EVIDENCE APPRAISAL CONTENT

Evidence-Appraisal Boot Camp

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Roughly half (the best part) of this course was initially developed by Mike Allan,
Practical Evidence for Informed Practice,
ACFP, U of A Dept of Family Med

For Course Material Please Go To
https://therapeuticseducation.org/boot-camp

Course Material

1. Evidence Appraisal Content
2. Evidence Appraisal Work Book

For Course Material Please Go To
https://therapeuticseducation.org/boot-camp

The Schedule

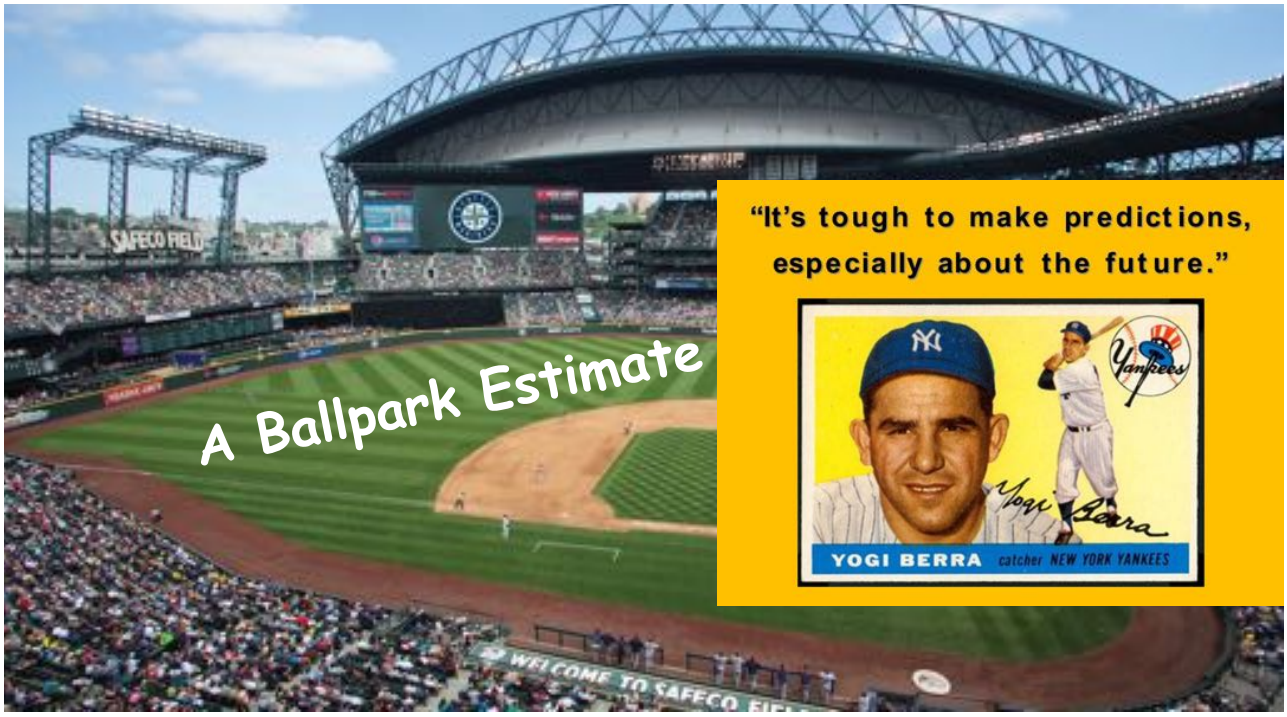
- Welcome and philosophy
- How to critically appraise an RCT in 10 minutes
- You do “it” - in pairs
- Homework review
- Meta-analyses
- Numbers, numbers, numbers workbook
- Lunch
- Meta-analysis workbook
- Please ask questions at any time - this is your chance to make mistakes/have things clarified/ OK to go off topic somewhat

Healthcare should be all about
Figuring out AND Explaining about

The Chance of Something Happening
WITH NO TREATMENT
VS
The Chance of Something Happening
WITH TREATMENT

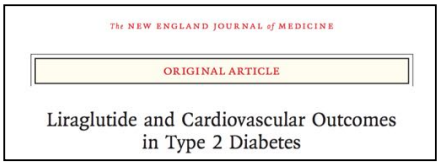
over a period of time

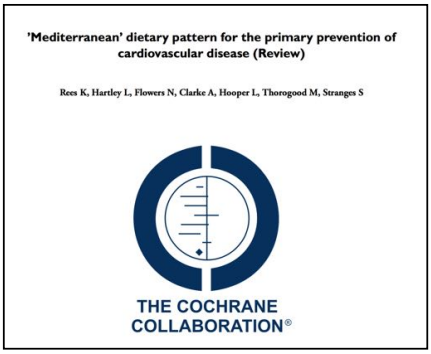
It's really THAT simple

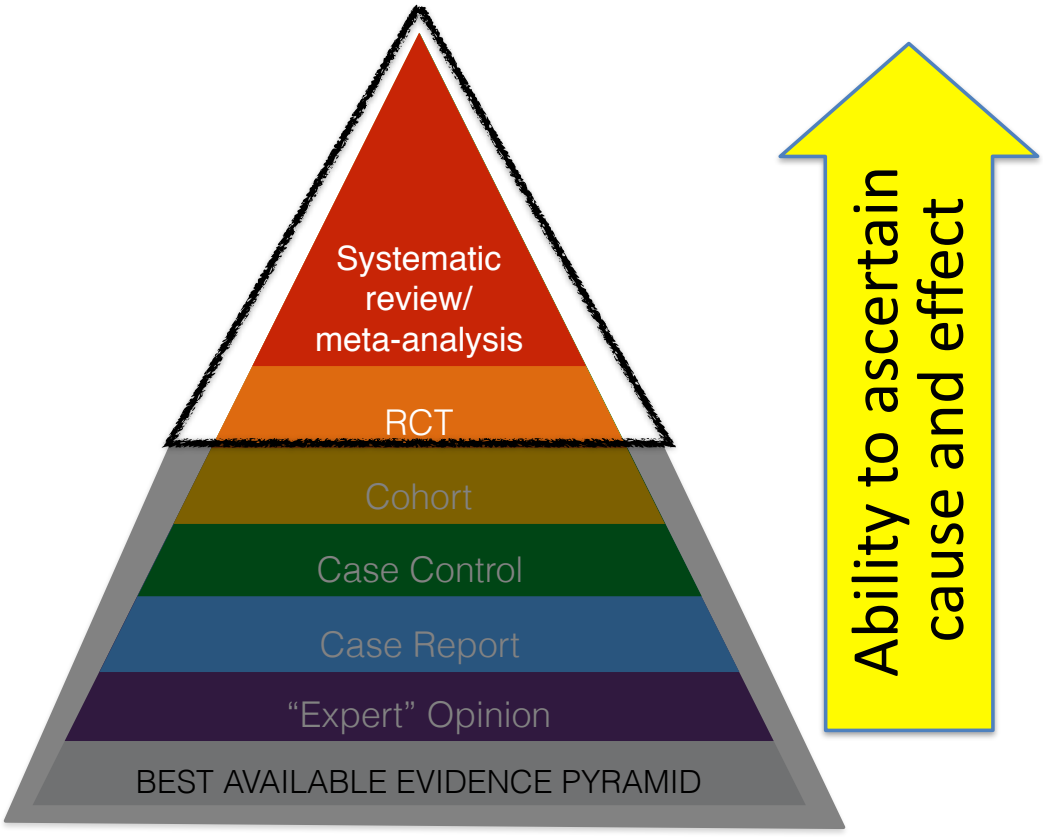


Trials almost never include people exactly like the person in front of you - genetic mongrels
All results from individual trials or meta-analyses are by definition ballpark estimates

PHAR 131/231 OVERALL COURSE OBJECTIVE
Develop Your Ability to Assess Health Claims







