Critical Analysis Problem 2 - August 2019

(20 marks)

Please read the following abstract and tables and answer the questions based on this information and your other knowledge.

‘Oral versus depot antipsychotic drugs for schizophrenia—A critical systematic review and meta-analysis of randomised long-term trials

Claudia Leucht, Stephan Heres, John M. Kane, Werner Kissling, John M. Davis, Stefan Leucht
Schizophrenia Research 127 (2011) 83–92

ABSTRACT:

Objective: Non-adherence is a major problem in the treatment of schizophrenia. Depot antipsychotic drugs are thought to reduce relapse rates by improving adherence, but a systematic review of long-term studies in outpatients is not available.

Method: We searched the Cochrane Schizophrenia Group's register, ClinicalTrials.gov, Cochrane reviews on depot medication, and the reference sections of included studies for randomised controlled trials lasting at least 12 months in outpatients that compared depot with oral antipsychotics in schizophrenia. Data on relapse (primary outcome), rehospitalisation, nonadherence, and dropout due to any reason, inefficacy of treatment and adverse events were summarised in a meta-analysis using a random-effects model…

Results: Ten studies with 1700 participants met the inclusion criteria. Depot formulations significantly reduced relapses with relative and absolute risk reductions of 30% and 10%, respectively (RR 0.70, CI 0.57–0.87, NNT 10, CI 6–25, P=0.0009), and dropout due to inefficacy (RR 0.71, CI 0.57–0.89). Limited data on non-adherence, rehospitalisation and dropout due to any reason and adverse events revealed no significant differences. There were several potential sources of bias such as limited information on randomisation methods, problems of blinding and different medications in the depot and oral groups.

Discussion: Depot antipsychotic drugs significantly reduced relapse. Due to a number of methodological problems in the single trials the evidence is, nonetheless, subject to possible bias.’

Based on the abstract, the quote below and your other knowledge choose the best option to answer the question.

Question 2.01

(1 mark)

'There were several potential sources of bias such as limited information on randomisation methods, problems of blinding and different medications in the depot and oral groups'

Which type of bias is reduced by use of randomisation to treatment?

A. Attribution bias.
B. Attrition bias.
C. Citation bias.
D. Confounding variables bias.
E. Observer bias.
F. Publication bias.
G. Recall bias.
H. Selection bias.

Answer: **H.** Selection bias**.**

Based on the abstract and your other knowledge choose the best option to answer the question.

Question 2.02

(1 mark)

Which type of bias is reduced by a placebo-controlled study?

A. Attribution bias.
B. Attrition bias.
C. Citation bias.
D. Confounding variables bias.
E. Observer bias.
F. Publication bias.
G. Recall bias.
H. Selection bias.

Answer: **A.** Attribution bias**.**

Based on the abstract and your other knowledge choose the best option to answer the question.

Question 2.03

(1 mark)

Which type of bias can be explored using funnel plots?

A. Attribution bias.
B. Attrition bias.
C. Citation bias.
D. Confounding variables bias.
E. Observer bias.
F. Publication bias.
G. Recall bias.
H. Selection bias.

Answer: **F.** Publication bias.

Ref: Egger et all 1997

Based on the abstract, the quote below and your other knowledge choose the best option to answer the question.

Question 2.04

(1 mark)

‘The most frequent other potential bias was the use of different antipsychotics in the depot than in the oral group.’
(Barnes et al., 1983; Falloon et al., 1978; Li et al., 1996; Gaebel et al., 2010 and Potapov et al., 2008).

Which type of bias is being discussed in this quote?

A. Attribution bias.
B. Attrition bias.
C. Citation bias.
D. Confounding variables bias.
E. Observer bias.
F. Publication bias.
G. Recall bias.
H. Selection bias.

Answer: **A.** Attribution bias.

Based on the abstract and your other knowledge choose the best option to answer the question.

Question 2.05

(1 mark)

Which term describes the performance of a medication under ideal and controlled circumstances?

A. Effectiveness.

B. Efficacy.

C. Efficiency.

D. Impact analysis.

E. Outcome analysis.

F. Utility analysis.

Answer: **B.** Efficacy.

Based on the abstract and your other knowledge choose the best option to answer the question.

