Critical appraisal of randomised controlled trials

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3 steps to appraising an RCT

1. **Find an RCT that addresses your clinical question**
2. **Assess risk of bias and determine if results are trustworthy**
3. **Determine if the effect is significant and generalizable**

A&E clinical scenario

3 days of fever, sore throat, and headache

Neck stiffness, photophobia, confusion

Elevated CRP and white blood count

Cloudy; 30% of blood glucose; raised protein & white cell count

What is the Diagnosis? What is your next test?

Should we start this patient on steroids to improve clinical outcomes?

Clinical question? (PICO)

- 22 year old female
- Bacterial meningitis
  - 3 days of fever, sore throat, headache, neck stiffness, photophobia, confusion
  - CSF: cloudy; 30% of blood glucose; raised protein and white cell count
- Should we start steroid treatment to improve clinical outcomes?

(PICO)

- Population: In adults with acute bacterial meningitis…
- Intervention: does treatment with steroids…
- Comparison: compared to no steroids…
- Outcome: reduce the likelihood of poor outcome?
- What kind of evidence do we want?

Levels of evidence for testing effectiveness of a therapy/treatment

What is a randomized controlled trial?

- A study in which participants are randomly allocated to an experimental or comparison group
- Experimental group get an intervention
- The comparison group gets something different (no intervention, a placebo, different intervention)
- Outcomes in each group are compared to determine the effect of the intervention

What’s so special about RCTs?

Randomisation = equal groups

Steroid   No steroid

- Only difference should be the intervention

- Infer causality: can attribute differences in outcomes to the differences in the treatment

1. Find an RCT that addresses your clinical question

PubMed Clinical Queries

Results of searches on this page are limited to specific clinical research areas. For comprehensive searches, use PubMed directly.

dexamethasone and bacterial meningitis | Search

Clinical Study Categories

Category: Therapy

Scope: Narrow

Results: 5 of 58

Corticosteroids for managing tuberculous meningitis.
Prasad K, Singh MB, Ryan H.
Cochrane Database Syst Rev. 2016 Apr 28; 4:CD002244. Epub 2016 Apr 28.

Streptococcus suis Meningitis: A Systematic Review and Meta-analysis.
van Samkar A, Brouwer MC, Schultsz C, van der Ende A, van de Beek D.
PLoS Negl Trop Dis. 2015; 9(10):e0004191. Epub 2015 Oct 27.

Adjuvant treatment with dexamethasone plus anti-C5 antibodies improves outcome of experimental pneumococcal meningitis: a randomized controlled trial.
Kasanmoentalib ES, Valls Seron M, Morgan BP, Brouwer MC, van de Beek D.
J Neuroinflammation. 2015 Aug 15; 12:149. Epub 2015 Aug 15.

Dexamethasone and long-term survival in bacterial meningitis.
Fritz D, Brouwer MC, van de Beek D.
Neurology. 2012 Nov 27; 79(22):2177-9. Epub 2012 Nov 14.

Single dose oral dexamethasone versus multi-dose prednisolone in the treatment of acute exacerbations of asthma in children who attend the emergency department: study protocol for a randomized controlled trial.
Cronin J, Kennedy U, McCoy S, An Fhailí SN, Crispino-O'Connell G, Hayden J, Wakai A, Walsh S, O'Sullivan R.
Trials. 2012 Aug 21; 13:141. Epub 2012 Aug 21.

Systematic Reviews

Results: 5 of 44

The role of adjunctive dexamethasone in the treatment of bacterial meningitis: an updated systematic meta-analysis.
Shao M, Xu P, Liu J, Liu W, Wu X.
Patient Prefer Adherence. 2016; 10:1243-9. Epub 2016 Jul 14.

Investigation of the Selection and Timing of Pharmacological Therapy in Community-Acquired Bacterial Meningitis.
Sheley J, Willman D, Downen J, Bergman S.
P T. 2016 Jul; 41(7):437-41.

Corticosteroids for managing tuberculous meningitis.
Prasad K, Singh MB, Ryan H.
Cochrane Database Syst Rev. 2016 Apr 28; 4:CD002244. Epub 2016 Apr 28.

Adjuvant corticosteroids for reducing death in neonatal bacterial meningitis.
Ogunlesi TA, Odigwe CC, Oladapo OT.
Cochrane Database Syst Rev. 2015 Nov 11; (11):CD010435. Epub 2015 Nov 11.

Streptococcus suis Meningitis: A Systematic Review and Meta-analysis.
van Samkar A, Brouwer MC, Schultsz C, van der Ende A, van de Beek D.
PLoS Negl Trop Dis. 2015; 9(10):e0004191. Epub 2015 Oct 27.