Need different evidence for different questions

It’s a Mindset

SCIENCE: NOT JUST FOR SCIENTISTS

We believe *that science is a human endeavour; it’s a way to ask questions about the world and test them out. It’s not just a list of facts;* ***it’s a mindset*** *owned by anyone who approaches the world in an* ***open-minded, sceptical, logical, systematic, empirically-oriented, tentative and curious way.*** *It applies in the natural and social sciences, as well as technology, engineering and mathematics.*

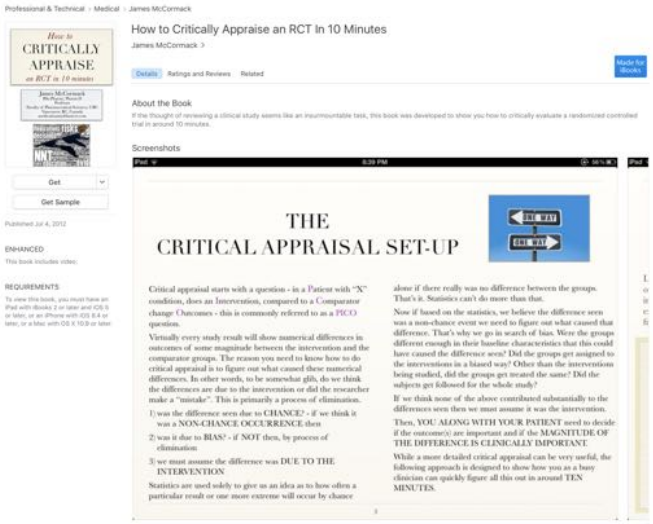
EVIDENCE APPRAISAL CONTENT

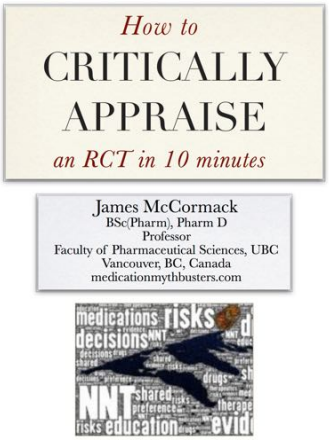
How To Critically Appraise

an RCT in 10 minutes

http://wiki.ubc.ca/Evidence_Appraisal_Integrated_Activities

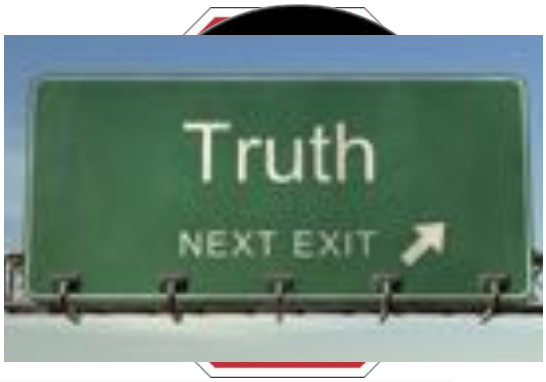
Links to a free iBook or pdf of this section





Effects of Intensive Glucose Lowering in Type 2 Diabetes

The Action to Control Cardiovascular Risk in Diabetes Study Group*



ABSTRACT

BACKGROUND

Epidemiologic studies have shown a relationship between glycated hemoglobin levels and cardiovascular events in patients with type 2 diabetes. We investigated whether intensive therapy to target normal glycated hemoglobin levels would reduce cardiovascular events in patients with type 2 diabetes who had either established cardiovascular disease or additional cardiovascular risk factors.

METHODS

In this randomized study, 10,251 patients (mean age, 62.2 years) with a median glycated hemoglobin level of 8.1% were assigned to receive intensive therapy (targeting a glycated hemoglobin level below 6.0%) or standard therapy (targeting a level from 7.0 to 7.9%). Of these patients, 38% were women, and 35% had had a previous cardiovascular event. The primary outcome was a composite of nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes. The finding of therapy after a mean of 3.5 years of follow-up.

therapy group (hazard ratio, 1.22; 95% CI, 1.01 to 1.46; P=0.04). Hypoglycemia requiring assistance and weight gain of more than 10 kg were more frequent in the intensive-therapy group (P<0.001).

CONCLUSIONS

As compared with standard therapy, the use of intensive therapy to target normal glycated hemoglobin levels for 3.5 years increased mortality and did not significantly reduce major cardiovascular events. These findings identify a previously

Let's recap

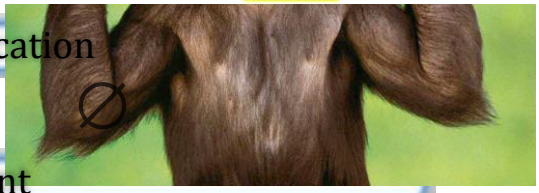
- Look at the Abstract
- Read the title
- Look at what was studied
- Look at the outcomes
- Read the conclusions

random

All 10,251 patients were randomly assigned

blind

premature death, blindness, kidney failure



allocation

∅

intent

✗

?

Analyses of primary and secondary outcomes were performed with the use of time-to-event methods according to the intention-to-treat principle, and occurrences of these outcomes in the

follow

✓

of patients within the previous 12 months; 50 patients (0.5%, including 26 patients in the intensive-therapy group and 24 in the standard-therapy group) were lost to follow-up, and 162 patients

✓

Supported by grants (N01-HC-95178, N01-HC-95179, N01-HC-95180, N01-HC-95181, N01-HC-95182, N01-HC-95183, N01-HC-95184, IAA-Y1-HC-9035, and IAA-Y1-HC-1020) from the National Heart, Lung, and Blood Institute; by other components of the National Institutes of Health, including the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute on Aging, and the National Eye Institute; by the

Abbott, GE Healthcare, SOLVAY, ALLERGAN, gsk, Roche, Baxter, JANSSEN PHARMACEUTICAL LTD, sanofi aventis, BD, MERCK SHARP & DOHME, Boots, NOVARTIS, SCHWARZ PHARMA, élan, Pfizer, Bristol-Myers Squibb, Lilly, Schering-Plough, Wyeth

tis, King, Takeda, and Sanofi-Aventis, lecture fees from Novartis, and grant support from Novartis, Hamilton Health, and Abbott; Dr. Genuth, receiving consulting fees from Merck, Mannkind, Sanofi-Aventis, and Novartis and lecture fees from Lilly and having an equity interest in Bristol-Myers Squibb; Dr. Grimm, receiving lecture fees from Merck, Pfizer, and Novartis; and Dr. Probstfield, receiving consulting fees from King and grant support from King and Sanofi-Aventis. No other potential conflict of interest relevant to this article was reported.

Primarily funded by the National Institutes of Health

Let's recap

- Randomized
- Blinded
- Allocation concealment
- Intention to treat
- Follow-up
- Conflicts of interest

MUCH OF THE REST OF THE TEXT

- INTRODUCTION
- "MOST" OF THE METHODS
- STATISTICAL TESTS
- DISCUSSION

Patient Characteristics

Table 1. Characteristics of the Patients at Baseline.*

Variable	Intensive Therapy (N=5128)	Standard Therapy (N=5123)
Age (yr)	62.2±6.8	62.2±6.8
Female sex (%)	38	38
Median duration of diabetes (yr)	10	10
Previous cardiovascular event (%)	35.6	34.8
Previous congestive heart failure (%)	4.9	4.8
Race or ethnic group (%) †		
White	64.4	64.5
Black	19.7	18.9
Hispanic	7.0	7.4
Education (%)		
Less than high school	15.7	14.0
High-school graduate	26.1	26.7
Some college	32.7	32.9
College degree or higher	25.5	26.4
Cigarette-smoking status (%)		
Current	14.3	13.7
Former	44.4	44.0
Never	41.3	42.3
Weight (kg)	93.5±18.7	93.6±18.7
Body-mass index	32.2±5.5	32.2±5.5
Waist circumference (cm)	106.8±14.5	106.8±13.8
Blood pressure (mm Hg)		
Systolic	136.2±17.0	136.5±17.2
Diastolic	74.8±10.6	75.0±10.7
Medications (%)		
Insulin	34.1	35.7
Metformin	59.7	60.0
Any sulfonylurea	50.8	49.4
Any thiazolidinedione	19.5	19.2
Any antihypertensive agent	84.9	86.0
Angiotensin-converting-enzyme inhibitor	53.0	53.0
Aspirin	54.8	54.1
Beta-blocker	28.7	29.9
Any thiazide diuretic	26.5	26.4
Statin	61.7	62.4
Glycated hemoglobin (%)		
Mean	8.3±1.1	8.3±1.1
Median	8.1	8.1
Fasting serum glucose (mg/dl)	174.9±56.0	175.7±56.5
Cholesterol (mg/dl)		
Total	183.3±42.1	183.3±43.4
Low-density lipoprotein	104.9±34.0	104.9±33.8
High-density lipoprotein		
Women	47.2±13.0	46.9±12.2
Men	38.4±9.5	38.8±9.8
Median triglyceride (mg/dl)	156	154

