

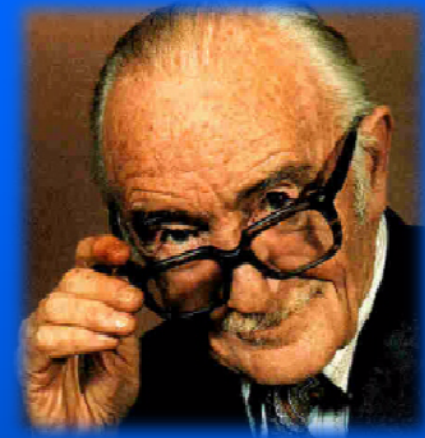
# Systematic Reviews and The Cochrane Library

*Phil Hahn*

Queen's University Co-site Representative  
Canadian Cochrane Centre

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# Archie Cochrane



*“It is surely a great criticism of our profession that we have not organized a critical summary, by specialty, adapted periodically, of all relevant randomized controlled trials.” (1979)*

# Cochrane Collaboration

- A world wide group of health care professionals (October 1993)
- Goal: To prepare, maintain and disseminate, up-to-date reviews by specialty, of all RCTs (or the best available evidence) in all areas of medicine.

# Cochrane Review Group

- **Group of experts with an interest in a health problem area**
- **Work to prepare and maintain systematic reviews of specified health care problems**
- **Willing and able to review all relevant research on specified topic**
- **Keep it up to date**

# 52 Review Groups

## *Women's Health:*

- Breast Cancer
- Fertility Regulation (Contraception)
- Gynaecologic Cancer
- Incontinence
- Menstrual Disorders & Subfertility
- Neonatal
- Pregnancy & Child Birth

# World-wide Network



# Cochrane Centres



- Amsterdam
- Australia
- Brazil
- Canada (Ottawa)
- China
- Belgium
- Columbia
- Finland
- Germany
- Italy
- Netherlands
- Norway
- Russia
- South Africa
- Spain
- United Kingdom
- United States
- Venezuela

# 18 Network Sites



## *Ontario Sites*

*(Representatives)*

- **University of Western Ontario**

*Currently Vacant (November 23, 2010)*

- **McMaster University**

*Currently Vacant*

- **University of Toronto**

*Joseph Beyene, Prakesh Shah*

- **Queen's University**

*Phil Hahn, Tanveer Towheed*

- **University of Ottawa**

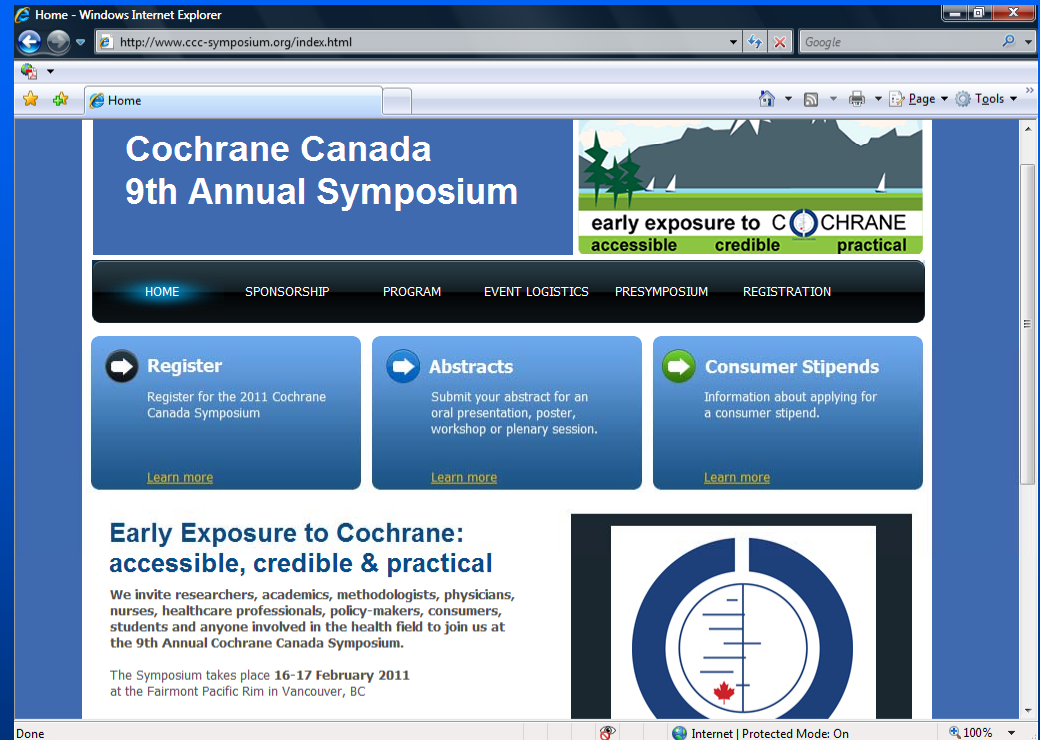
*Peter Tugwell, George Wells*

# Cochrane Colloquium

- 1993 *Oxford, United Kingdom*
- 1994 *Hamilton, Canada*
- 1995 *Oslo, Norway*
- 1996 *Adelaide, Australia*
- 1997 *Amsterdam, The Netherlands*
- 1998 *Baltimore, USA*
- 1999 *Rome, Italy*
- 2000 *Cape Town, South Africa*
- 2001 *Lyon, France*
- 2002 *Stavanger, Norway*
- 2003 *Barcelona, Spain*
- 2004 *Ottawa, Canada*
- 2005 *Melbourne, Australia*
- 2006 *Dublin, Ireland*
- 2007 *Sao Paulo, Brazil*
- 2008 *Freiburg, Germany*
- 2009 *Singapore*
- 2010 *Keystone, Colorado, USA*
- 2011 *Madrid, Spain (19-22 October)*
- 2012 *Nanning, China*

# Cochrane Symposia (Canada)

- 1999 Hamilton
- 2001 Edmonton
- 2003 Hamilton
- 2005 Montreal
- 2007 Ottawa
- 2008 Edmonton
- 2009 Halifax
- 2010 Ottawa
- 2011 Vancouver