See all (44)

Medical Genetics

Topic: All

Results: 5 of 29

Impact of corticosteroids on experimental meningococcal sepsis in mice.
Levy M, Antunes A, Fiette L, Deghmane AE, Taha MK.
Steroids. 2015 Sep; 101:96-102. Epub 2015 Jun 9.

LTA4H genotype is associated with susceptibility to bacterial meningitis but is not a critical determinant of outcome.
Dunstan SJ, Tram TT, Thwaites GE, Chau TT, Phu NH, Hien TT, Farrar JJ, Wolbers M, Mai NT.
PLoS One. 2015; 10(3):e0118789. Epub 2015 Mar 23.

Bacterial meningitis.
Heckenberg SG, Brouwer MC, van de Beek D.
Handb Clin Neurol. 2014; 121:1361-75.

Listeria monocytogenes sequence type 6 and increased rate of unfavorable outcome in meningitis: epidemiologic cohort study.
Koopmans MM, Brouwer MC, Bijlsma MW, Bovenkerk S, Keijzers W, van der Ende A, van de Beek D.
Clin Infect Dis. 2013 Jul; 57(2):247-53. Epub 2013 Apr 16.

Genetic variation in GLCCI1 and dexamethasone in bacterial meningitis.
Brouwer MC, van der Ende A, Baas F, van de Beek D.
J Infect. 2012 Nov; 65(5):465-7. Epub 2012 Jul 11.

See all (29)

This column displays citations pertaining to topics in medical genetics

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VOLUME 347 NOVEMBER 14, 2002 NUMBER 20

DEXAMETHASONE IN ADULTS WITH BACTERIAL MENINGITIS

JAN DE GANS, PH.D., AND DIEDERIK VAN DE BEEK, M.D., FOR THE EUROPEAN DEXAMETHASONE IN ADULTHOOD BACTERIAL MENINGITIS STUDY INVESTIGATORS*

ORIGINAL ARTICLE

Dexamethasone in Vietnamese Adolescents and Adults with Bacterial Meningitis

Nguyen Thi Hoang Mai, M.D., Tran Thi Hong Chau, M.D., Guy Thwaites, M.D., Ly Van Chuong, M.D., Dinh Xuan Sinh, M.D., Ho Dang Trung Nghia, M.D., Phung Quoc Tuan, M.D., Nguyen Duy Phong, M.D., Nguyen Hoan Phu, M.D., To Song Diep, M.D., Nguyen van Vinh Chau, M.D., Nguyen Minh Duong, M.D., James Campbell, Constance Schultsz, M.D., Chris Parry, M.D., M. Estee Torok, M.D., Nicholas White, F.R.C.P., Nguyen Tran Chinh, M.D., Tran Tinh Hien, M.D., Kasia Stepniewska, Ph.D., and Jeremy J. Farrar, F.R.C.P.

N Engl J Med 2007; 357:2431-2440 | December 13, 2007 | DOI: 10.1056/NEJMoa070852

1. Find an RCT that addresses your clinical question

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N Engl J Med 2007; 357:2431-2440 | December 13, 2007 | DOI: 10.1056/NEJMoa070852

- High proportion of Meningitis in Asia (and the study) due to *Streptococcus suis*
- *S. suis* not a common cause of meningitis in high-income countries
- Different standard of care

1. Find an RCT that addresses your clinical question

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- **Population:** Age 17 years or older; suspected meningitis; cloudy CSF, bacteria on Gram staining OR leukocyte >1000 per mm^3; Netherlands, Belgium, Germany, Austria, Denmark

- **Intervention:** Dexamethasone (10mg) every 6 hours for 4 days (first dose with or before antibiotics)

- **Comparison:** Placebo

- **Primary Outcome:** Glasgow outcome scale

2. Assess the risk of bias and decide if the results are trustworthy

Validity

- Internal validity: the extent to which the study is free from bias
- Bias: systematic differences between groups
  - i.e. Sicker patients in one group
- Bias can be introduced because of the design, conduct, or analysis of studies
- Low risk of bias: we can attribute differences in outcomes to the differences in the treatment given and not other variables (confounding)

Internal Validity…External Validity

- If a study is internally valid we then assess the study's <u>external validity a.k.a. generalizability</u>

- <u>External validity:</u> the extent to which the results apply outside the study setting
  - Can you use the results in your situation?
  - Assess whether your patients/setting are similar enough to those in the study

Cochrane Handbook for Systematic Reviews of Interventions

THE COCHRANE

Show

Chapter 8: Assessing risk of bias in included studies

Editors: Julian PT Higgins, Douglas G Altman and Jonathan AC Sterne on behalf of the Cochrane Statistical Methods Group and the Cochrane Bias Methods Group.

