explicit published criteria

The medical review article: state of the science

Mulrow CD *Ann Intern Med* 1987 106(3):485-8

- Specific purpose of review stated
- Sources & methods of citation search identified
- Explicit inclusion / exclusion criteria
- Methodological validity assessment of material in the review
- Information systematically integrated with explication of data limitations and inconsistencies
- Information integrated & weighted or pooled metrically
- Summary of pertinent findings
- Specific directives for new research

The medical review article: state of the science

Mulrow CD *Ann Intern Med* 1987 106(3):485-8

- Results: n=50
 - 3 criteria satisfied (n=17)
 - 4-5 criteria satisfied (n=32)
 - 6 criteria satisfied (n=1)
 - Clearly specified purposes (n = 40)
 - Conclusions (n=37)
 - Future research directives (n= 21)

The medical review article: state of the science

Mulrow CD *Ann Intern Med* 1987 106(3):485-8

- Integrating information
 - Qualitative synthesis (n = 43)
 - Quantitative synthesis (n = 3)
- Clearly specified methods of identifying, selecting, and validating included information (n=1)

The medical review article: state of the science

Mulrow CD *Ann Intern Med* 1987 106(3):485-8

- Conclusion:

Current medical reviews do not routinely use scientific methods to identify, assess, and synthesize information.

Recognition of Value of Systematic Reviews in Developed Countries

Clinical Guideline development:

Grade 1A Evidence Hierarchy ranking

Research governance

*“It is essential that existing sources of evidence, **especially systematic reviews**, are considered carefully prior to undertaking research.”*

*Research Governance Framework For Health and Social Care
(Section 2.3.1) 2nd ed. publ Department of Health 2005*

Contribution to Clinical Practice

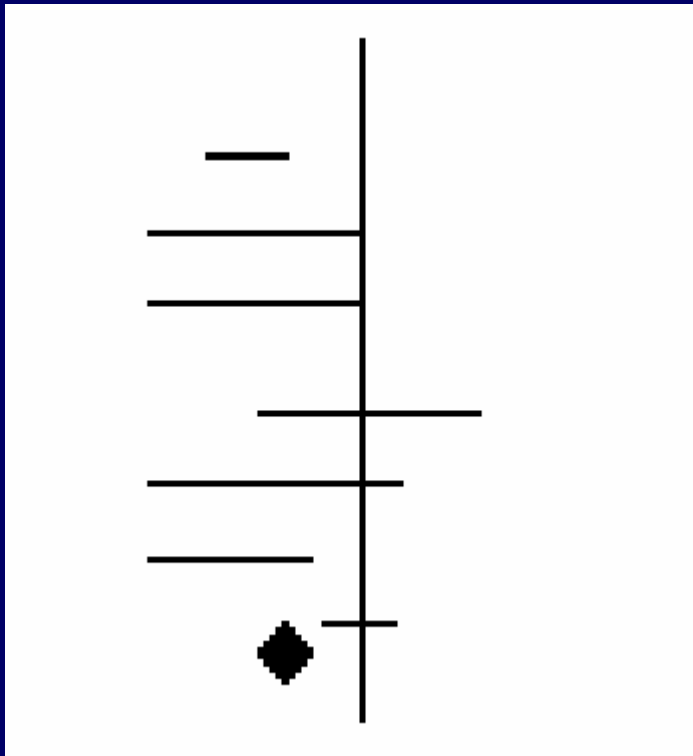
- Provide reliable (unbiased) evidence of effects and effectiveness of interventions
- Identifies treatment effects previously not apparent when trials were considered in isolation
- Facilitate reviews of cost effectiveness

Contribution to Clinical Research

- Identify all relevant research in topic area
- Identify gaps in our knowledge
- Minimises wasteful duplication of effort
- Identifies methodological difficulties
- Protects patients from badly designed/unnecessary research

Establish a baseline:

Prophylactic corticosteroids for pre-term birth (First published 1989)



Crowley P. Prophylactic corticosteroids for pre-term birth (Cochrane Review). In: *The Cochrane Library*, Issue 4, 2003.