# Casa (House) Battlo (1904)

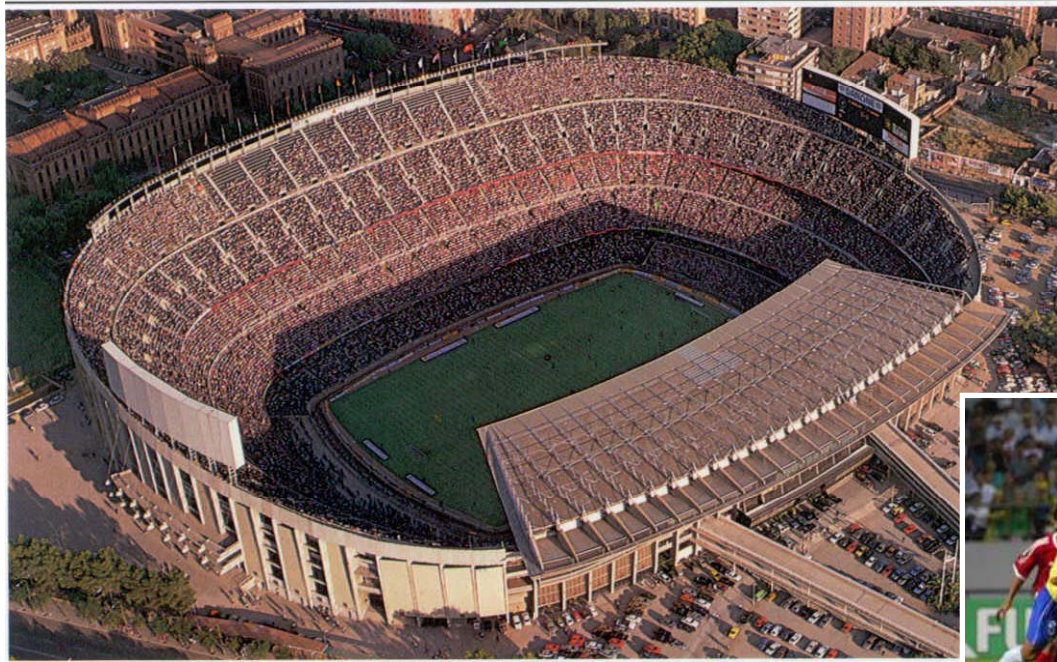
*Architect Antoni Gaudi*



# Barcelona 2003

Ronaldinho

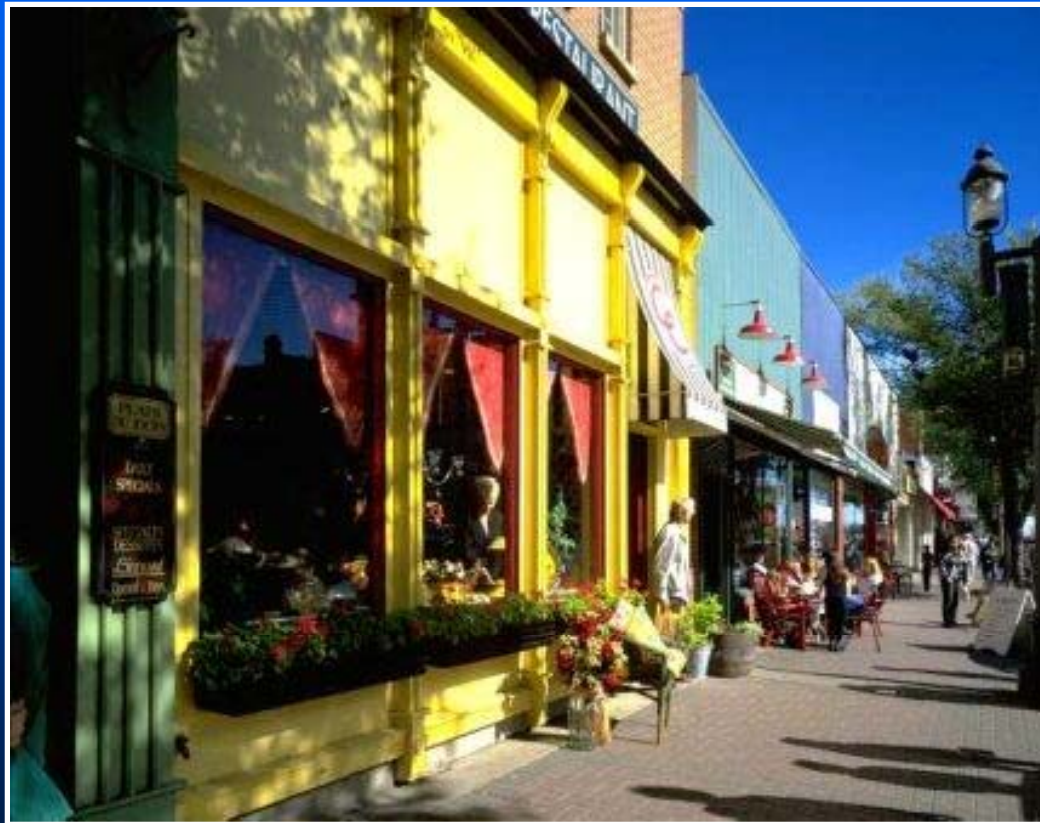
**Estadi F.C. Barcelona**



***F.C. Barcelona (3)  
Real Murcia (0)***



# Whyte Avenue: Old Stathcona



Coffee Shops  
Pubs  
Boutiques  
Book Stores  
Antiques  
People

Edmonton 2008



# Systematic Review

- **Involves the application of scientific strategies, in ways that limit bias, to the assembly, critical appraisal, and synthesis of all relevant studies that address a specific clinical question.**

**Deborah Cook et al.**

**Systematic Reviews: Synthesis of Best Evidence for Clinical Decisions. Annals of Internal Medicine 1997;126:376-380.**

# Meta-analysis

- Type of systematic review that uses statistical methods to combine and summarize the results.