Key points

- Problems with the design and execution of individual studies of healthcare interventions raise questions about the validity of their findings; empirical evidence provides support for this concern.
- An assessment of the validity of studies included in a Cochrane review should emphasize the risk of bias in their results, i.e. the risk that they will overestimate or underestimate the true intervention effect.
- Numerous tools are available for assessing methodological quality of clinical trials. We recommend against the use of scales yielding a summary score.
- The Cochrane Collaboration recommends a specific tool for assessing risk of bias in each included study. This comprises a judgement and a support for the judgement for each entry in a 'Risk of bias' table, where each entry addresses a specific feature of the study. The judgement for each entry involves assessing the risk of bias as 'low risk', as 'high risk, or as 'unclear risk', with the last category indicating either lack of information or uncertainty over the potential for bias.
- Plots of 'Risk of bias' assessments can be created in RevMan.
- In clinical trials, biases can be broadly categorized as selection bias, performance bias, detection bias, attrition bias, reporting bias and other biases that do not fit into these categories.
- For parallel group trials, the features of interest in a standard 'Risk of bias' table of a Cochrane review are sequence generation (selection bias), allocation sequence concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective outcome reporting (reporting bias) and other potential sources of bias.
- Detailed considerations for the assessment of these features are provided in this chapter.

Chapter 8

Table 8.4.a: A common classification scheme for bias

Type of bias	Description	Relevant domains in the Collaboration's 'Risk of bias' tool
Selection bias.	Systematic differences between baseline characteristics of the groups that are compared.	• Sequence generation. • Allocation concealment.
Performance bias.	Systematic differences between groups in the care that is provided, or in exposure to factors other than the interventions of interest.	• Blinding of participants and personnel. • Other potential threats to validity.
Detection bias.	Systematic differences between groups in how outcomes are determined.	• Blinding of outcome assessment. • Other potential threats to validity.
Attrition bias.	Systematic differences between groups in withdrawals from a study.	• Incomplete outcome data
Reporting bias.	Systematic differences between reported and unreported findings.	• Selective outcome reporting (see also Chapter 10).

Rapid risk of bias checklist

A. Was the method of randomization truly random?
B. Was allocation adequately concealed?
C. Were groups comparable at the start?

D. Were patients and practitioners providing care blinded?
E. Was outcome assessment blinded or were outcomes objective?

F. Was there minimal loss to follow-up & losses explained?
G. Was an intention-to-treat analysis conducted?

Think about how the bias could affect the outcome

- Will it make the intervention seem more or less beneficial?
- Will it have a big impact or little impact on the effect estimates?

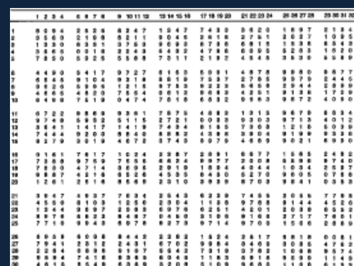
Selection bias

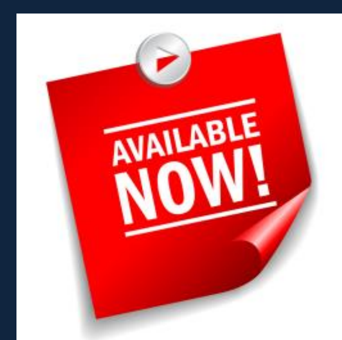
- Systematic differences between baseline characteristics of the groups

- Want comparable groups at the start

A. Random sequence generation
B. Concealed allocation

A. Generation of an unpredictable allocation sequence





B. Adequate allocation concealment

- Patients and investigators enrolling patients shouldn't know which group the next patient is going to; can't know the sequence

- Biased if participant's decision to provide consent or a recruiter's decision to enrol a participant is influenced by knowledge of which group a patient would be in if they participated

B. Adequate allocation concealment

Best

Central telephone/computer

Doubtful

Things that can be tampered with (numbered, opaque, sealed envelopes)

Allocation concealment impacts results

BMJ. 2008 Mar 15; 336(7644): 601–605. PMCID: PMC2267990
Published online 2008 Mar 3. doi: 10.1136/bmj.39465.451748.AD

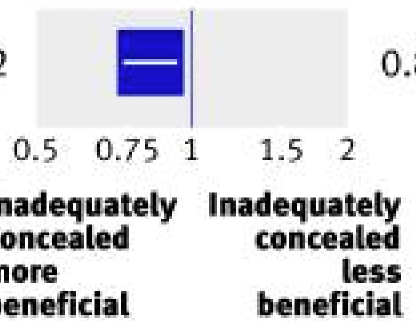
Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study