No "clinical" differences

N = 5,100

Age 62
Female 38%
Diabetes 10 years
Previous CV event 35%
White 65%
Smoker 14%
BMI 32
BP 136/75
A1C 8.3%
Total Chol 183 or 4.7

Let's recap

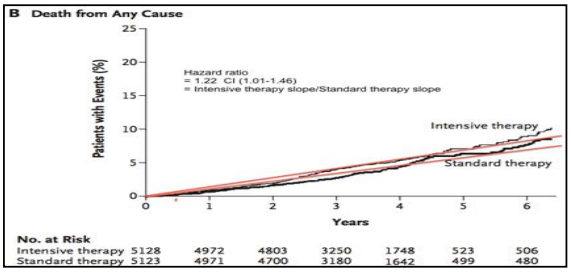
- Differences between groups
- Baseline characteristics

Similar but different relatives

Relative risk/risk ratio (RR) - ratio of two probabilities (%) at one point in time - treatment/control

- eg 8% vs 10% - RR = 8/10 = 0.8
- most useful in low probability events

Hazards ratio (HR) - ratio of two hazard rates (slopes) over a time period



Odds ratio (OR) - ratio of two odds (25/1) - typically used in case-control studies - typically the incidence is not known

OR is a reasonable estimate of the **RR** if a disease is "rare" <~15% but treating an **OR** as if it were an accurate estimate of the **RR** will typically overestimate both the likely benefits and harms of treatment

Main Patient Outcomes

Table 4. Primary and Secondary Outcomes.*

Outcome	A1c = 6.4% no. of patients (%)	A1c = 6.4% % per yr	A1c = 7.5% no. of patients (%)	A1c = 7.5% % per yr	Hazard Ratio (95% CI)	P Value
Primary outcome	352 (6.9)	2.11	371 (7.2)	2.29	0.90 (0.78–1.04)	0.16
Secondary outcome						
Death						
Any cause	257 (5.0)	1.41	203 (4.0)	1.14	1.22 (1.01–1.46)	0.04
Cardiovascular causes	135 (2.6)	0.79	94 (1.8)	0.56	1.33 (1.04–1.70)	0.02
Nonfatal myocardial infarction	186 (3.6)	1.11	235 (4.6)	1.45	0.76 (0.62–0.92)	0.004
Nonfatal stroke	67 (1.3)	0.39	61 (1.2)	0.37	1.06 (0.75–1.50)	0.74
Fatal or nonfatal congestive heart failure	152 (3.0)	0.90	124 (2.4)	0.75	1.18 (0.93–1.49)	0.17
Causes of death						
Any	257 (5.0)	1.41	203 (4.0)	1.14	1.22 (1.01–1.46)	0.04
Unexpected or presumed cardiovascular disease†	86 (1.7)		67 (1.3)			
Fatal myocardial infarction†	19 (0.4)		13 (0.3)			
Fatal congestive heart failure†	23 (0.4)		16 (0.3)			
Fatal procedure†						
For cardiovascular disease	10 (0.2)		3 (0.1)			
For noncardiovascular disease	1 (<0.1)		3 (0.1)			
Fatal arrhythmia†	4 (0.1)		10 (0.2)			
Fatal stroke†	9 (0.2)		11 (0.2)			
Other cardiovascular disease†	8 (0.2)		10 (0.2)			
Cancer	65 (1.3)		63 (1.2)			
Condition other than cancer or cardiovascular disease‡	50 (1.0)		35 (0.7)			
Undetermined	7 (0.1)		11 (0.2)			

Primary outcome = nonfatal myocardial infarction or nonfatal stroke or death from cardiovascular causes

	Intensive therapy	Standard therapy	Hazard Ratio	Hazard Ratio 95% CI	Relative Risk
Primary outcome (%)	6.9	7.2	0.9	0.78-1.04	0.96
Death (%)	5	4	1.22	1.01-1.46	1.25
Non-fatal MI (%)	3.6	4.6	0.76	0.62-0.92	0.78
Non-fatal stroke (%)	1.3	1.2	1.06	0.75-1.50	1.08
CHF (%)	3	2.4	1.18	0.93-1.49	1.25

Let's recap

- Primary outcomes
- Other outcomes
- Differences
  - Absolute numbers
  - Relative numbers
  - Confidence intervals

Adverse Events

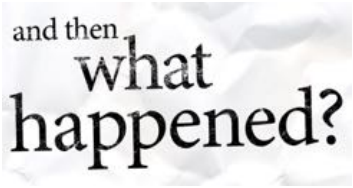


Table 3. Adverse Events, Clinical Measures, Tobacco Use, and Use of Nonglycemic Medication after Randomization.*

Variable	Intensive Therapy (N=5128)	Standard Therapy (N=5123)	P Value†
Adverse events			
Hypoglycemia — no. (%)			
Requiring medical assistance	538 (10.5)	179 (3.5)	<0.001
Requiring any assistance	830 (16.2)	261 (5.1)	<0.001
Fatal or nonfatal heart failure — no. (%)	152 (3.0)	124 (2.4)	0.10
Motor vehicle accident in which patient was driver — no./total no. (%)	9/5033 (0.2)	14/5036 (0.3)	0.40
Any nonhypoglycemic serious adverse event — no. (%)	113 (2.2)	82 (1.6)	0.03
Fluid retention — no./total no. (%)‡	3541/5053 (70.1)	3378/5054 (66.8)	<0.001
Clinical measures			
Weight gain >10 kg since baseline — no./total no. (%)	1399/5036 (27.8)	713/5042 (14.1)	<0.001
Alanine aminotransferase >3 times ULN — no./total no. (%)§	51/5065 (1.0)	77/5061 (1.5)	0.02
Low-density lipoprotein cholesterol — mg/dl¶	90.8±3		
Blood pressure — mm Hg¶			
Systolic	126.4±1		
Diastolic	66.9±1		

	Intensive therapy	Standard therapy	Hazard Ratio	Hazard Ratio 95% CI
Primary outcome (%)	6.9	7.2	0.9	0.78-1.04
Death (%)	5	4	1.22	1.01-1.46
Non-fatal MI (%)	3.6	4.6	0.76	0.62-0.92
Non-fatal stroke (%)	1.3	1.2	1.06	0.75-1.50
CHF (%)	3	2.4	1.18	0.93-1.49
Hypoglycemia (%)	10.5	3.5		
Serious adverse event	2.2	1.6		
Weight gain >10kg	27.8	14.1		

Let's recap

- Adverse outcomes
- Any other outcomes
- Differences
  - Absolute numbers
  - Relative numbers
  - Confidence intervals