Deborah Cook et al.

Systematic Reviews: Synthesis of Best Evidence for Clinical Decisions. *Annals of Internal Medicine* 1997;126:376-380.

# Narrative Review

- A summary of research that lacks explicit descriptions of systematic methods.
- Deal with a broad range of issues related to a topic rather than a specific clinical question.
- Summary is most often qualitative (no overall effect size).

Deborah Cook et al.

Systematic Reviews: Synthesis of Best Evidence for Clinical Decisions. *Annals of Internal Medicine* 1997;126:376-380.

# Systematic Review... 5 Steps

1. State objective as a focused clinical question.

Three parts:

1. *A patient with a problem*
2. *An intervention or exposure (compared to)*
3. *An outcome*

# Systematic Review... 5 Steps

1. State objective as a focused clinical question.

## Example:

1. *In women expected to deliver preterm*
2. *do corticosteroids (compared to) placebo*
3. *reduce the incidence of infant mortality and RDS?*

# Systematic Review

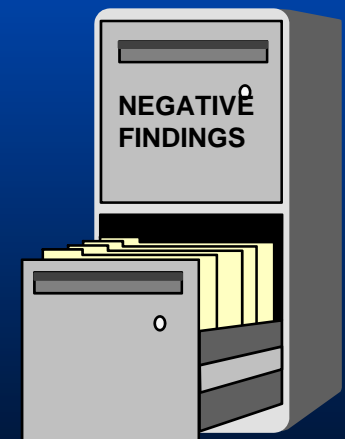
## 2. Apply eligibility criteria.

- *Randomized trials only*
- *Corticosteroid drugs*
- *Women expected to deliver preterm as a result of:*
  - *spontaneous preterm labour*
  - *prelabour rupture of the membranes preterm*
  - *elective preterm delivery.*

# Systematic Review

## 3. Search for all studies that meet criteria.

- *Electronic literature search (Medline, Embase)*
- *Hand-search journals*
- *Contact researchers directly for unpublished studies (publication bias)*



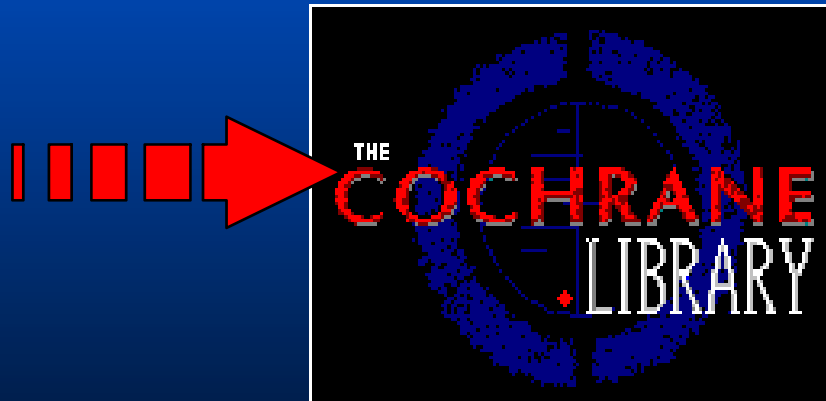
# Systematic Review

4. Synthesize the results with a meta-analysis (if appropriate)

*Using Review Manager (RevMan)*

# Systematic Review

5. Prepare a structured report for inclusion into the Cochrane Database of Systematic Reviews



Updated every 3 months

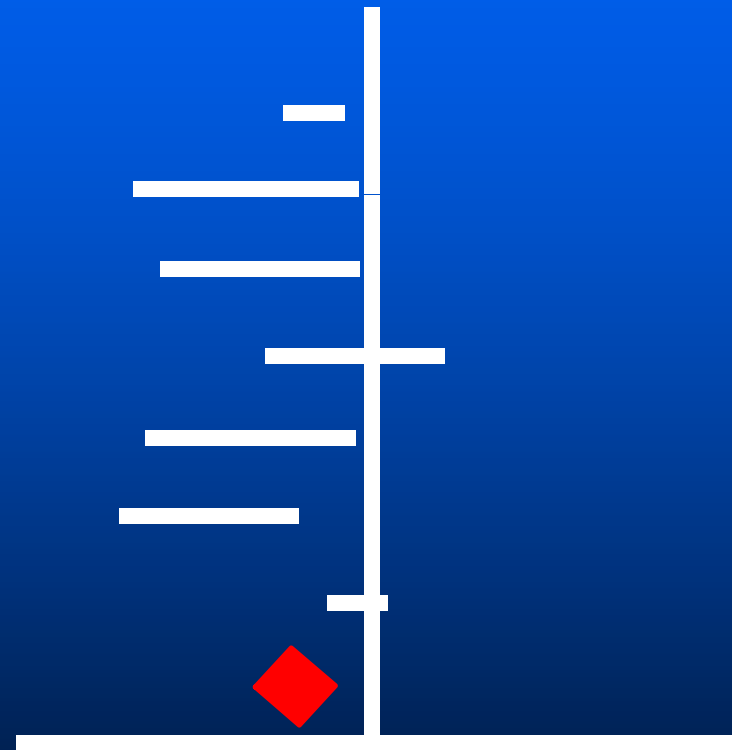
# What's in The Cochrane Library?