Allocation concealment and estimates of intervention effects

We included 102 meta-analyses in our analysis of associations between allocation concealment and estimates of intervention effects (fig 1). Of the 804 trials in these meta-analyses, 272 (34%) had adequate allocation concealment. Overall, intervention effect estimates were exaggerated by 17% in the trials with inadequate or unclear allocation concealment compared with those with adequate allocation concealment

exaggerated by 17%

Allocation concealment impacts results

Comparison (No of meta-analyses)	No of trials*	Ratio of odds ratios	Ratio of odds ratios (95% CI)	P value of test of interaction	Variability in bias† (P value)
Overall (102)	532 v 272		0.83 (0.74 to 0.93)	–	0.11 (<0.001)

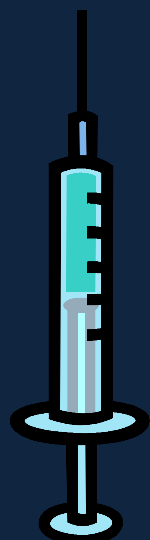
* Inadequately or unclearly concealed *v* adequately concealed

† Between-meta-analysis heterogeneity variance

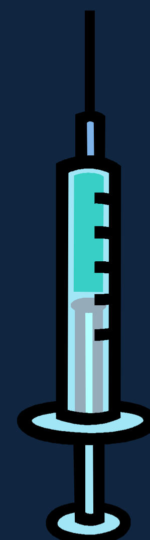
Treatment

Patients were randomly assigned to receive dexamethasone sodium phosphate (Oradexon), at a dose of 10 mg given every six hours

Dexamethasone,
n=157



OR



Placebo,
n=144

A. Method of randomisation?

B. Adequate allocation concealment?

C. Were groups comparable at the start?

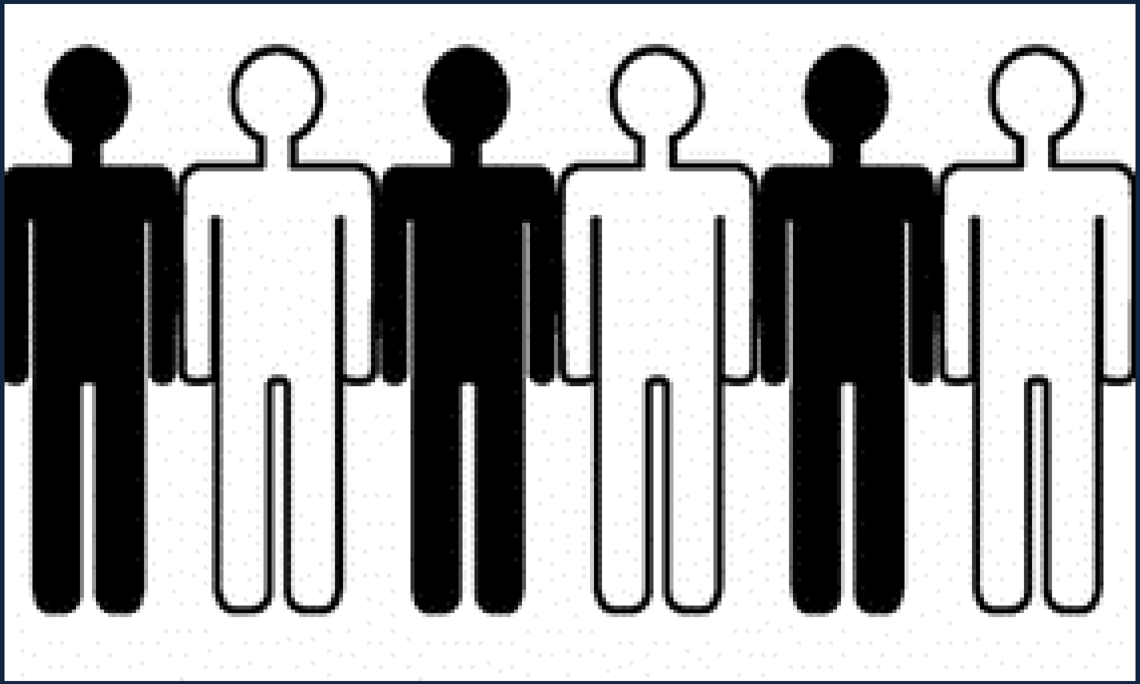
Balanced treatment assignments within each hospital were achieved with the use of a computer-generated list of random numbers in blocks of six. The code was not broken until the last patient to be enrolled had completed eight weeks of follow-up. Treatment assignments were concealed from all investigators, but in an emergency, investigators had access to the sealed, opaque envelopes containing the assignments; two emergencies occurred. Patients were