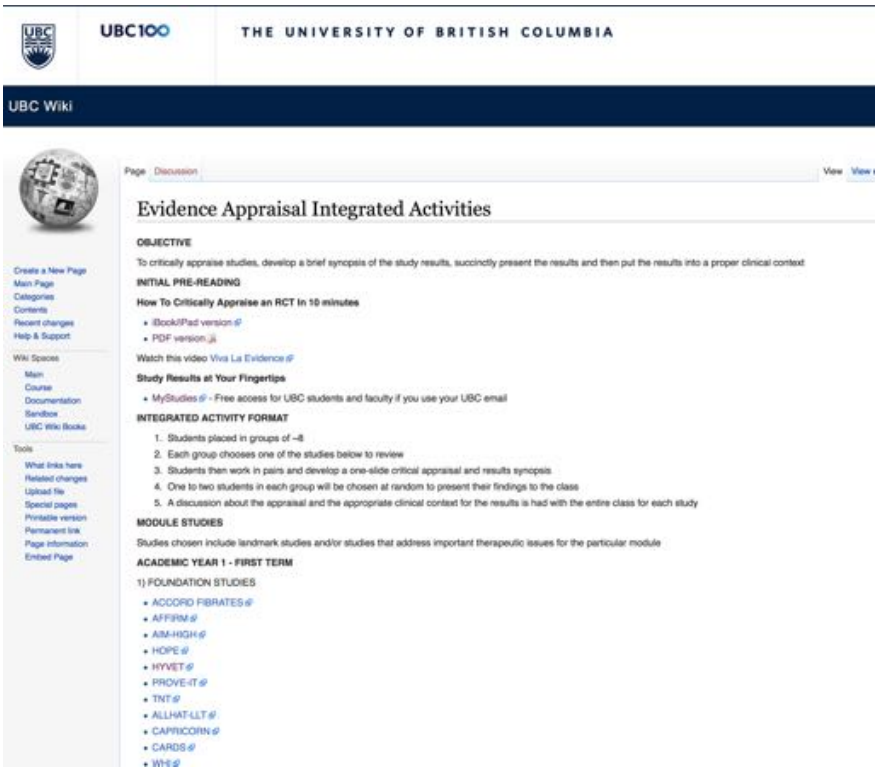
Randomised
Non-blinded
Allocation concealment?
Intention-to-treat
Follow-up

N=10,251 - 3.5 years

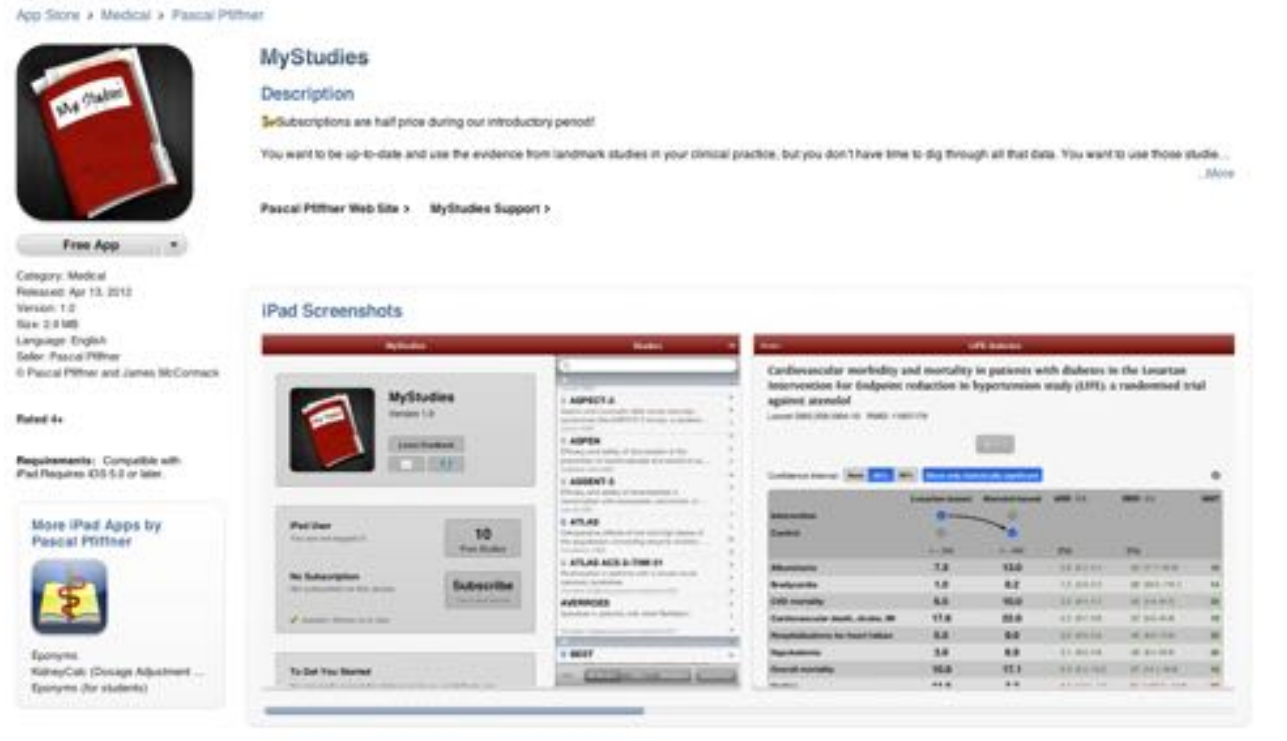
Age 62, Female 38%, Diabetes 10 years, Previous CV event 35%, White 65%, Smoker14%, BMI 32, BP136/75, A1C 8.3, Total Chol 183

	Intensive therapy	Standard therapy	Hazard Ratio	Hazard Ratio 95% CI
Primary outcome (%)	6.9	7.2	0.9	0.78-1.04
Death (%)	5	4	1.22	1.01-1.46
Non-fatal MI (%)	3.6	4.6	0.76	0.62-0.92
Non-fatal stroke (%)	1.3	1.2	1.06	0.75-1.50
CHF (%)	3	2.4	1.18	0.93-1.49
Hypoglycemia (%)	10.5	3.5		
Serious adverse event	2.2	1.6		
Weight gain >10kg	27.8	14.1		

http://wiki.ubc.ca/Evidence_Appraisal_Integrated_Activities



mystudies.org



Meta-Analysis

Meta-Analysis

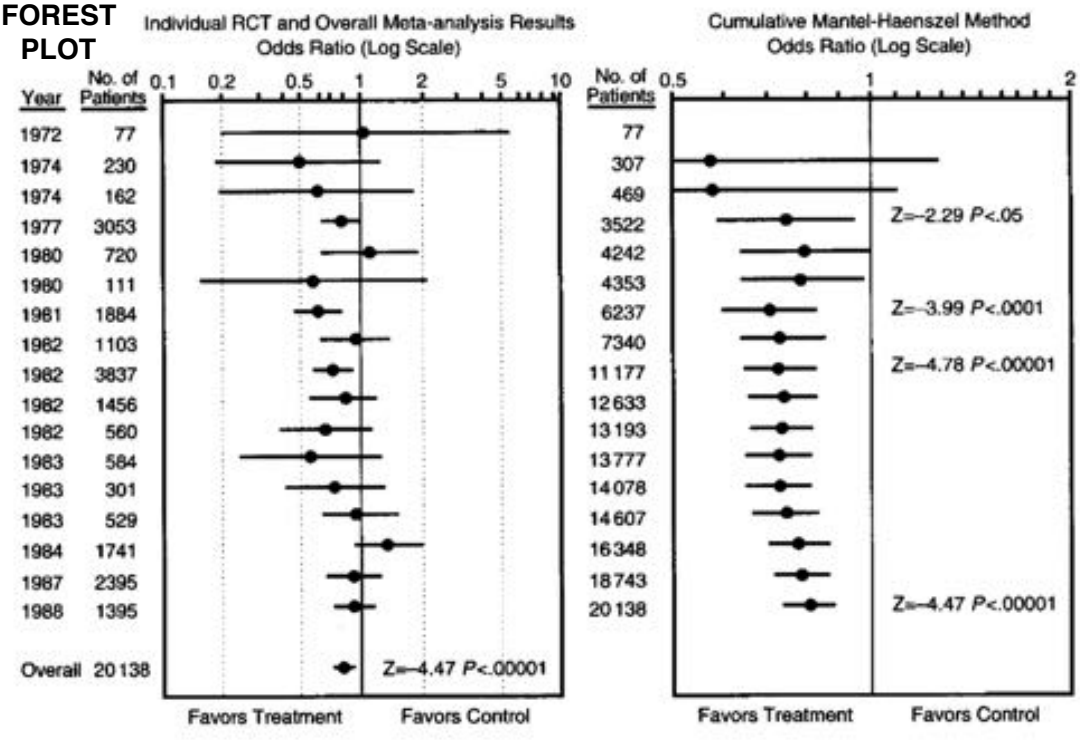
MA's "started" in 1976

Critics - "An exercise in Mega-Silliness"