Issue 4, 2009

- **Cochrane Database of Systematic Reviews**
  - 4,027 complete reviews
  - 1,906 protocols
- **Database of Abstracts of Reviews of Effects (DARE)**  
(Other reviews in the literature. Quality-assessed.)
  - 11,447 structured abstract / commentary
- **Controlled Trials Register**
  - 600,472 abstracts



# Presentation of Results



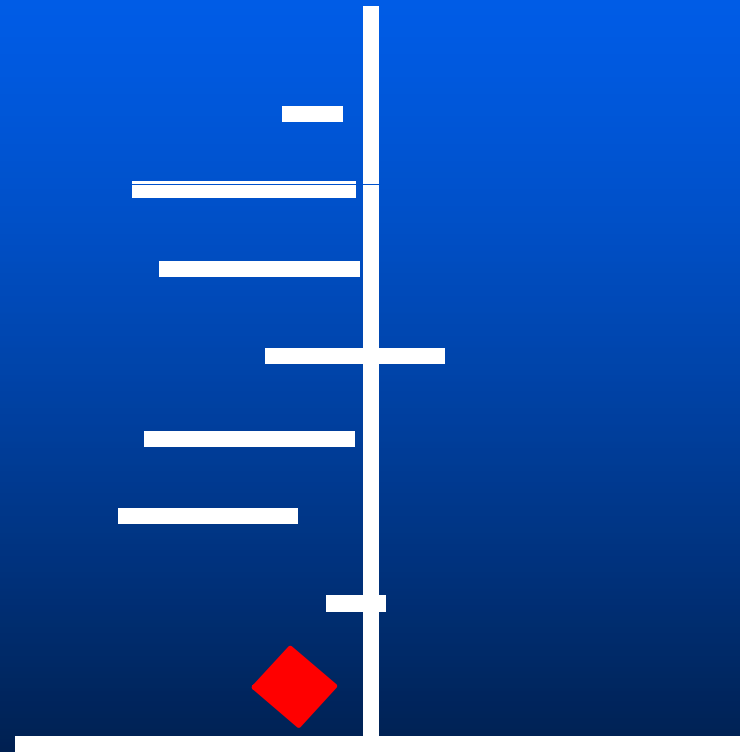
# 7 RCTs: Corticosteroids for Preterm Delivery

## Outcome: Neonatal Death

Each horizontal line represents the results of one trial.

The shorter the line the more certain the estimate.

The diamond represents the pooled results.



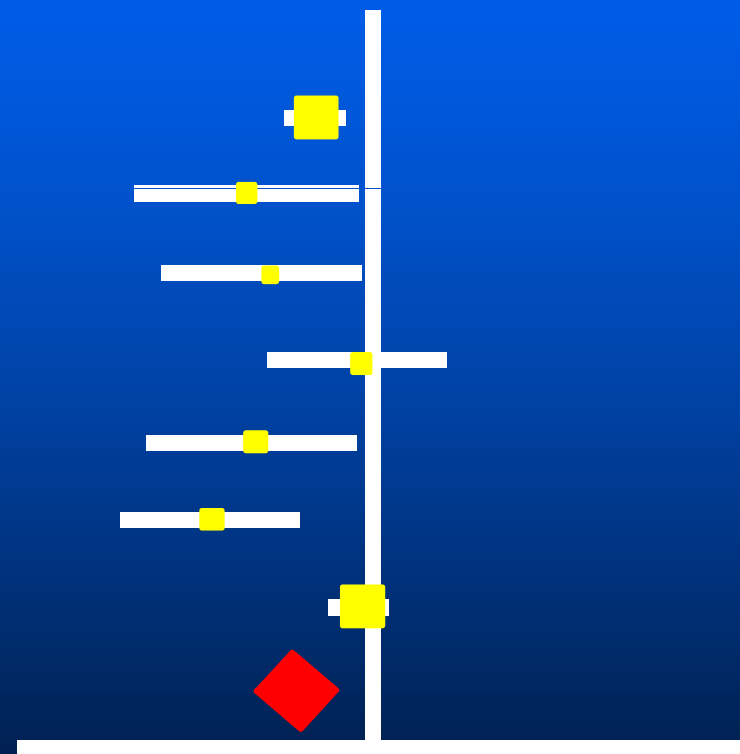
# 7 RCTs: Corticosteroids for Preterm Delivery

## Outcome: Neonatal Death

Centre of horizontal line is the point estimate - Odds ratio.

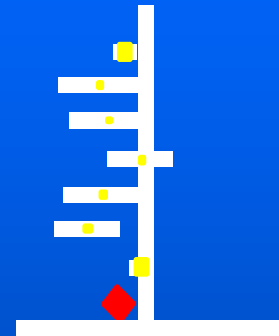
Size of square - Sample size.

The length of the horizontal line represents the 95% CI.



# 7 RCTs: Corticosteroids for Preterm Delivery

## Outcome: Neonatal Death



Odds Ratio (OR)

$$\text{OR} = \frac{\text{odds of an event (death) in treatment group}}{\text{odds of an event (death) in control group}}$$

$$\text{Odds} = \frac{\text{number of times an event occurs}}{\text{number of times an event does not occur}}$$

When event rate is small (10% or less)

Odds Ratio is approximately the same as a Relative Risk.

# OR versus RR

## *Corticosteroids versus Placebo*

Group:	OUTCOME = DEATH		Total
	Yes	No	
Treatment	129	1641	1770
Control	204	1543	1747

# OR versus RR

## *Corticosteroids versus Placebo*

Group:	OUTCOME = DEATH		Total
	Yes	No	
Treatment	129	1641	1770
Control	204	1543	1747

$$RR = 129/1770 \text{ divided by } 204/1747 = 0.62$$

Incidence

7.3%

11.7%

# OR versus RR

## *Corticosteroids versus Placebo*

Group:	OUTCOME = DEATH		<del>Total</del>
	Yes	No	
Treatment	129	1641	<del>1770</del>
Control	204	1543	<del>1747</del>