Table 1: Baseline characteristics

Characteristic	Dexamethasone Group (N=157)	Placebo Group (N=144)
Age — yr	44±18	46±20
Male sex — no. (%)	89 (57)	80 (56)
Basis for eligibility — no. (%)		
Bacteria in CSF on Gram's staining	116 (74)	99 (69)
No bacteria in CSF on Gram's staining but CSF white-cell count >1000 per mm³	38 (24)	42 (29)
Cloudy CSF only	3 (2)	3 (2)
Duration of symptoms before admission — hr		
Median	24	24
Range	1–336	1–167
Seizures — no. (%)	15 (10)	7 (5)
Findings on admission		
CSF pressure — cm of water†	37±13	34±14
Score on Glasgow Coma Scale‡		
Median	12	12
Range	3–14	3–14
Score <8, indicating coma — no. (%)	25 (16)	23 (16)
Papilledema — no. (%)§	6 (7)	9 (10)
Cranial-nerve palsy — no. (%)	14 (9)	18 (12)
Hemiparesis — no. (%)	10 (6)	12 (8)
CSF culture — no. (%)¶		
Streptococcus pneumoniae	58 (37)	50 (35)
Neisseria meningitidis	50 (32)	47 (33)
Other bacteria	12 (8)	17 (12)
Negative bacterial culture	35 (23)	30 (21)
Indexes of CSF inflammation		
White-cell count — per mm³		
Mean ±SD	8185±12,541	7438±10,688
Median	3667	3498
Range	7–123,000	3–76,000
Protein — g/liter	4.3±3.0	4.7±3.2
Glucose — mg/dl‖	27±31	27±29
Positive blood culture — no. (%)**	72 (53)	60 (47)

Balanced treatment assignments within each hospital were achieved with the use of a computer-generated list of random numbers in blocks of six. The code was not broken until the last patient to be enrolled had completed eight weeks of follow-up. Treatment assignments were concealed from all investigators, but in an emer-

Block randomisation attempts to ensure equal group sizes



Performance bias

- Systematic differences in how patients are treated and in how patients behave during a study (other than the intervention)

- Goal is equal treatment/behaviour other than the intervention

D. Were patients and practitioners providing care blinded?

Blinding impacts the results

BMJ. 2008 Mar 15; 336(7644): 601–605. PMCID: PMC2267990
Published online 2008 Mar 3. doi: 10.1136/bmj.39465.451748.AD

Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study

Blinding and estimates of intervention effects

Figure 2 shows the associations between blinding and estimates of intervention effects, based on 76 meta-analyses containing 746 trials, of which 432 (58%) were blinded. Overall, estimates of intervention effects were exaggerated by 7% in non-blinded compared with blinded trials (ratio of odds ratios 0.93 (0.83 to

exaggerated by 7%

D. Were patients and practitioners providing care blinded?

Methods We conducted a prospective, randomized, double-blind, multicenter trial of adjuvant treatment with dexamethasone, as compared with placebo, in

intravenously for four days, or placebo that was identical in appearance to the active drug. The study medication was given 15 to 20

bers in blocks of six. The code was not broken until the last patient to be enrolled had completed eight weeks of follow-up. Treatment

Performance bias

- Other differences in treatment?

ance to the active drug. The study medication was given 15 to 20 minutes before the parenteral administration of antibiotics. After the interim analysis, the protocol was amended to allow administration of the study medication with the antibiotics.

Detection bias

- Systematic differences in how outcomes are determined?

- Goal: outcomes assessed the same way for both groups

E. Was outcome assessment blinded or were outcomes objective

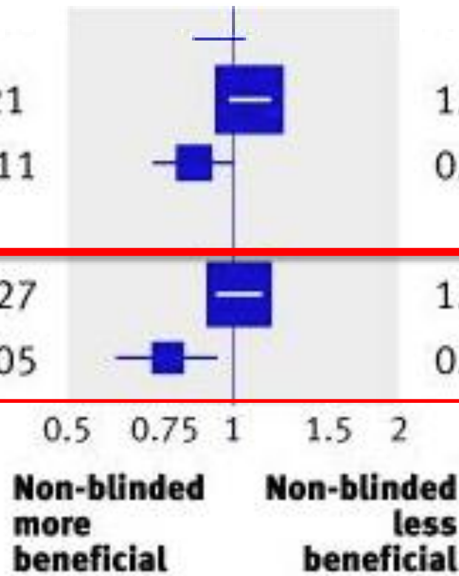
- Objective: cannot be influenced by investigators' judgment
- Death, preterm birth, etc.