"Garbage in = Garbage out"

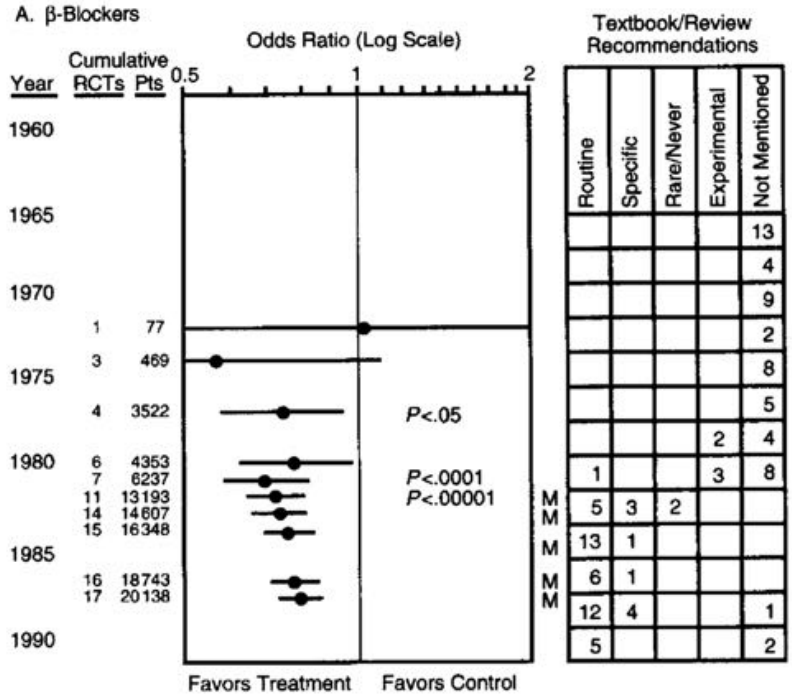
Effect of beta-blockers on mortality after a heart attack

FOREST PLOT



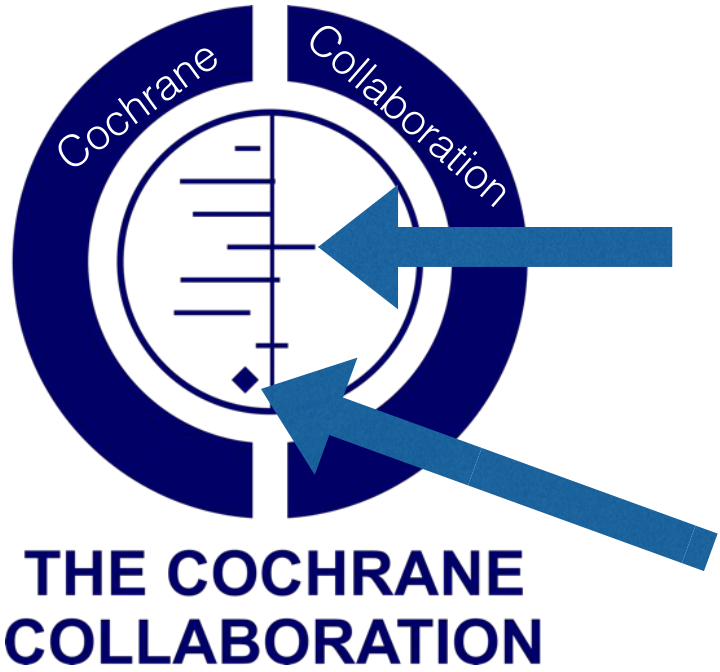
JAMA 1992;268:240-248

Effect of beta-blockers on mortality after a heart attack



JAMA 1992;268:240-248

Started in 1993



THE COCHRANE COLLABORATION

Systematic review of RCTs of a short, inexpensive course of a corticosteroid given to women about to give birth too early.
7 studies

Neonatal death reduced by 31% - RR 0.69
Absolute difference 5%

Number of Cochrane Reviews

TOTAL

2016/15	Total reviews	Total protocols	Total reviews and protocols
Issue 1 2016	6471	2460	9201
Issue 2	6791	2432	9227
Issue 3 2015	6355	2380	8735
Issue 4	6388	2411	[illegible]
Issue 5	6421	[illegible]	[illegible]
Issue 6	[illegible]	[illegible]	8901
Issue 7	[illegible]	2432	8937
Issue 8	6538	2425	8963
Issue 9	6583	2432	9017
Issue 10	6621	2429	9050
Issue 11	6670	2427	9099
Issue 12	6715	2426	9143

~7000

NEW

2016/2015	New reviews	Updated reviews	Withdrawn reviews	Conclusions changed
Issue1 2016	28	31	6	6
Issue2	49	31	[illegible]	[illegible]
Issue3 2015	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	11
Iss[illegible]	[illegible]	[illegible]	5	6
Issue[illegible]	[illegible]	35	3	11
Issue9	46	51	5	14
Issue10	37	40	9	10
Issue11	49	35	5	10
Issue12	44	35	9	6

Each issue
~35 new reviews
~35 updated
~5 withdrawn
~10 conclusions changed

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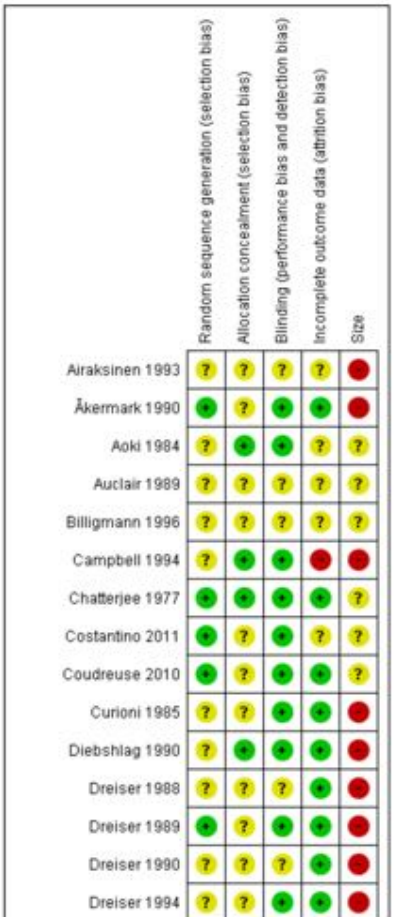
Summary of Findings

Topical NSAIDs compared with topical placebo for acute musculoskeletal pain in adults

Patient or population: adults with strains, sprains, or muscle pull
Settings: community
Intervention: topical NSAID (topical diclofenac, ibuprofen, and ketoprofen gels only shown here for efficacy)
Comparison: topical placebo