**OR = 129/1641 divided by 204/1543 = 0.59**

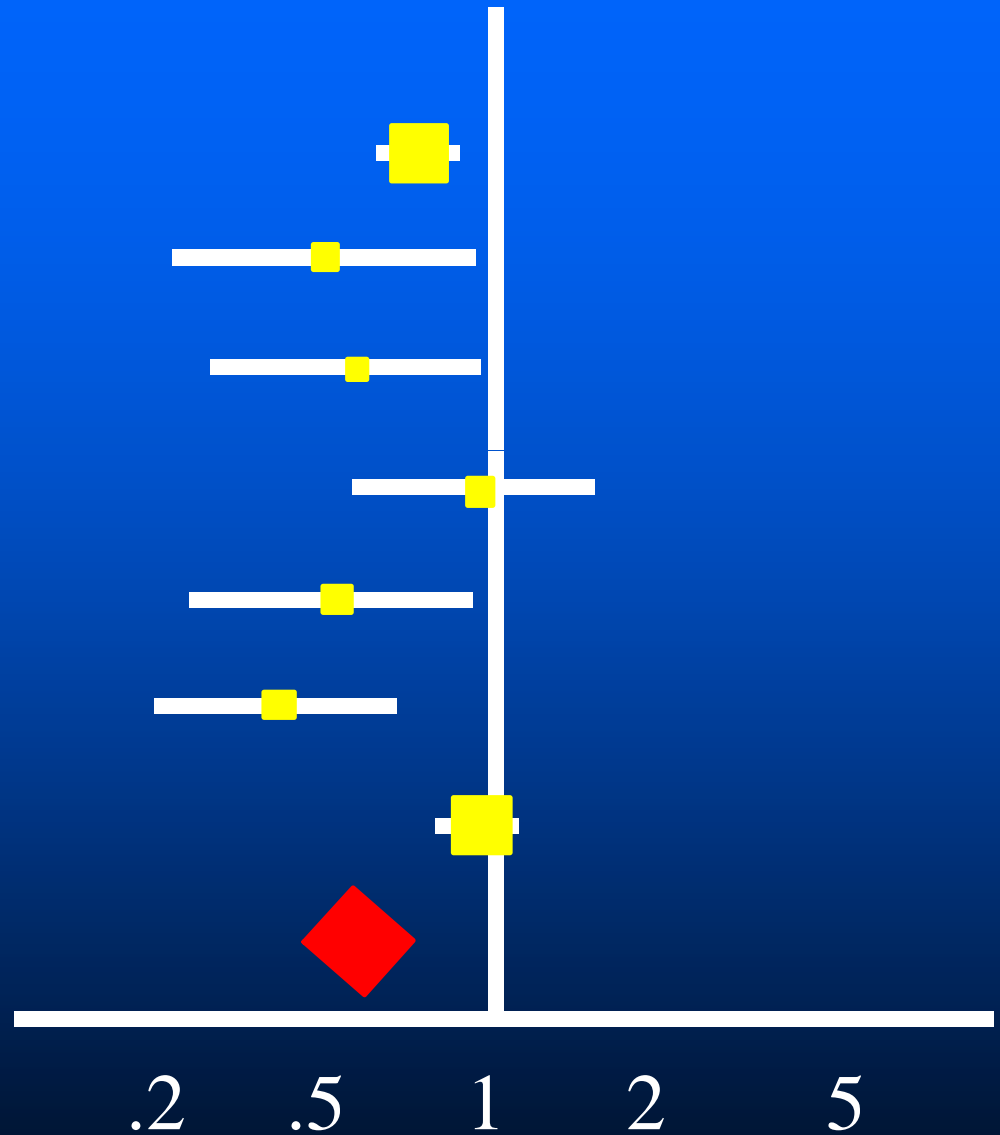
**RR = 129/1770 divided by 204/1747 = 0.62**