Image shows 7 RCTs (1972-82)

Corticosteroids v Placebo

Horizontal = Trial

Vertical = No difference

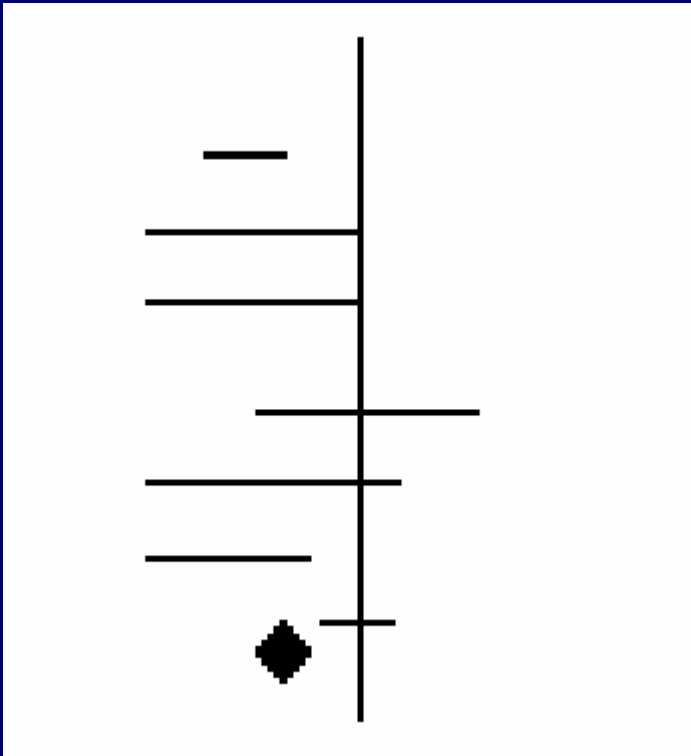
Diamond = combined results

Crowley P. Prophylactic corticosteroids for preterm birth (Cochrane Review).

- 7 trials conducted 1972-1980
- 40 % reduction in infant mortality and morbidity
- 6 further trials before systematic review published in 1989 eventually changed UK practice

Establish a baseline:

Prophylactic corticosteroids for pre-term birth (First published 1989)



Crowley P. Prophylactic corticosteroids for pre-term birth (Cochrane Review). In: *The Cochrane Library*, Issue 4, 2003. Chichester, UK: John Wiley & Sons, Ltd.

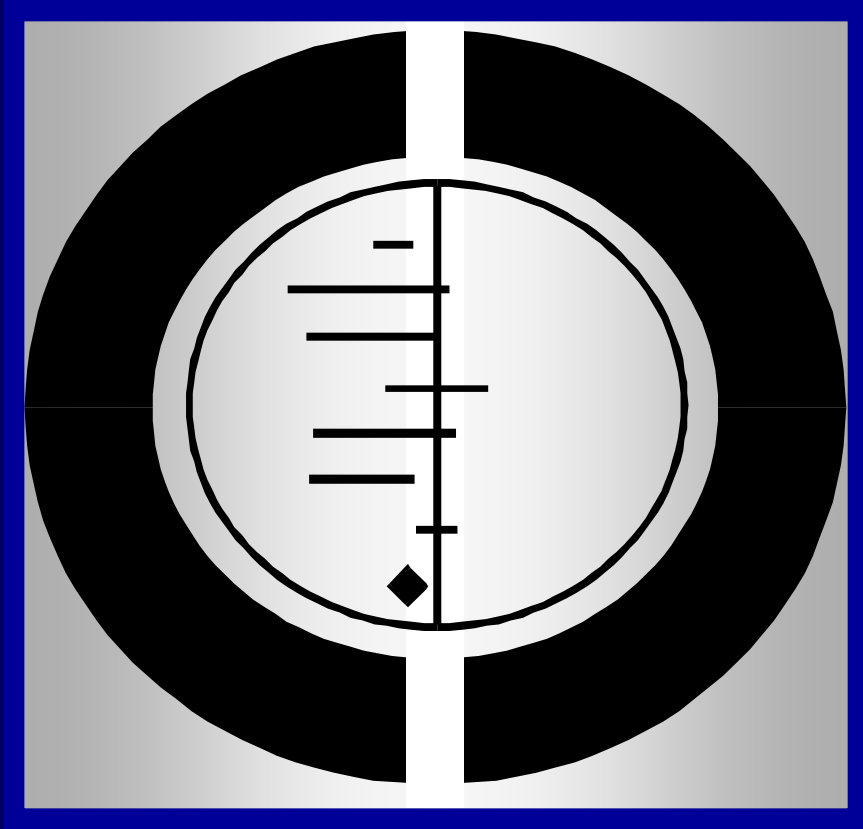
Image shows 7 RCTs (1972-82)