Outcomes	Probable outcome with intervention	Probable outcome with comparator	RR, NNT, NNTp, or NNH (95% CI)	No of studies, participants	Quality of the evidence (GRADE)	Comments
Topical diclofenac gel (as Emulgel) Clinical success (eg 50% reduction in pain)	780 in 1000	200 in 1000	RR 3.4 (2.7 to 55) NNT 1.8 (1.5 to 2.1)	2 studies 314 participants	High	Consistent results in 2 moderately sized recent studies of high quality
Topical ibuprofen gel Clinical success (eg 50% reduction in pain)	420 in 1000	160 in 1000	RR 2.7 (1.7 to 4.2) NNT 3.9 (2.7 to 6.7)	2 studies 241 participants	Moderate	Modest effect size and numbers of participants
Topical ketoprofen gel Clinical success (eg 50% reduction in pain)	720 in 1000	330 in 1000	RR 2.2 (1.7 to 2.8) NNT 2.5 (2.0 to 3.4)	5 studies 348 participants	Moderate	Modest effect size and numbers of participants, but studies small, with none recent
All topical NSAIDs Local adverse events	46 in 1000	50 in 1000	RR 1.0 (0.80 to 1.2) NNH not calculated	42 studies 6125 participants	High	Large number of studies and participants with consistent results
All topical NSAIDs Systemic adverse events	32 in 1000	35 in 1000	RR 1.0 (0.7 to 1.3) NNH not calculated	38 studies 5372 participants	High	Large number of studies and participants with consistent results
All topical NSAIDs Withdrawals - adverse events	11 in 1000	11 in 1000	RR 1.0 (0.7 to 1.7) NNH not calculated	42 studies 5790 participants	High	Large number of studies and participants with consistent results

Author's assessment of the risk of bias



Characteristics of Studies

WOSCOPS

Methods	Randomised trial.	
Participants	6595 men with hypercholesterolaemia based in Scotland aged 45-64 (mean age 55). < 10% with clinical evidence of CVD	
Interventions	40 mg pravastatin versus placebo; follow-up 4.9 years.	
Outcomes	Primary outcome: composite of non-fatal MI and CHD death. Single outcomes included total mortality, fatal CVD events, cholesterol, revascularisations, non-fatal MI and CHD death and adverse events	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Blocks of random numbers and treatment assigned randomly
Allocation concealment (selection bias)	Low risk	All trial personnel remained unaware of the participant's treatment assignment throughout the study
Blinding (performance bias and detection bias) All outcomes	Low risk	Double-blind: participants and personnel
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT used, 30% drop-outs reported
Selective reporting (reporting bias)	Low risk	
Other bias	Unclear risk	Funded by pharmaceutical industry

Data and Analyses

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total Mortality	13	48060	Odds Ratio (M-H, Fixed, 95% CI)	0.86 [0.79, 0.94]
2 Total Number of CHD Events	14	48049	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.67, 0.80]
3 Number of Fatal CHD Events	10	46094	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.70, 0.96]
4 Number of Non-fatal CHD Events	11	40977	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.59, 0.76]
5 Total Number of CVD Events	9	23805	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.70, 0.81]
6 Number of Fatal CVD Events	5	34012	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.72, 0.96]
7 Number of Non-fatal CVD Events	2	8696	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.62, 0.96]
8 Total Number of Stroke Events	10	40295	Risk Ratio (M-H, Fixed, 95% CI)	0.78 [0.68, 0.89]
9 Number of Fatal Stroke Events	3	27238	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.18, 2.23]
10 Number of Non-fatal Stroke Events	5	28097	Risk Ratio (M-H, Fixed, 95% CI)	0.69 [0.58, 0.83]
11 Total Number of Fatal and Non-fatal CHD, CVD and Stroke Events	4	35254	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.58, 0.73]
12 Number of Study Participants who underwent Revascularisation	7	42403	Risk Ratio (M-H, Fixed, 95% CI)	0.62 [0.54, 0.72]

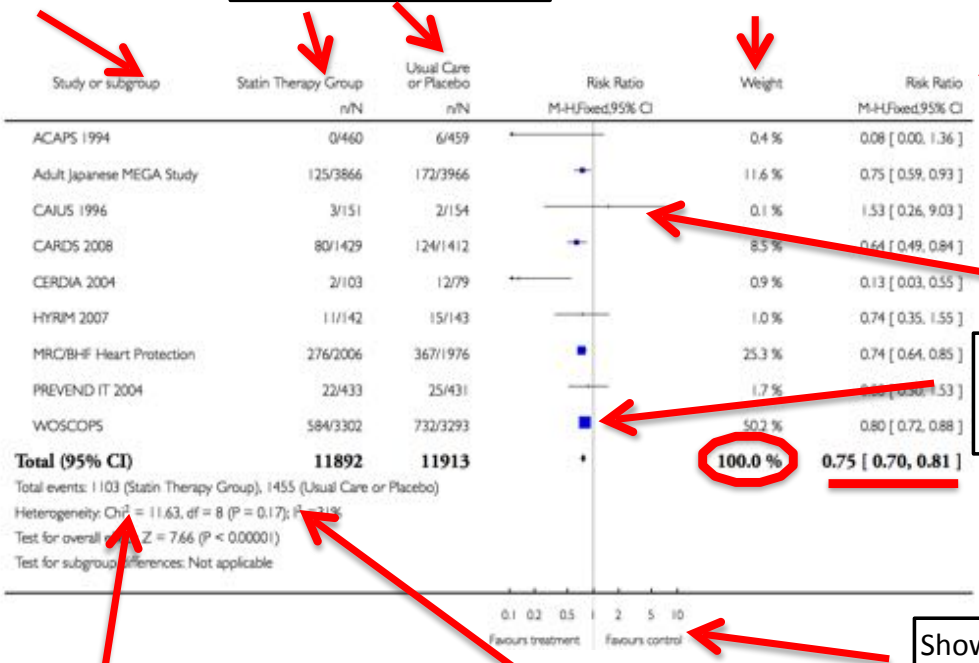
Mantel–Haenszel - statistical method
Random (assumes the studies are different) is more conservative than fixed (assumes trials are the same)

Included studies (ideally would have citation)

Includes the number of events & total included in each group

How much each study contributes (weight)

The actual (numeric) results for each study



Tiny square= small study

Big square= Big study and/or lots of events

Heterogeneity given & I^2 stat available

Final numbers of events and total included in each arm (can do "cheater" NNT)

Shows what side is "better" for treatment or control

CD004816 2013

McCormack et al. BMC Medical Research Methodology 2013, 13:134
http://www.biomedcentral.com/1471-2288/13/134

BMC Medical Research Methodology

DEBATE Open Access

How confidence intervals become confusion intervals

James McCormack[1], Ben Vandermeer[2] and G Michael Allan[3*]

BMC Medical Research Methodology 2013;13:134

Do statins reduce mortality in primary prevention?

Studer et al.: "reduced risks of overall and cardiac mortality"**YES**

Thavendiranathan et al.: [does not decrease]"overall mortality"**NO**

Mills et al.: "an important role in preventing all-cause mortality"**YES**

Brugts et al.: "associated with significantly improved survival"**YES**

Ray et al.: "did not find evidence for the benefit … on all-cause mortality"**NO**

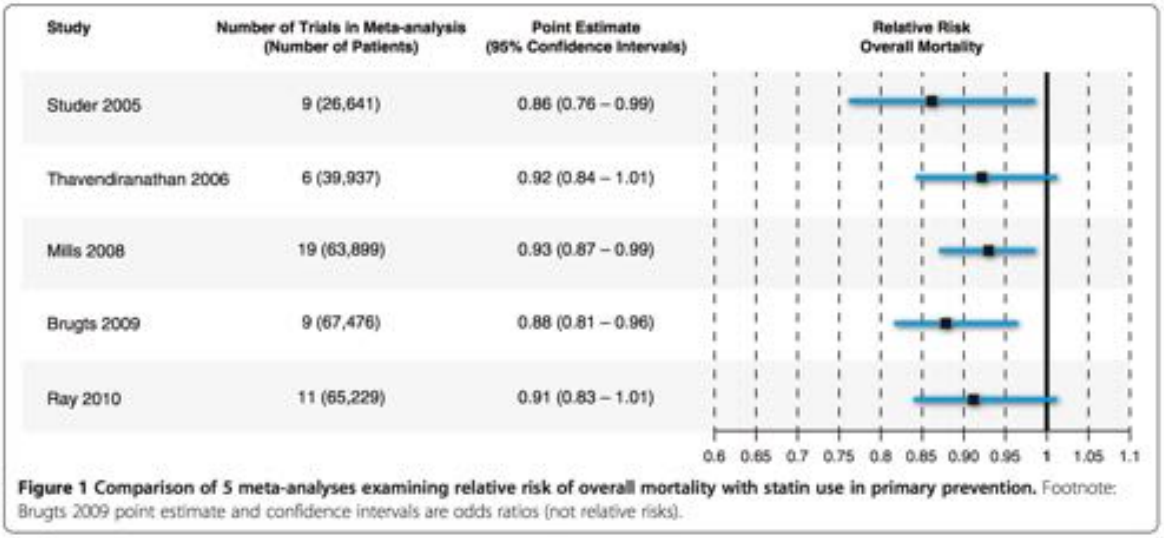


Figure 1 Comparison of 5 meta-analyses examining relative risk of overall mortality with statin use in primary prevention. Footnote: Brugts 2009 point estimate and confidence intervals are odds ratios (not relative risks).