**(7.3%)**

**(11.7%)**

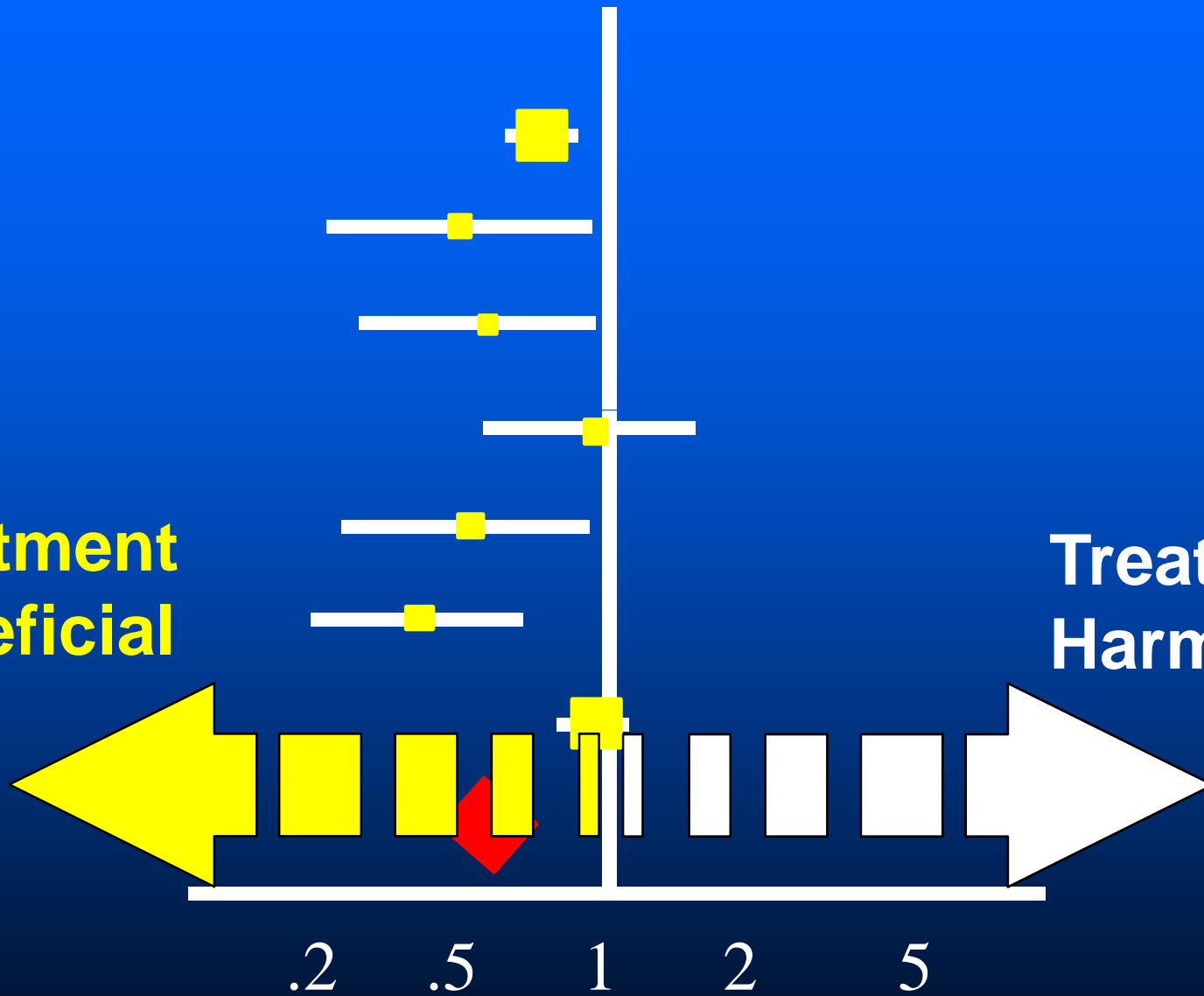
Vertical Line - Line of Unity

OR or RR = 1 (no risk)