BMJ. 2008 Mar 15; 336(7644): 601–605. PMCID: PMC2267990
Published online 2008 Mar 3. doi: 10.1136/bmj.39465.451748.AD

Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study

Comparison (No of meta-analyses)	No of trials*	Ratio of odds ratios (95% CI)	P value of test of interaction	Variability in bias† (P value)
All cause mortality (18)	79 *v* 121	1.04 (0.95 to 1.14)	0.011	0.01 (0.27)
Other outcomes (58)	235 *v* 311	0.83 (0.70 to 0.98)		0.18 (‹0.001)
Objective outcomes (44)	210 *v* 227	1.01 (0.92 to 1.10)	0.01	0.08 (‹0.001)
Subjective outcomes (32)	104 *v* 205	0.75 (0.61 to 0.82)		0.14 (0.001)

Ratio of odds ratios



* Non-blinded *v* blinded

† Between-meta-analysis heterogeneity variance

- Were outcome assessments blinded?

bers in blocks of six. The code was not broken until the last patient
to be enrolled had completed eight weeks of follow-up. Treatment

Other outcome considerations

- Relevant for patients?
- Valid and reliable?
- Sample size calculation: was the study "powered" to detect a difference?

Outcomes

- Primary outcome
  - Glasgow Outcome Score 1 - 4 eight weeks after randomisation (unfavourable outcome)
  - 1: death, 2: vegetative state, 3: severe disability, 4: moderate disability
- Secondary outcomes
  - Death
  - Focal neurological abnormalities
  - Hearing loss (audiologic examination)
  - GI bleed
  - Fungal infection
  - Herpes zoster
  - Hyperglycaemia

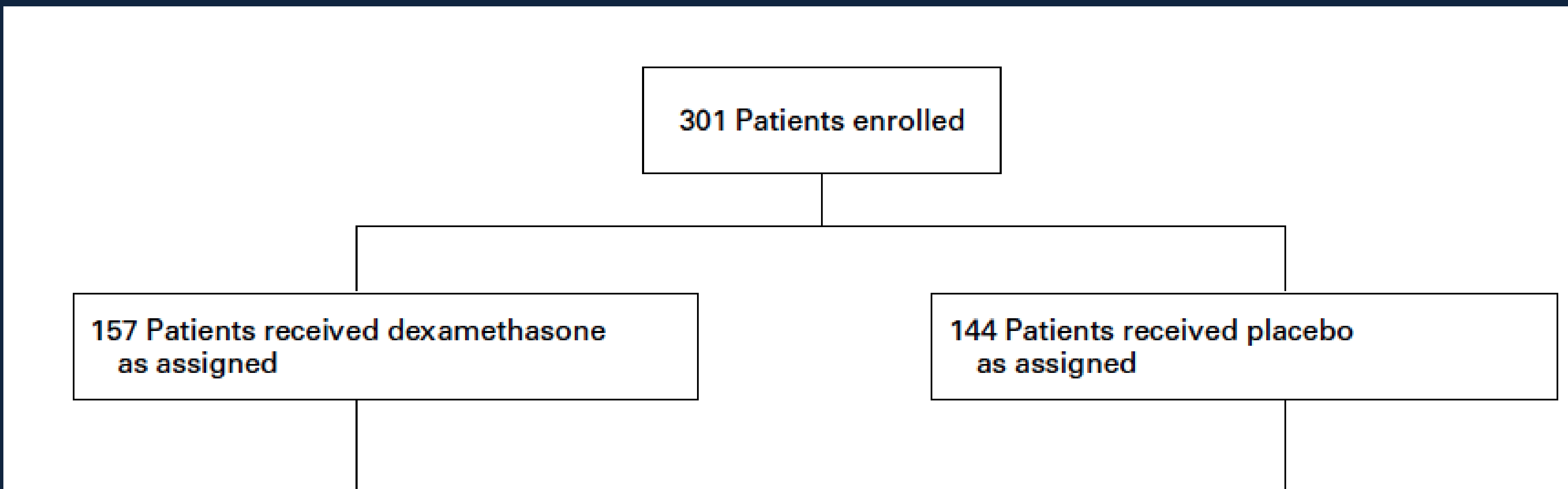
outcome as a score of 1 to 4. The Glasgow Outcome Scale has frequently been used in trials involving stroke and other brain injuries. It is a well-validated scale with good interobserver agreement.[13,14]

Sample size calculation

Was there a sample size calculation?

Did the study include enough participants?