Heterogeneity

If confidence intervals for the results of individual studies have poor overlap, this generally indicates the presence of statistical heterogeneity

Thresholds for the interpretation of I^2 can be misleading but

0% - no heterogeneity

25% - low heterogeneity

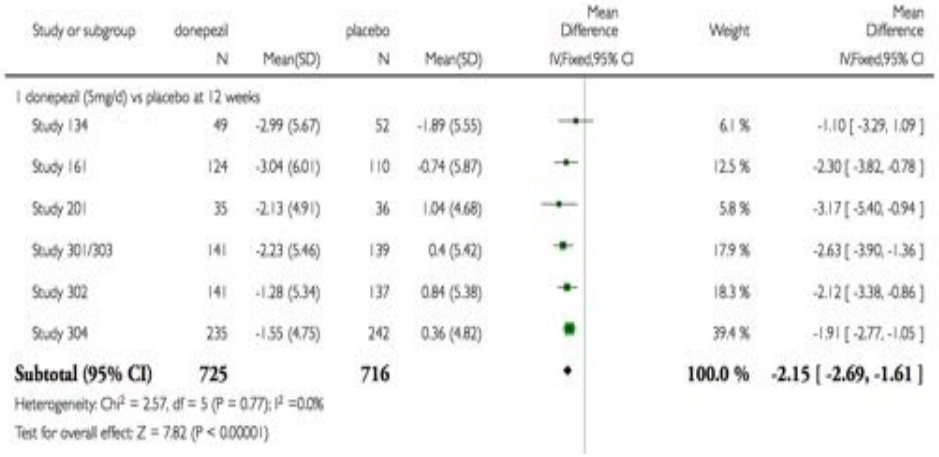
50% - moderate heterogeneity

75% - high heterogeneity

Significant heterogeneity

- differences between studies seem to exist
- it may be invalid to pool the results and generate a single summary result
- look for the variation in the studies
- investigate sources of heterogeneity - do subgroup analysis, look at characteristics of the studies
- account for heterogeneity

Statistical significance Yes; Heterogeneity No



Study or subgroup	donepezil N	Mean(SD)	placebo N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 donepezil (5mg/d) vs placebo at 12 weeks							
Study 134	49	-2.99 (5.67)	52	-1.89 (5.55)		6.1 %	-1.10 [-3.29, 1.09]
Study 161	124	-3.04 (6.01)	110	-0.74 (5.87)		12.5 %	-2.30 [-3.82, -0.78]
Study 201	35	-2.13 (4.91)	36	1.04 (4.68)		5.8 %	-3.17 [-5.40, -0.94]
Study 301/303	141	-2.23 (5.46)	139	0.4 (5.42)		17.9 %	-2.63 [-3.90, -1.36]
Study 302	141	-1.28 (5.34)	137	0.84 (5.38)		18.3 %	-2.12 [-3.38, -0.86]
Study 304	235	-1.55 (4.75)	242	0.36 (4.82)		39.4 %	-1.91 [-2.77, -1.05]
Subtotal (95% CI)	**725**		**716**			**100.0 %**	**-2.15 [-2.69, -1.61]**

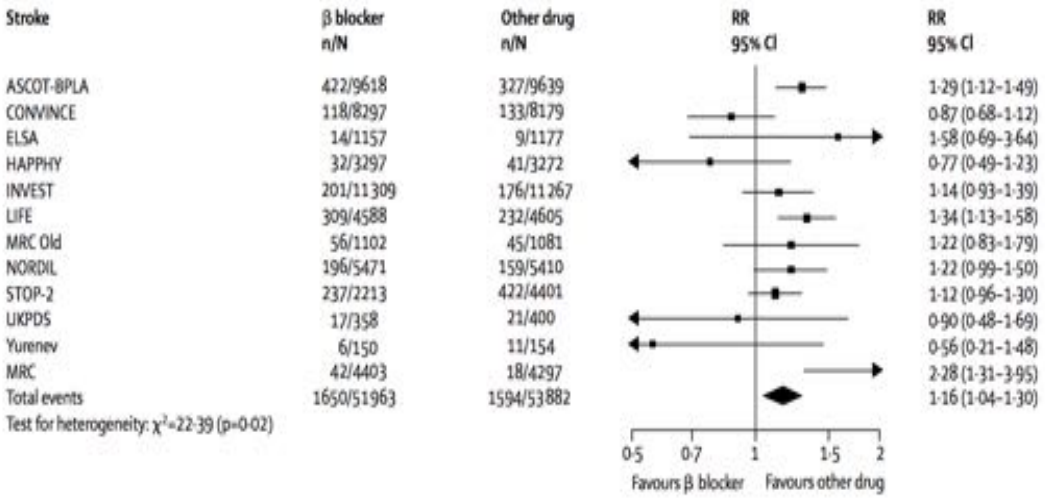
Heterogeneity: $Chi^2 = 2.57$, df = 5 (P = 0.77); $I^2 = 0.0\%$

Test for overall effect: Z = 7.82 (P < 0.00001)

ADAS-cog changes with donepezil in dementia

Cochrane Database Syst Rev. 2006 Jan 25;(1):CD001190.

Statistical significance Yes; Heterogeneity Yes



Stroke	β blocker n/N	Other drug n/N	RR 95% CI	RR 95% CI
ASCOT-BPLA	422/9618	327/9639		1·29 (1·12–1·49)
CONVINCE	118/8297	133/8179		0·87 (0·68–1·12)
ELSA	14/1157	9/1177		1·58 (0·69–3·64)
HAPPHY	32/3297	41/3272		0·77 (0·49–1·23)
INVEST	201/11 309	176/11 267		1·14 (0·93–1·39)
LIFE	309/4588	232/4605		1·34 (1·13–1·58)
MRC Old	56/1102	45/1081		1·22 (0·83–1·79)
NORDIL	196/5471	159/5410		1·22 (0·99–1·50)
STOP-2	237/2213	422/4401		1·12 (0·96–1·30)
UKPDS	17/358	21/400		0·90 (0·48–1·69)
Yurenev	6/150	11/154		0·56 (0·21–1·48)
MRC	42/4403	18/4297		2·28 (1·31–3·95)
Total events	1650/51963	1594/53882		1·16 (1·04–1·30)
Test for heterogeneity: χ^2=22·39 (p=0·02)				

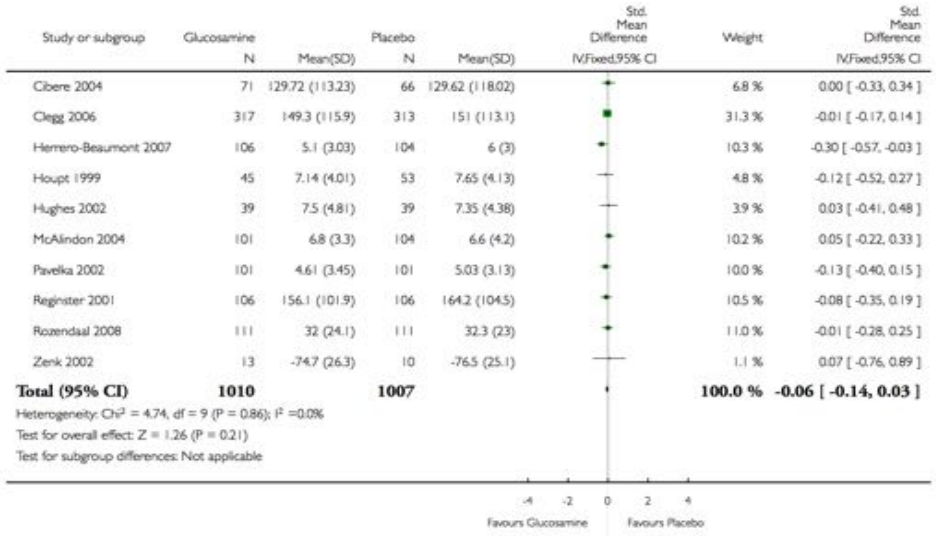
0·5 0·7 1 1·5 2

Favours β blocker Favours other drug

Beta-blockers vs other drugs in hypertension for stroke

Lancet. 2005 Oct 29-Nov 4;366(9496):1545-53.

