

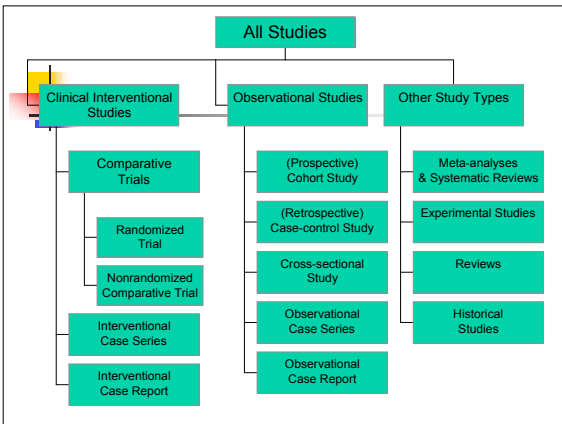
Meta-analysis

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Meta-analysis

(Customarily now refers only to analysis of randomized trials)
(Systematic review = analysis of all available publications)

- The process of using statistical methods to combine results of randomized trials, which individually may not demonstrate statistically significant differences between study groups, to derive more clear trends.
[critically dependent on quality of collected studies & bias control]





The Cochrane Collaboration is an international non-profit organization that aims to help people make well-informed decisions about healthcare by preparing, maintaining and promoting the accessibility of "systematic reviews" of the effects of healthcare interventions

What does the Cochrane Collaboration do?

- Prepare and maintain systematic reviews
- Educate investigators in performing reviews
- Contribute to Cochrane's CENTRAL database of controlled trials (~350,000)
- Build trials registers (eg, eyes and vision)
- Encourage use of Cochrane reviews

Cochrane Eyes and Vision Group

- 1 of 49 disease-specific review groups
- Editorial base at Moorfields Eye Hospital, London
- Prepare and maintain reviews of all interventions used to prevent or treat eye diseases and/or visual impairment which have been evaluated by controlled trials

How to do a Cochrane systematic review?

Select a topic and formulate a focused question


- ✓ Register the title
- ✓ Perform a comprehensive literature search
- ✓ Identify a co-reviewer (minimize bias)
- ✓ Prepare the protocol (peer review)
- ✓ Publish on *The Cochrane Library*
- ✓ Prepare the review (peer review)
- ✓ Publish on *The Cochrane Library*
- ✓ Respond to comments/criticism
- ✓ Keep the review up-to-date
- ✓ Submit for publication in journals

Protocol

- Title
- Background
- Objectives
- Criteria for including studies
- Search strategy
- Methods of the review


Literature Search

- Electronic data-bases:
 - MEDLINE
 - EMBASE
 - Cochrane Library
 - LILACS
 - Personal
- Hand Search
- Companies; manufacturers
- Published & unpublished




The Review = The protocol +...

- Description of studies
- Methodological quality
- Results
- Discussion
- Reviewers conclusions...
 - Implications for practice and research



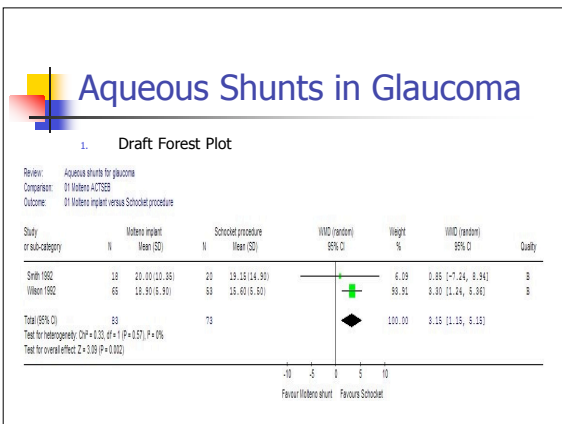
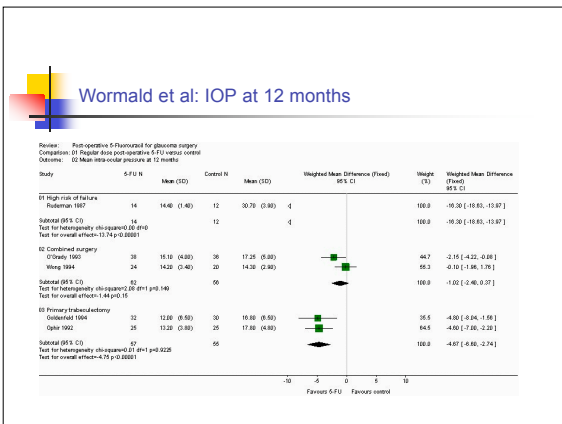
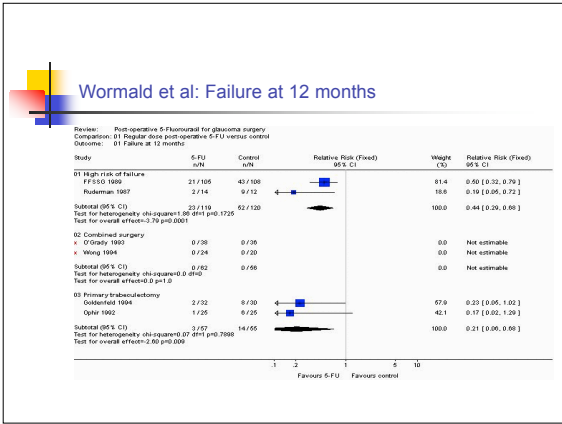
Principal Methodological Issues (Biases) considered across collected publications