Calculation of the required sample size was based on the assumption that dexamethasone would reduce the proportion of patients with an unfavorable outcome from 40 to 25 percent. With a two-sided test, an alpha level of 0.05, and a power of 80 percent, the analysis required 150 patients per group. The analysis of outcomes


301 Patients enrolled
157 Patients received dexamethasone as assigned
144 Patients received placebo as assigned

Attrition bias

- Systematic differences in withdrawals from the study

F. Was there minimal loss to follow-up & losses explained?

G. Was an intention-to-treat analysis conducted?

- Goal: groups should be equal at the end of the study

F. Minimal loss to follow-up and losses explained

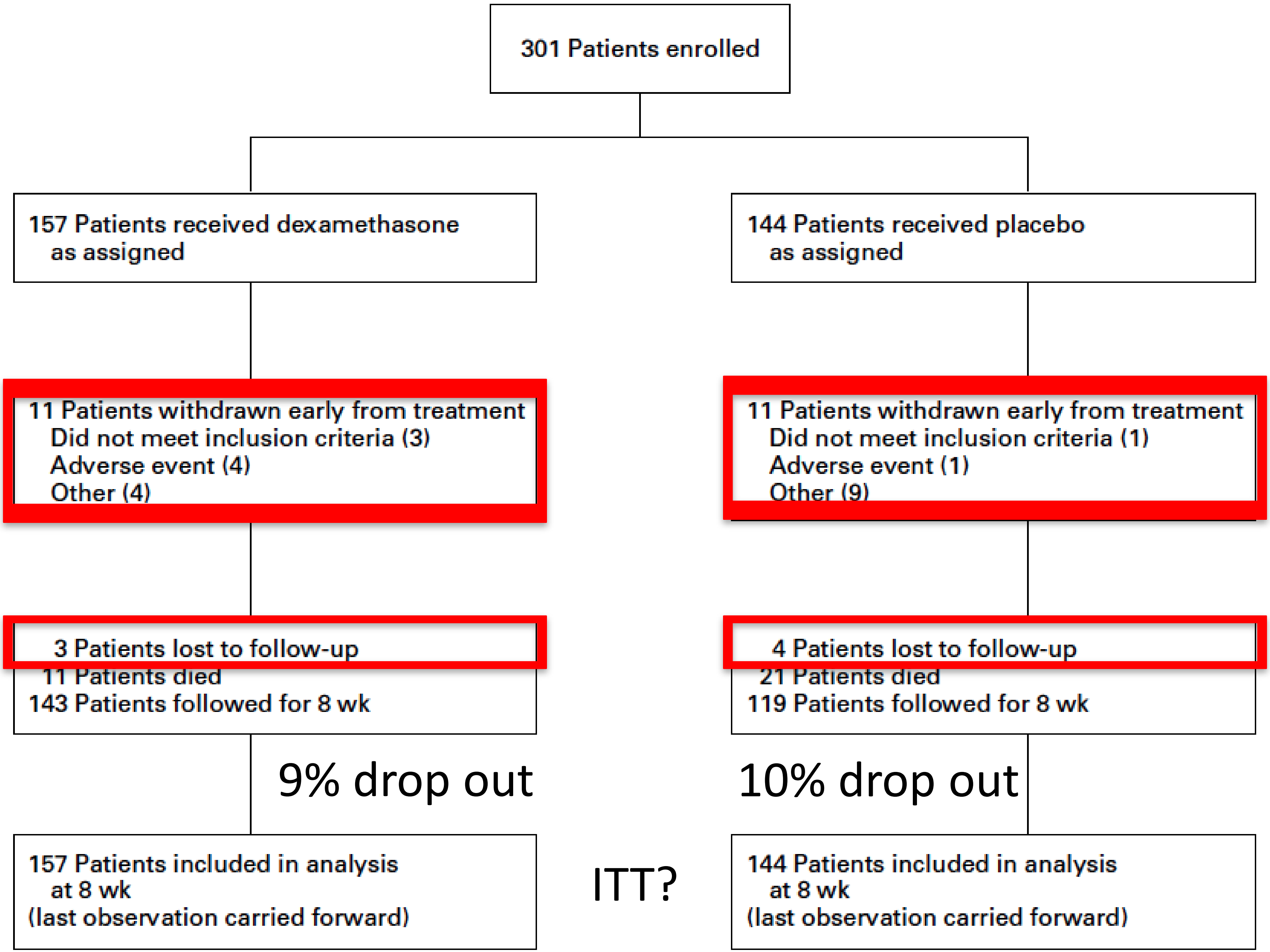
- “5-and-20 rule of thumb” for follow-up
  - <5% little bias
  - 5 to 20% small bias
  - >20% poses serious threats to validity

G. Intention-to-treat analysis

- Once a patient is randomised, he/she is analysed in their assigned group
- Regardless of status: lost to follow-up, never received treatment, or crossed over
- Benefit: groups stay equal, maintain power, estimate of "real world" effectiveness
- Missing data
  - Last observation carried forward
  - Multiple imputation