Question 2.06

(1 mark)

Which term describes the utility of studying outcomes in usual clinical practice?

A. Effectiveness assessment.
B. Efficacy assessment.
C. Efficiency assessment.
D. Impact analysis.
E. Outcome analysis.
F. Utility analysis.

Answer: **A.** Effectiveness assessment.

Based on the abstract and your other knowledge choose the best option to answer the question.

Question 2.07

(1 mark)

Which term most accurately describes the purpose of this systematic review of randomised controlled studies?

A. Effectiveness assessment.

B. Efficacy assessment.

C. Efficiency assessment.

D. Impact analysis.

E. Outcome analysis.

F. Utility analysis.

Answer: **B.** Efficacy assessment.

Based on the abstract and your other knowledge choose the best option to answer the question.

Question 2.08

(1 mark)

Which term describes the aspect of a study which estimates the probability of a Type 2 error?

A. Effectiveness.

B. Efficacy.

C. Efficiency.

D. Impact analysis.

E. Outcome analysis.

F. Utility analysis.

Answer: **C.** Efficiency.

Based on the abstract, the quote below and your other knowledge choose the best option to answer the question.

Question 2.09

(1 mark)

'In several studies adherence was enhanced by home visits if the patients did not show up for their appointments (Falloon et al., 1978; Schooler et al., 1980) or in any case (Del Giudice et al., 1975). Falloon et al. (1978) explicitly excluded non-adherent patients and Rifkin et al. (1977) excluded those who had not regularly attended the aftercare clinic.'

The finding of a …. result.

Which term describes the most important outcomes risk of excluding from analysis non adherent or non-attending patients?

A. False negative.

B. False positive.

C. True negative.

D. True positive.

Answer: **B.** False positive.

Based on the abstract, the quote below and your other knowledge choose the best option to answer the question.

Question 2.10

(1 mark)

'We based the analyses on intention to treat data whenever available'.

The finding of a …. result.

Which of the terms describes the most important outcome that is enhanced by the intention to treat protocol?

A. False negative.

B. False positive.

C. True negative.

D. True positive.

Answer: **D.** True positive.

Ref: West J Emerg Med. 2017 Oct; 18(6): 1075–1078.
Published online 2017 Sep 18. doi: 10.5811/westjem.2017.8.35985
Understanding the Intention-to-treat Principle in Randomized Controlled Trials
C. Eric McCoy, MD, MPH

Based on the abstract and your other knowledge choose the best option to answer the question.

Question 2.11

(1 mark)

Which of the statistical tests or analyses would demonstrate robustness of the outcomes in view of inconsistencies between RCTs?

A. Chi².
B. Confidence interval.
C. I².
D. Odds ratio.
E. Risk ratio.
F. Sensitivity analysis.
G. Tau².

Answer: **F.** Sensitivity analysis.

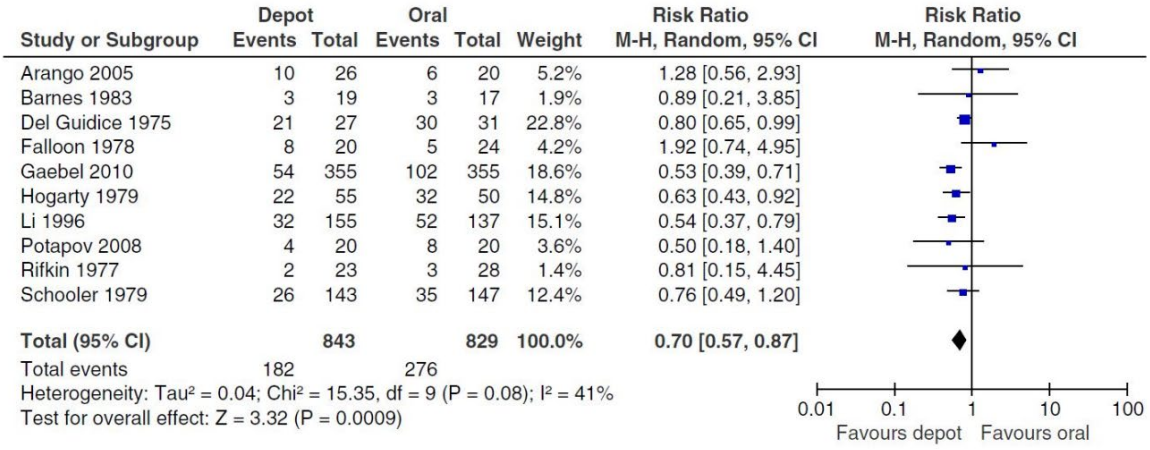
Based on the abstract, the quote below, Figure 1 below and your other knowledge choose the best option to answer the question.