Corticosteroids v Placebo

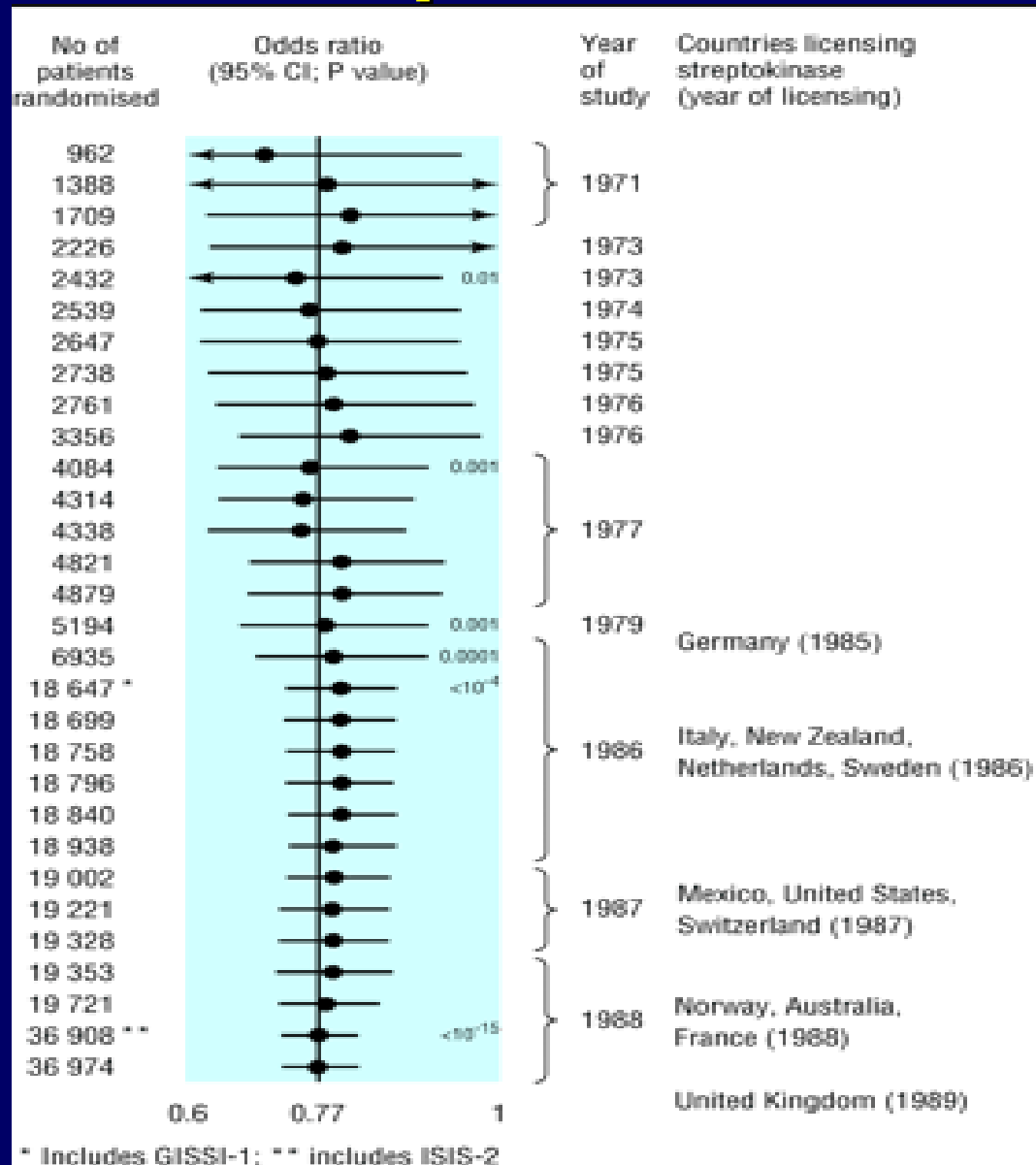
Horizontal = Trial

Vertical = No difference

Diamond = combined results



Reducing duplication: Streptokinase for MI



Lau J, Antman EM, Jimenez-Silva J, Kupelnick B, Mosteller F, Chalmers T.

Cumulative meta-analysis of therapeutic trials for myocardial infarction.

NEJM 1992;327:248-54

Reducing duplication: Streptokinase for MI

- 33 trials evaluating this therapy were performed between 1959 and 1988.
- We found that a consistent, statistically significant reduction in total mortality (Odds ratio, 0.74; 95%CI, 0.59-0.92) was achieved in 1973 after only 8 trials involving 2,432 patients had been completed.
- The results of the 25 subsequent trials which enrolled 34, 542 patients through 1988 had little or no effect on the odds ratio but simply narrowed the 95% confidence interval.

Identifying treatment effects that were previously not apparent

The Human Albumin Review

- HA solutions used in the emergency treatment of shock and other conditions where restoration of blood vol. is urgent, in burns & hypoproteinaemia.
- Identify all RCTs of human albumin or plasma protein fraction (PPF) administration (albumin/PPF versus no albumin/PPF, or a crystalloid solution).
- HA solutions are more expensive than other colloids and crystalloids

The Albumin Reviewers (Alderson P, Bunn F, Lefebvre C, Li Wan Po A, Li L, Roberts I, Schierhout G). Human albumin solution for resuscitation and volume expansion in critically ill patients (Cochrane Review).

Identifying treatment effects that were previously not apparent

The Human Albumin Review

- Identified 31 RCTs (1973-2001)
- For each patient category the risk of death in the albumin treated group was higher than in the comparison group
- Overall, the risk of death in patients receiving albumin was 14% compared to 9% in the control groups, an increase in the risk of death of 5% (2% - 8%).

Identifying treatment effects that were previously not apparent

The Human Albumin Review

- There is no evidence that albumin administration reduces the risk of death in critically ill patients with hypovolaemia, burns or hypoalbuminaemia, and a strong suggestion that it may increase the risk of death. These data suggest that the use of human albumin in critically ill patients should be urgently reviewed and that it should not be used outside the context of a rigorously conducted randomised controlled trial.

Need for systematic reviews

- Important effects of health care not identified promptly
- Uninformed research agenda
- Prevent duplication of effort
- Promising leads may be missed
- People using health services will otherwise be ill-served

Benefits of Systematic Reviews

- Provide unbiased assessment of the effects and effectiveness of health care interventions
- Informs investment decisions
- With political will, help prevent wasteful deployment of scarce resources

Are the current systematic reviews in cancer appropriate for Developing Countries?