Statistical significance No; Heterogeneity No



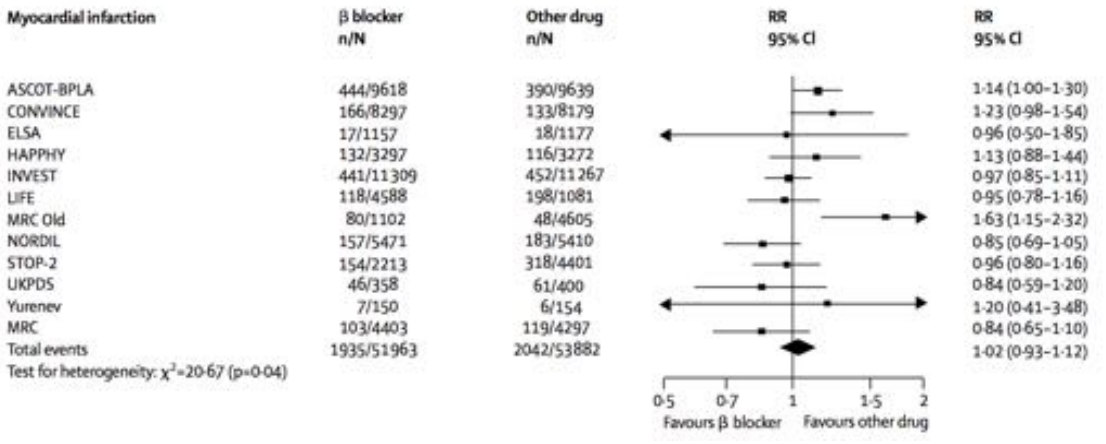
Study or subgroup	Glucosamine N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Cibere 2004	71	129.72 (113.23)	66	129.62 (118.02)		6.8 %	0.00 [-0.33, 0.34]
Clegg 2006	317	149.3 (115.9)	313	151 (113.1)		31.3 %	-0.01 [-0.17, 0.14]
Herrero-Beaumont 2007	106	5.1 (3.03)	104	6 (3)		10.3 %	-0.30 [-0.57, -0.03]
Houpt 1999	45	7.14 (4.01)	53	7.65 (4.13)		4.8 %	-0.12 [-0.52, 0.27]
Hughes 2002	39	7.5 (4.81)	39	7.35 (4.38)		3.9 %	0.03 [-0.41, 0.48]
McAlindon 2004	101	6.8 (3.3)	104	6.6 (4.2)		10.2 %	0.05 [-0.22, 0.33]
Pavelka 2002	101	4.61 (3.45)	101	5.03 (3.13)		10.0 %	-0.13 [-0.40, 0.15]
Reginster 2001	106	156.1 (101.9)	106	164.2 (104.5)		10.5 %	-0.08 [-0.35, 0.19]
Rozendaal 2008	111	32 (24.1)	111	32.3 (23)		11.0 %	-0.01 [-0.28, 0.25]
Zenk 2002	13	-74.7 (26.3)	10	-76.5 (25.1)		1.1 %	0.07 [-0.76, 0.89]
Total (95% CI)	**1010**		**1007**			**100.0 %**	**-0.06 [-0.14, 0.03]**

Heterogeneity: Ch^2 = 4.74, df = 9 (P = 0.86); I^2 =0.0%
Test for overall effect: Z = 1.26 (P = 0.21)
Test for subgroup differences: Not applicable

Glucosamine vs Placebo for OA pain, high quality studies

Cochrane Database Syst Rev. 2005 Apr 18;(2):CD002946.

Statistical significance No; Heterogeneity Yes



Myocardial infarction	β blocker n/N	Other drug n/N	RR 95% CI	RR 95% CI
ASCOT-BPLA	444/9618	390/9639		1·14 (1·00–1·30)
CONVINCE	166/8297	133/8179		1·23 (0·98–1·54)
ELSA	17/1157	18/1177		0·96 (0·50–1·85)
HAPPHY	132/3297	116/3272		1·13 (0·88–1·44)
INVEST	441/11 309	452/11 267		0·97 (0·85–1·11)
LIFE	118/4588	198/1081		0·95 (0·78–1·16)
MRC Old	80/1102	48/4605		1·63 (1·15–2·32)
NORDIL	157/5471	183/5410		0·85 (0·69–1·05)
STOP-2	154/2213	318/4401		0·96 (0·80–1·16)
UKPDS	46/358	61/400		0·84 (0·59–1·20)
Yurenev	7/150	6/154		1·20 (0·41–3·48)
MRC	103/4403	119/4297		0·84 (0·65–1·10)
Total events	1935/51963	2042/53882		1·02 (0·93–1·12)

Test for heterogeneity: χ^2=20·67 (p=0·04)

Beta-blockers vs other drugs in hypertension for MI

Lancet. 2005 Oct 29-Nov 4;366(9496):1545-53.

EVIDENCE APPRAISAL WORK BOOK

YOUR ANSWERS WILL INVOLVE NOT ONLY

Numbers

BUT ALSO

Clinical Judgement

AND

Personal opinion

What is in the DM trials?

	Number	Mean Age	Duration of DM	Past CVD	Weight in 2nd Meta
UKPDS 33 (1998)	3,867 (4209*)	53.2	New	2%	23.9
UKPDS 34 (1998)	753 (4209*)	53.2	New	2%	
ACCORD (2008)	10,251	62.2	8.3	35%	21.5
ADVANCE (2008)	11,140	66	7.5	32%	28.2
VADT (2009)	1791	60.4	11.5	40%	11.9
UGDP (1978)	414	52.7	New	6%	11.8

* The n used in the BMJ meta for UKPDS combined

What is in those Vitamin D trials?

Study	Country	Endpoint	Age
Camargo (2012)	Mongolia	Acute RI	10
Jorde (2012)	Norway	Influenza	63
Laaksi (2010)	Finland	URTI	18-28
Li-Ng (2009)	USA	URI*	59
Manaseki-Holland (2010)	Afghanistan	pneumonia	0-3
Manaseki-Holland (2012)	Afghanistan	pneumonia	0-1
Murdoch (2012)	New Zealand	Colds	47
Urashima (2010)	Japan	Flu	10.2

URI* = 2 or more of fever, cough, productive sputum or change in sputum color and quantity, muscle aches, nausea or vomiting

What is in those Vitamin D trials?

Let's look specifically at Urashima (Am J Clin Nutr 2010;91:1255-60)

	Vitamin D		Placebo		Relative Risk*
	n (167)	%	n (167)	%	
Influenza A	18	11%	31	19%	0.58 (0.34-0.996)
Influenza B	39	23%	28	17%	1.39 (0.90-2.15)
Influenza Like Illness	8	5%	9	5%	-
Total	65	38.9%	68	40.7%	0.96 (0.73-1.24)

* Using http://www.hutchon.net/ConfidRR.htm for RR (& CI) estimation