- Selection Bias (concealment of allocation)
- Performance Bias (masking of providers?)
- Detection Bias (evaluators masked?)
- Attrition Bias (follow-up & compliance similar in control & study groups?)



After protocol....

- Assess search results
- Assess quality of studies
- Extract data
- Contacting trialists
- Data entry (RevMan)
- Summarize results
- Sensitivity analyses
- Final report





Aqueous Shunts in Glaucoma

Example: Comparing baseline and final IOP values

Double-plate Molteno vs. Schocket

- Wilson RP, Cantor L, Katz LJ, Schmidt CM, Steinmann WC, Allee S. Aqueous shunts, Molteno versus Schocket. Ophthalmology 1992;99:672-678.
(included mean IOP at baseline & six months with SD)
- Smith MF, Sherwood MB, McGorray SP. Comparison of the double-plate Molteno drainage implant with the Schocket procedure. Arch Ophthalmol 1992;110:1246-1250.
(provided mean change in IOP & SD but no follow-up time)

How to pool data?

- Estimate SD for mean change in IOP for two groups in Wilson 1992.



Aqueous Shunts in Glaucoma

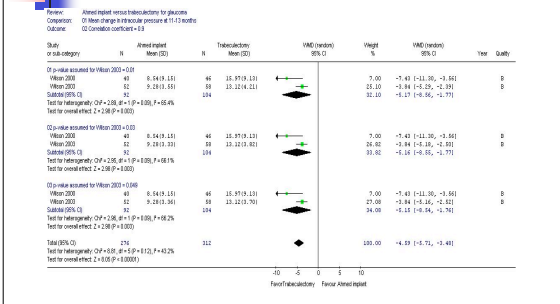
(Ahmed vs Trabeculectomy)

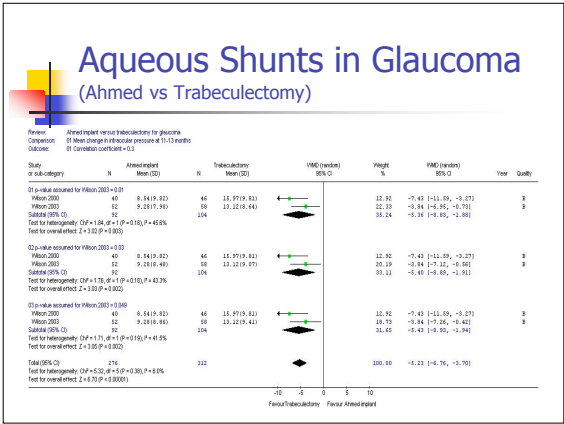
- Wilson MR, Mendis U, Paliwal A, Haynatzka V. Long-term follow-up of primary glaucoma surgery with Ahmed glaucoma valve implant versus trabeculectomy. American Journal of Ophthalmology 2003;136:464-470.
- Wilson MR, Mendis U, Smith SD, Paliwal A. Ahmed glaucoma valve implant vs trabeculectomy in the surgical treatment of glaucoma: A randomized clinical trial. American Journal of Ophthalmology 2000;130:267-273.



Aqueous Shunts in Glaucoma

(Ahmed vs Trabeculectomy)





- ## Meta-analysis
- Advantage
 - Increased statistical power across small studies
 - Disadvantages
 - Publication bias (published/unpublished)
 - Variations in quality of available/selected studies
 - Important individual issues may be masked by synthesis of data
 - Lack of uniform standards (terminology, methodology, data-analysis)

- ## Lack of Standard Terminology/concepts Re: Aqueous Shunt RCTs (and all other glaucoma topics)
- Definitions of Success/Failure
 - Small numbers of cases (without sample size/power statements)
 - Variable randomization methods; random number tables best; quasi-randomization: alternating assignments; coin toss
 - Unclear statements about "ITT" vs. "as treated" analysis; variable accounting for loss to follow-up
 - Variable follow-up intervals (12 weeks - years); lack of individual-specific IOP data in favor of summary graphs; survival curves; data plots
 - Group analyses less useful than individual-specific data for meta-analysis
 - Incomplete (inconsistent) Demographics