- Different cancers
- Different genetic populations, demographic profiles
- Limited or no access to reviewed technology
- Invalid assumptions about infrastructure
- Different health care delivery systems

Building an evidence base

- Register of Studies (all types)
- Train content experts in review methodology
- Database of Systematic Reviews
- Effective dissemination
- Build evidence-based business case for infrastructure investment

Building a Register of Studies

- All types of scientific studies
- Prioritise relevance to high incidence or mortality cancers
- Coded for review
- Comprehensive search programme
 - Databases

Databases: Identifying omissions in indexing by country

1. Neoplasms (explode all subheadings)
2. Cancer
3. #1 and #2
4. COUNTRY.in
5. CITY.in
6. #4 and #5
7. #3 and #5
8. #3 and #6
9. #7 not #8

Indexing by country

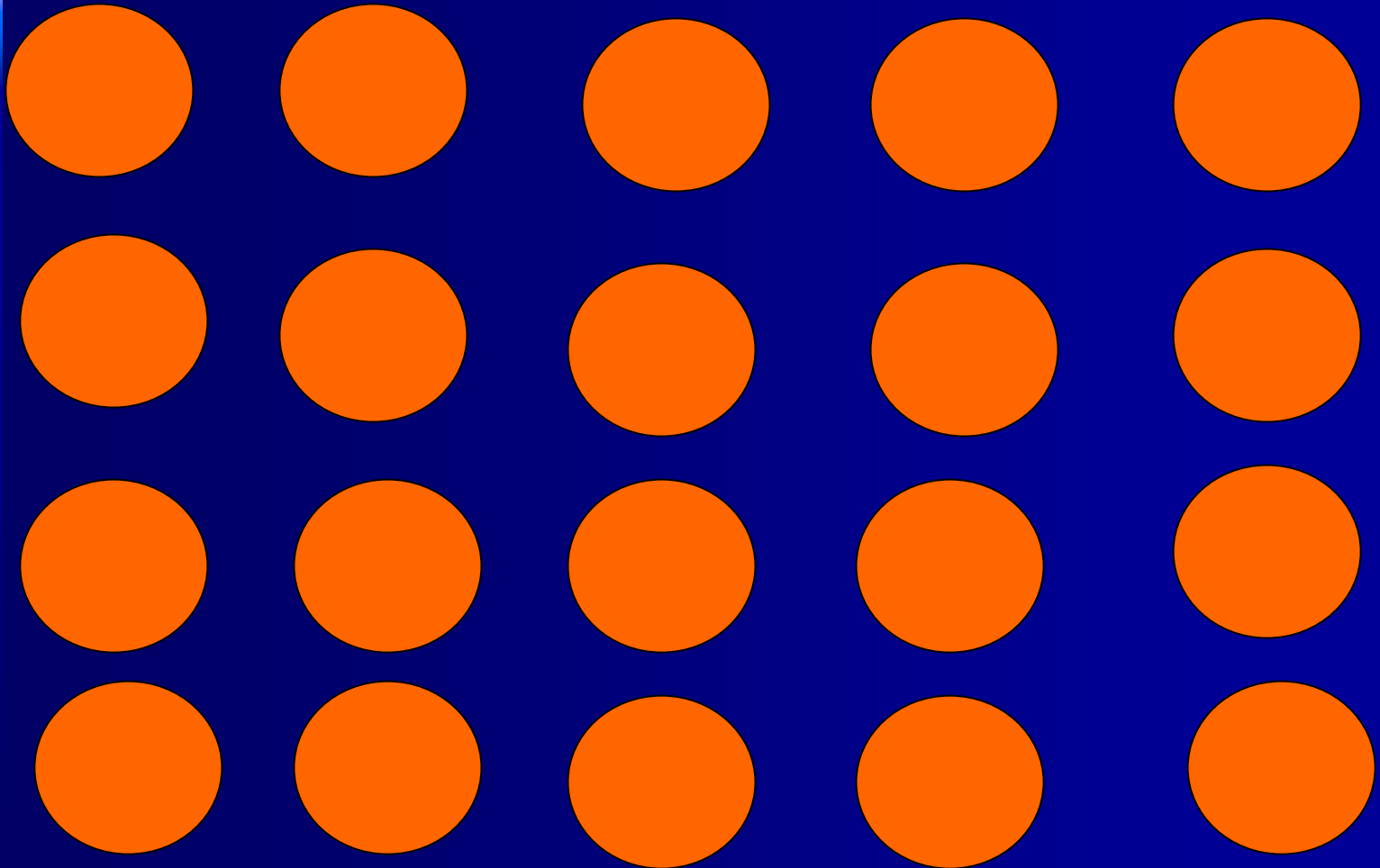
Medline: 1996- 4th week January
2007

■ Cairo	200
■ Egypt and Cairo	193
■ Difference	7 (3.5%)
■ Chennai	162
■ Chennai and India	153
■ Difference	9 (5.5%)
■ Cape Town	149
■ Cape Town and South Africa	139
■ Difference	10 (6.7%)

Information Glut

20,000 sources

2 million articles p.a.