Question 2.12

(2 marks)

'The primary outcome was the number of participants relapsed as defined in the original studies…'

Figure 1 Relapse



Study or Subgroup	Depot Events	Depot Total	Oral Events	Oral Total	Weight	Risk Ratio M-H, Random, 95% CI
Arango 2005	10	26	6	20	5.2%	1.28 [0.56, 2.93]
Barnes 1983	3	19	3	17	1.9%	0.89 [0.21, 3.85]
Del Guidice 1975	21	27	30	31	22.8%	0.80 [0.65, 0.99]
Falloon 1978	8	20	5	24	4.2%	1.92 [0.74, 4.95]
Gaebel 2010	54	355	102	355	18.6%	0.53 [0.39, 0.71]
Hogarty 1979	22	55	32	50	14.8%	0.63 [0.43, 0.92]
Li 1996	32	155	52	137	15.1%	0.54 [0.37, 0.79]
Potapov 2008	4	20	8	20	3.6%	0.50 [0.18, 1.40]
Rifkin 1977	2	23	3	28	1.4%	0.81 [0.15, 4.45]
Schooler 1979	26	143	35	147	12.4%	0.76 [0.49, 1.20]
Total (95% CI)		**843**		**829**	**100.0%**	**0.70 [0.57, 0.87]**
Total events	182		276			

Heterogeneity: Tau² = 0.04; Chi² = 15.35, df = 9 (P = 0.08); I² = 41%
Test for overall effect: Z = 3.32 (P = 0.0009)

Fig. 1. Relapse footnote: in Li et al. the allocation of 28 out of 320 participants was unclear, reducing the total number of participants from 1700 to 1672. Events = the number of participants with a relapse, Total = the total number of participants in this group.

Which of the statistical analyses in Figure 1 is affected by the weighting applied to each study?

A. Chi².

B. Confidence interval.

C. I².

D. Odds ratio.

E. Risk ratio.

F. Sensitivity analysis.

G. Tau².

Answer: **E.** Risk ratio.

Based on the abstract, the quote below, Figure 1 below and your other knowledge choose the best option to answer the question.

Question 2.13

(1 mark)

'The primary outcome was the number of participants relapsed as defined in the original studies…'