F. Was there minimal loss to follow-up and were the reasons explained?

G. Did they do an ITT analysis?


301 Patients enrolled
157 Patients received dexamethasone as assigned
144 Patients received placebo as assigned
11 Patients withdrawn early from treatment
Did not meet inclusion criteria (3)
Adverse event (4)
Other (4)
11 Patients withdrawn early from treatment
Did not meet inclusion criteria (1)
Adverse event (1)
Other (9)
3 Patients lost to follow-up
11 Patients died
143 Patients followed for 8 wk
4 Patients lost to follow-up
21 Patients died
119 Patients followed for 8 wk
9% drop out
10% drop out
157 Patients included in analysis at 8 wk
(last observation carried forward)
ITT?
144 Patients included in analysis at 8 wk
(last observation carried forward)

Risk of bias done!

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation list, block size 6
Allocation concealment (selection bias)	Low risk	Allocation was concealed
Blinding (performance bias and detection bias) All outcomes	Low risk	The study was double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	Inclusion chart provided. Intention-to-treat analysis
Other bias	Low risk	No indication of other bias

3. Determine if the effect is significant and generalizable

What was the effect on the primary outcome?

Outcome and Culture Results	Dexamethasone Group	Placebo Group	Relative Risk (95% CI)†	P Value
Unfavorable outcome				
All patients	23/157 (15)	36/144 (25)	0.59 (0.37–0.94)	0.03

Plain English, no stats

GOS 1-4 “unfavorable outcome”
1: death
2: vegetative state
3: severe disability
4: moderate disability

Is the effect statistically significant?

Outcome and Culture Results	Dexamethasone Group	Placebo Group	Relative Risk (95% CI)†	P Value
Unfavorable outcome				
All patients	23/157 (15)	36/144 (25)	0.59 (0.37–0.94)	0.03

- P values
  - Probability that what you are observing is due to chance
  - <0.05 is statistically significant

- Confidence intervals
  - Range of values that likely include the real value
  - Repeat study 100 times, value would be in that range 95% of the time
  - Narrower the range, the more reliable
  - Statistically significant if range does not include 1 for a ratio or 0 for a difference

Different ways to describe the effect

Outcome and Culture Results	Dexamethasone Group	Placebo Group	Relative Risk (95% CI)†	P Value
Unfavorable outcome				
All patients	23/157 (15)	36/144 (25)	0.59 (0.37–0.94)	0.03

Relative measures use division (ratio of risk)

- 0.15/0.25= 0.59 (Relative risk)
- 0.59 - 1 = 0.41 (Expressed as a relative risk reduction)
  - Dexamethasone group had a 41% reduction in the risk of unfavorable outcome compared to the placebo group

Absolute measures use subtraction (difference in risk)

- 0.15 – 0.25 = 0.10 (Absolute risk reduction or risk difference)
- Number Needed to Treat to avoid ONE unfavourable outcome
- 1/risk difference = NNT (better description for clinical significance)
- 1/0.10 = 10 (treat 10 patients to avoid ONE unfavourable outcome)

Described the effect, assessed significance

What else do we want to know to make a decision?

Adverse events

Table 5. Adverse Events.

Event	Dexamethasone Group (N=157)	Placebo Group (N=144)	P Value
	no. (%)		
Gastrointestinal bleeding	2 (1)	5 (3)	0.27
Blood transfusion required	2 (1)	4 (3)	0.43
Stomach perforation	1 (1)	0	1.00
Hyperglycemia	50 (32)	37 (26)	0.24
Herpes zoster	6 (4)	4 (3)	0.75
Fungal infection	8 (5)	4 (3)	0.38

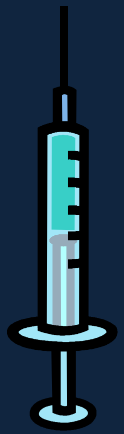
Generalizable effect that helps us decide on treatment?

- External validity: were the patients and setting in the study similar to ours?

- Consider patient characteristics, feasibility and features of the intervention, clinical setting and standards of routine care
  - Really selected patient populations
  - High vs. low income countries
  - Complex interventions

- European countries, adults, similar clinical presentation, likely similar standards of care

Decision



- 22 year old female
- Bacterial meningitis
  - 3 days of fever, sore throat, headache, neck stiffness, photophobia, confusion
  - CSF: cloudy; 30% of blood glucose; raised protein and white cell count
- Should we use steroid treatment to improve clinical outcomes?

Resources

- Cochrane
  - http://handbook.cochrane.org/chapter_8/8_assessing_risk_of_bias_in_included_studies.htm
- Centre for Evidence-Based Medicine
  - http://www.cebm.net/year-4-medical-students/

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Questions?

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