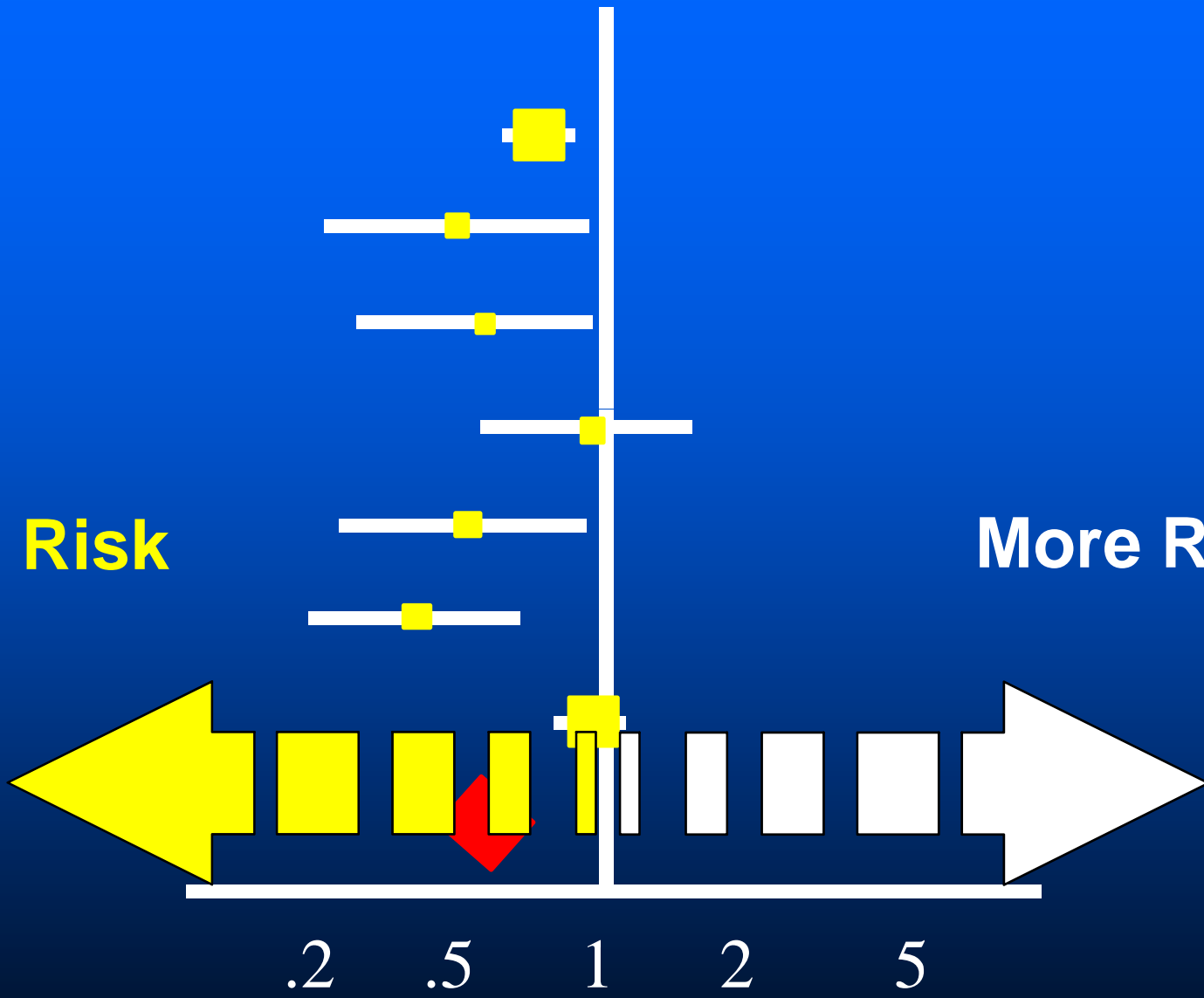
**Treatment  
Beneficial**

**Treatment  
Harmful**



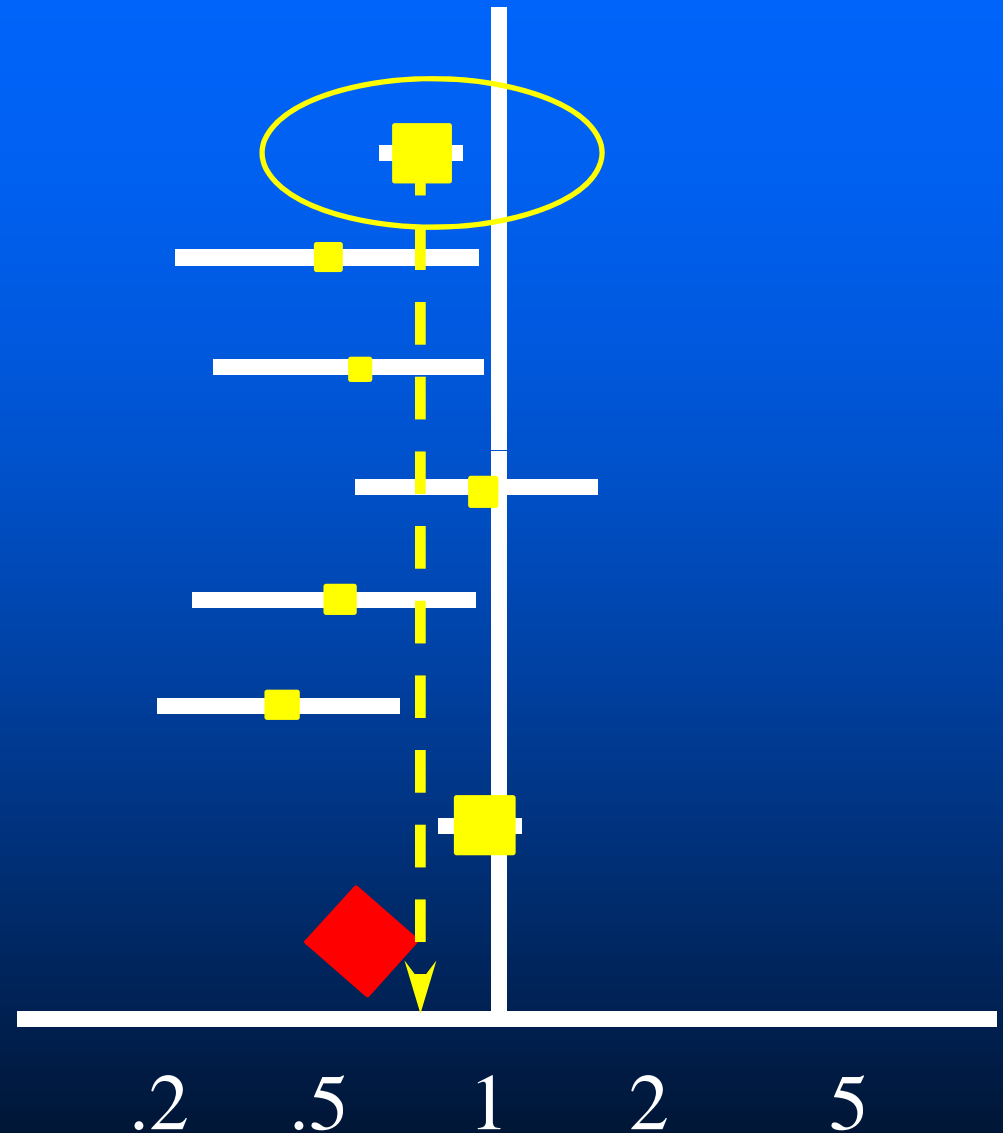
Less Risk

More Risk



# Odds ratio of 0.75

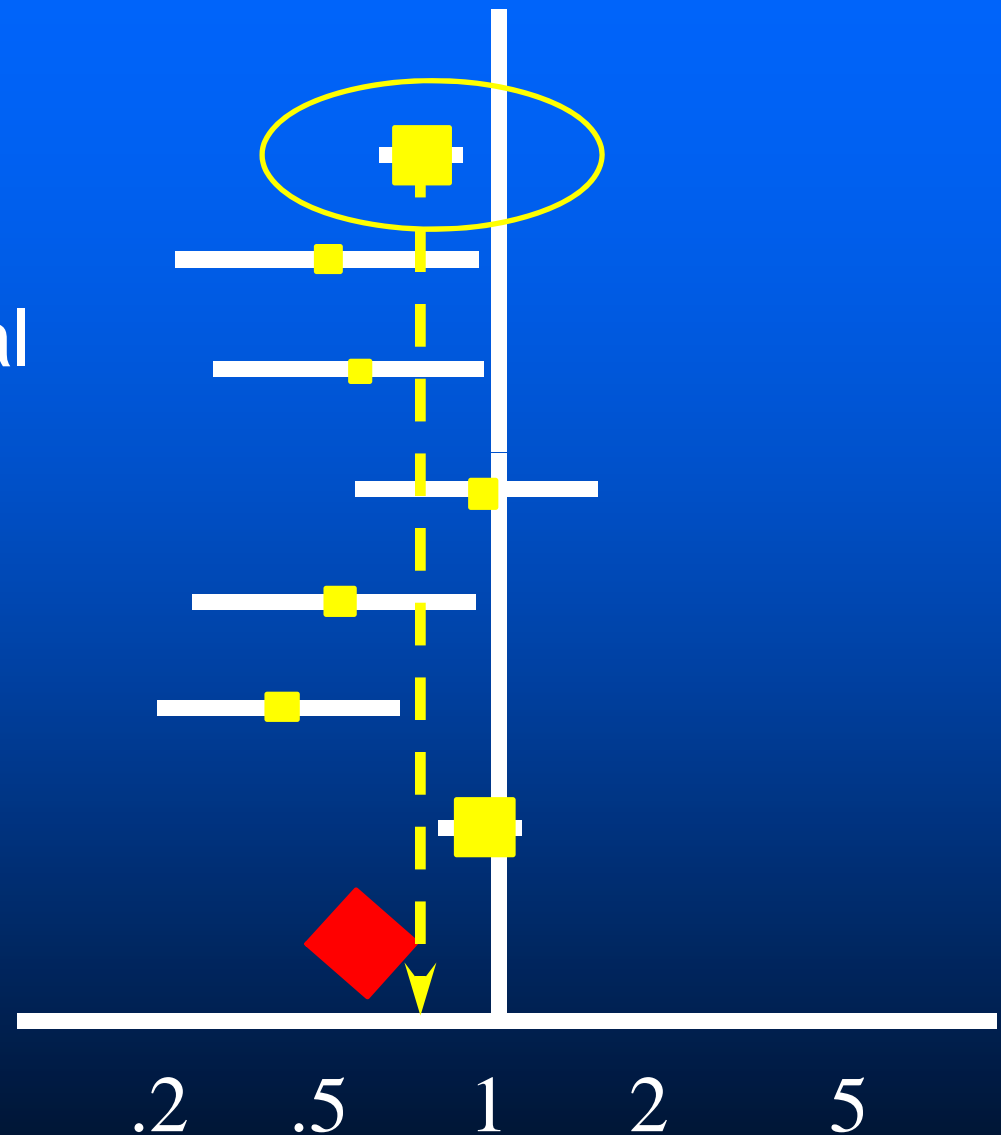
Corresponds to a 25% reduction in the odds of neonatal death attributable to corticosteroid intervention.