Figure 1 Relapse

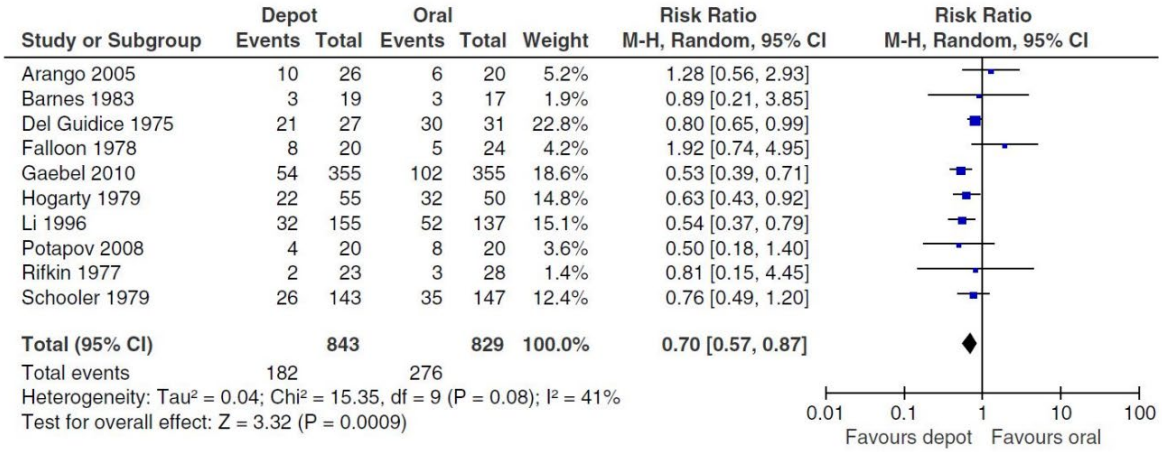


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Fig. 1. Relapse footnote: in Li et al. the allocation of 28 out of 320 participants was unclear, reducing the total number of participants from 1700 to 1672. Events = the number of participants with a relapse, Total = the total number of participants in this group.

Which of the statistical tests used in Figure 1 is a measure of inconsistency between the studies?

A. Chi^2.
B. Confidence interval.
C. I^2.
D. Odds ratio.
E. Risk ratio.
F. Sensitivity analysis.
G. Tau^2.

Answer: **C.** I^2.

Based on the abstract, the quote below, Figure 1 below and your other knowledge choose the best option to answer the question.

Question 2.14

(1 mark)

'The primary outcome was the number of participants relapsed as defined in the original studies…'

Figure 1 Relapse

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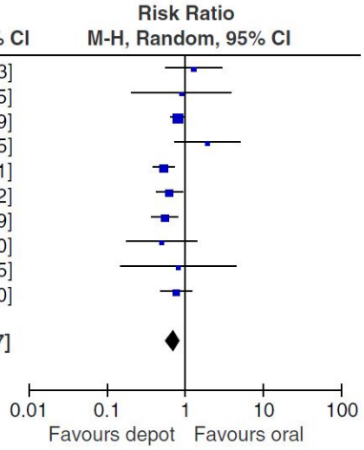

Fig. 1. Relapse footnote: in Li et al. the allocation of 28 out of 320 participants was unclear, reducing the total number of participants from 1700 to 1672. Events = the number of participants with a relapse, Total = the total number of participants in this group.

Which of the statistical tests in Figure 1 was applied to provide a range of values which probably includes the true value of the parameter?

A. Chi^2.

B. Confidence interval.

C. I^2.

D. Odds ratio.

E. Risk ratio.

F. Sensitivity analysis.

G. Tau^2.

Answer: **B.** Confidence interval.

Based on the abstract, Figure 1 below and your other knowledge choose the best option to answer the question.

Question 2.15

(1 mark)

Figure 1 Relapse

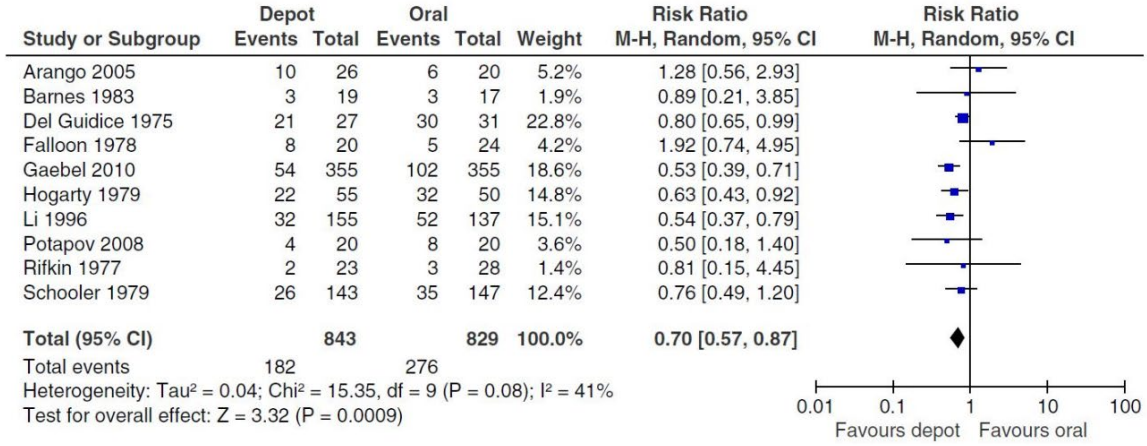

Fig. 1. Relapse footnote: in Li et al. the allocation of 28 out of 320 participants was unclear, reducing the total number of participants from 1700 to 1672. Events = the number of participants with a relapse, Total = the total number of participants in this group.