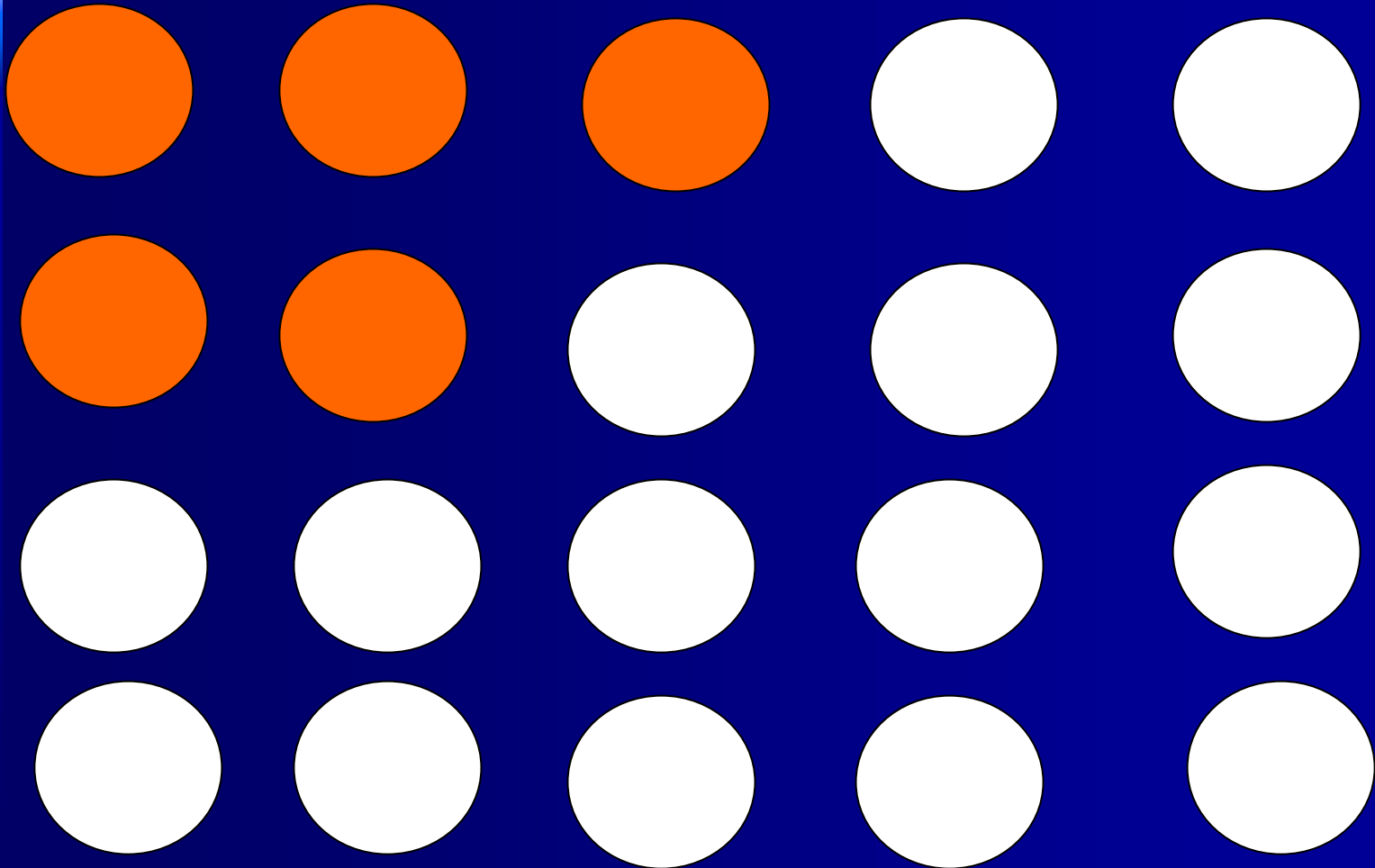
Journals indexed for Medline

5051 journals (November 2006)