**Odds ratio = 0.75**

95% Confidence Interval  
does not cross 1

Result is statistically  
significant.

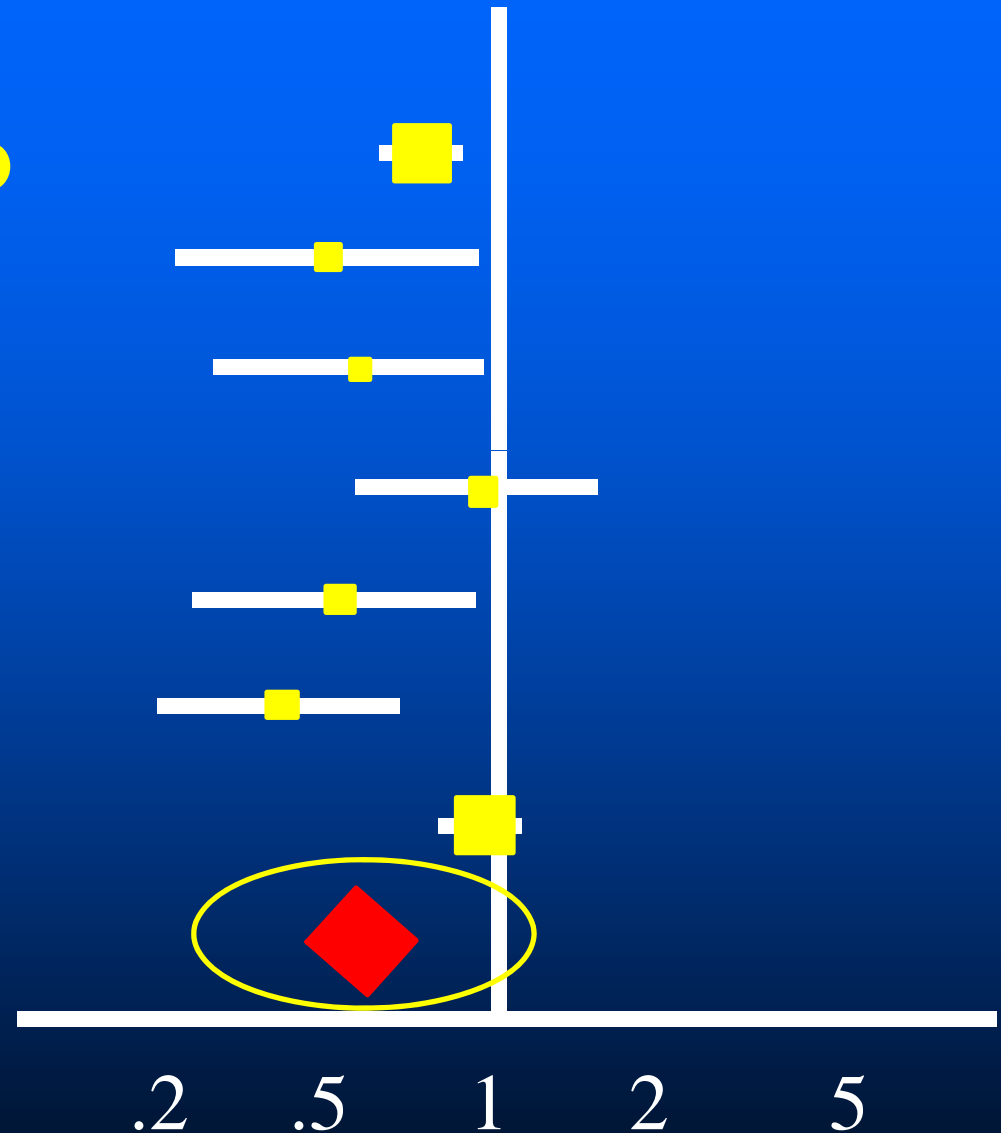


## Overall Odds Ratio

Odds ratio = 0.60

Corresponds to a 40% reduction in the odds of neonatal death.

Evidence available by 1982.



# Use of Corticosteroids prior to Preterm Delivery



- Systematic Review not published until 1989
  - Oxford Database of Perinatal Trials
- Many did not realize the treatment was so effective
  - ACOG Committee Opinion (No. 147) December 1994
  - SOGC Committee Opinion March 1995
  - ACOG Committee Opinion (No. 210) October 1998
  - ACOC Committee Opinion (No. 273) May 2003
  - SOGC Committee Opinion (No. 122) January 2003

# Cochrane Library

**The best single source of reliable evidence about the effects of health care in the world.**





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# Access to the Cochrane Library (Oct 07)

(Source, March 26, 2008: Mary Ellen Schaafma: Executive Director, CCN/C)

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Ecuador Algeria Cuba Honduras Poland Congo, R & DR  
Argentina Djibouti Panama Ghana Togo Cameroon Haiti Peru  
Guatemala Jamaica Dominican Rep Nigeria Sao Tome & Principe Liberia  
Somalia Armenia Mauritania St. Kitts and Nevis Bhutan Myanmar Dominica Azerbaijan  
Zambia Nepal El Salvador The Bahamas Sierra Leone Turkmenistan  
St. Vincent and The Grenadines Barbados India Kenya Netherland Antilles England Chile  
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Benin Benin Scotland Timor-Leste Mozambique Mongolia Colombia  
Bolivia Senegal Vietnam Mali Paraguay Sweden Yemen, Rep  
Georgia Nicaragua Virgin Islands Guyana Mexico Kiribati Sweden Finland  
Suriname Uzbekistan Cote D'Ivoire Bangladesh Mexico Kiribati Tajikistan Cambodia  
Wyoming

# Questions?