From Figure 1, which study has the range of confidence which suggests the lowest reliability of the findings?

A: Arango.

B: Barnes.

C: Del Guidice.

D: Fallon.

E: Hogarty.

F: Li.

G: Potapov.

H: Rifkin.

Answer: **H.** Rifkin.

Based on the abstract, Figure 1 below and your other knowledge choose the best option to answer the question.

Question 2.16

(1 mark)

Figure 1 Relapse

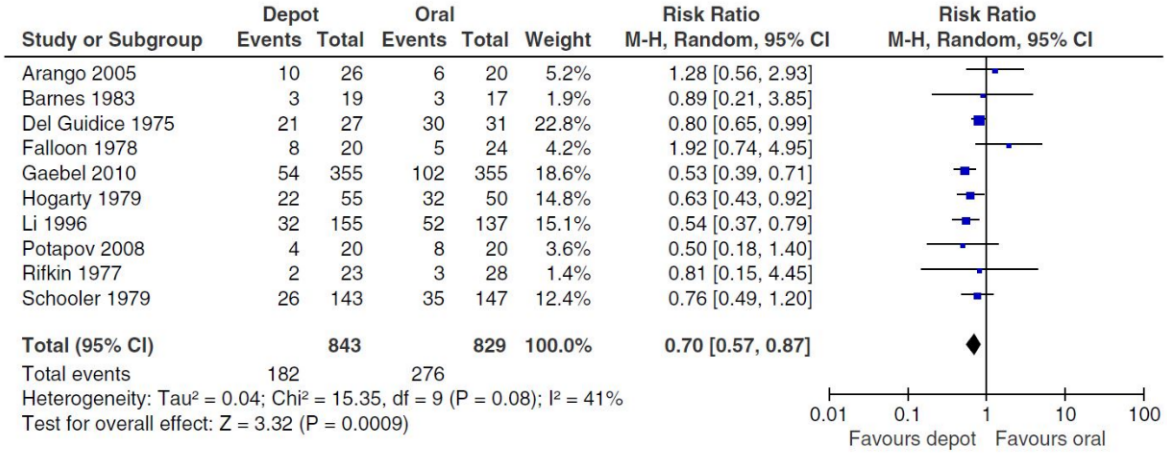

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Fig. 1. Relapse footnote: in Li et al. the allocation of 28 out of 320 participants was unclear, reducing the total number of participants from 1700 to 1672. Events = the number of participants with a relapse, Total = the total number of participants in this group.

From Figure 1, which study has the highest proportion of relapse events?

A: Arango.

B: Barnes.

C: Del Guidice.

D: Fallon.

E: Hogarty.

F: Li.

G: Potapov.

H: Rifkin.

Answer: **C.** Del Guidice.

Based on the abstract, the vignette below and your other knowledge choose the best option to answer the question.

Question 2.17

(2 marks)

'Depot formulations significantly reduced relapses with relative and absolute risk reductions of 30% and 10%, respectively (RR 0.70, CI 0.57–0.87, NNT 10, CI 6–25, P=0.0009), and dropout due to inefficacy (RR 0.71, CI 0.57–0.89).'

Which option is most correct regarding the NNT 10, CI 6-25,?

A. 10 subjects needed to be treated with a depot for one extra to benefit.

B. The number of subjects who needed to be treated for one extra to benefit was probably between 6 and 25.

C. The number of subjects who were harmed by the treatment is between 6-25.

D. The number of subjects harmed by the depot was much less than the number who benefitted.

E. The NNT =10 shows depot medications are proven to be much more successful than oral medications.

Answer: **B.** The number of subjects who needed to be treated for one extra to benefit was somewhere between 6 and 25.

Based on the abstract and your other knowledge choose the best option to answer the question.

Question 2.18

(1 mark)

Select the statement which reflects the highest level of generalisability that can be supported.

A. Evidence generalizable to the target population.

B Evidence generalizable to the target population with caveats.

C Evidence not generalizable to the target population.

D Insufficient evidence presented to answer the question.

Answer: **B.** Evidence generalizable to the target population with some caveats.