– Indexed on Index Medicus 4,447

– Non-IndexMedicus journals 604

**Medline database:
5,051 journals indexed
(12m + citations)**



Minimising bias

- Majority of Medline indexed journals are English language journals
- Non-English language reports indexed may not include abstracts
- Reports with statistically significant outcomes more likely to be published in English
- Very few conference proceedings indexed

Conference proceedings not indexed in Medline Indexed journals

Int J Radiation Oncol Biol Phys
1999-2003

No of RCTs/CCTs found:	291
No. of reports of trials indexed as trials	85
No. RCTs/CCTs indexed on MEDLINE but not as trials	3
No. RCTs/CCTs reported in conference proceedings & NOT indexed on MEDLINE	203
Total no. RCTs/CCTs not adequately indexed on MEDLINE as trials: 71%	206

Conference proceedings not indexed in Medline Indexed journals

Eur J Cancer 2001-2003

No of RCTs/CCTs found:	286
No. of reports of trials indexed as trials	44
No. of RCTs/CCTs indexed on MEDLINE but not as trials	0
No. RCTs/CCTs reported in conference proceedings & NOT indexed on MEDLINE	242
Total no. RCTs/CCTs not adequately indexed on MEDLINE as trials 85%	242

Building a Register of Studies

- Databases (General & regional)
- **Journals (indexed & non-indexed)**
- Conference proceedings

Conference proceedings

- Very few conference proceedings properly indexed on major databases
- Electronic conference proceedings hard to interrogate
- Bias between proceedings and full article

Building a Register of Studies

- Databases
- Journals (indexed & non-indexed)
- Conference proceedings
- **Dissertations & Theses**
- **Industry reports**
 - **WHO International Trials Platform**
- Unpublished studies
- Register of sources searched

Training & Knowledge Transfer

- Train local content experts in review methodology
- Local expertise of conditions and realities
- Able to critically appraise and comment upon evidence from the appropriate perspective
- Identify local implications for Clinical Practice and for Research

Database of Systematic Reviews

- Prioritised by available cancer registry incidence/mortality data
- Relevant to local conditions
- Address all aspects of cancer control and management (Prevention- Screening, Treatment -Palliative Care - Bereavement)
- Designed for use by decision-makers

Systematic reviews

Contribution to clinical practice information needs

- Effective care / Ineffective care
- Benefit or harm to patients
- No evidence of effectiveness
- Insufficient evidence to support clinical practice

Effective dissemination

- National provision
- User summaries
- Use media (scientific and general)

Securing political will

- Studies Register
 - Creation of a storehouse of knowledge
 - Identifiable voice in world literature
 - Highlight centres of research experience
- Training
 - Knowledge transfer to build on local expertise
 - Trained content experts with critical appraisal and systematic review skills

Securing political will

- Database of Systematic Reviews
 - Informs National Cancer Plan & investment in future clinical practice and research
 - Help direct scarce resources where the evidence shows that they're needed
 - Build evidence-based research agenda
 - Build up business case for investment in research infrastructure that will benefit clinical practice

Conclusions

- Developed countries 20 years ahead
- Results of cancer research in developing countries remains scattered and not easily accessible
- Needed: global search programme
- Needed: content experts with local experience to conduct resource-relevant systematic reviews
- Build evidence-based business case for investment in research and practice infrastructure

**Vannevar Bush,
U.S. Director of the Office of
Scientific Research & Development**

**“For a record to be useful to
Science it must be stored, it
must be maintained and
above all it must be
consulted.”**

Bush V As we may think. *Atlantic Monthly* June 1945