# The Royal College of Pathologists
# Journal article evaluation questions

# Previous exam questions

Dorrian CA, Toole, BJ, Alvarez-Madrazo S, Kelly A, Connell JMC, Wallace AM. A screening procedure for primary aldosteronism based on the Diasorin Liaison® automated chemiluminescent immunoassay for direct rennin. *Ann Clin Biochem*2010:**47**:195-199

- Produce a 200 word abstract for this paper, structured under the headings 'Background', 'Methods', Results' and 'Conclusions' (12)
- Explain why it was important to explore interference from prorenin in the Diasorin assay and outline the method used to do this. (8)
- What is the implication of the recently recognised higher prevalence of this condition on the diagnostic performance of this screening procedure? (16)
- Your laboratory currently measures plasma renin activity using a traditional manual radioimmunoassay for anngiotensin I. What are the advantages and disadvantages of replacing this with the Diasorin direct renin assay? (14)

ANSWER

The positive predictive value (PPV) of a test improves as prevalence increases. (2)

PPV=proportion of patients with a +ve test correctly diagnosed as disease positive. (2)

PPV = True Positives/(True positives + False positives)

- With a prevalence of 1% PPV of the test is 12.5%
- Whereas with a prevalence of 10% PPV increases to 62.5%. (4)

Negative predictive value (NPV) is proportion of patients with a –ve test correctly diagnosed as disease free.(2)

NPV = True Negatives/(True negatives + False negatives)

- NPV is 100% (2)

This performance is probably acceptable for a screening test, the purpose of which is to pick up all those who have the disease (in which case false positive rate is less important).(2)

Once patients are identified by the ARR screening test, a salt loading test is performed to further investigate the possibility of primary hyperaldosteronism (2)

**16 marks available**

# Previous exam questions

- Chronic Kidney Disease Consortium. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. Lancet 2010; 375: 2073-2081

- What is a meta-analysis? Describe the advantages and problems associated with this type of study, and measures taken by the authors to guard against the latter

(24)

- Describe the relationship between all-cause mortality and estimated GFR, and discuss possible reasons for this (10)
- The authors state „These findings suggest that the dipstick test is useful for risk stratification despite being a less precise measure of albuminuria.“ Is this conclusion justified? Explain your answer (6)
- Discuss whether the results support the current classification of Chronic Kidney Disease (10)

The Royal College of Pathologists

## Journal article evaluation questions

1. What type/design of study design is described (Observational, survey, cohort etc)

   Discuss suitability of study design to answer the question.

1. Comment on the potential for bias
2. List the statistical techniques used to analyse data and critical discuss the authors interpretation
3. Was the sample size justified and was it sufficient to answer the question.
4. Are the measurements of patient and/or laboratory data valid and reliable. Comment on possible alternatives
5. Are the basic data fully and adequately described. Suggest additional methods or measurements that could have been used.
6. PPV or NPV with a change in prevalence
7. List the different types of data used to characterise a patient or evaluate a response. Discuss how each type of data should be evaluated statistically.

9. Summarise the different methods used to select patients for a study.  How did the decisions the authors made influence the study.

10. Are there missing data and they fully explained?

11. This study found a statistically significant difference between the two groups, discuss whether this is clinically significant.

12. Explain how null findings are interpreted, if at all, and their clinical or laboratory significance.

13. What further studies should be done in this area and how should they be designed.

14. In this paper the author has used XX as a control. Is this optimal? Comment on how this alters the meaning of the result and suggestive alternative controls.

# How to read a paper

On this page you will find links to articles in the *BMJ* that explain how to read and interpret different kinds of research papers:

- Papers that go beyond numbers (qualitative research) Trisha Greenhalgh, Rod Taylor
- Papers that summarise other papers (systematic reviews and meta-analyses) Trisha Greenhalgh
- Papers that tell you what things cost (economic analyses) Trisha Greenhalgh
- Papers that report diagnostic or screening tests Trisha Greenhalgh
- Papers that report drug trials Trisha Greenhalgh
- Statistics for the non-statistician. II: "Significant" relations and their pitfalls Trisha Greenhalgh
- Statistics for the non-statistician Trisha Greenhalgh
- Assessing the methodological quality of published papers Trisha Greenhalgh
- Getting your bearings (deciding what the paper is about) Trisha Greenhalgh
- The Medline database Trisha Greenhalgh

About The BMJ

Editorial staff

Advisory panels

Publishing model

Complaints procedure

History of The BMJ online

Freelance contributors

Poll archive

Help for visitors to thebmj.com

# Proposal for Training Days

- Each training session to review a journal so that repetition improves skills
- Will help to establish the depth of knowledge needed
- Proforma for how to review an article
- Cover essential topics including:

Study types, power calculations, the correct statistical tools

# Journal interpretation

- What is the question to be answered?
- Whom is the study about?
- Type of study
- Was the design appropriate?
- Was systematic bias avoided?
- Statistics and sample size
- Conclusions

Vitamin D and mortality: meta-analysis of individual participant data from a large consortium of cohort studies from Europe and the United States. BMJ 2014;348:g3656

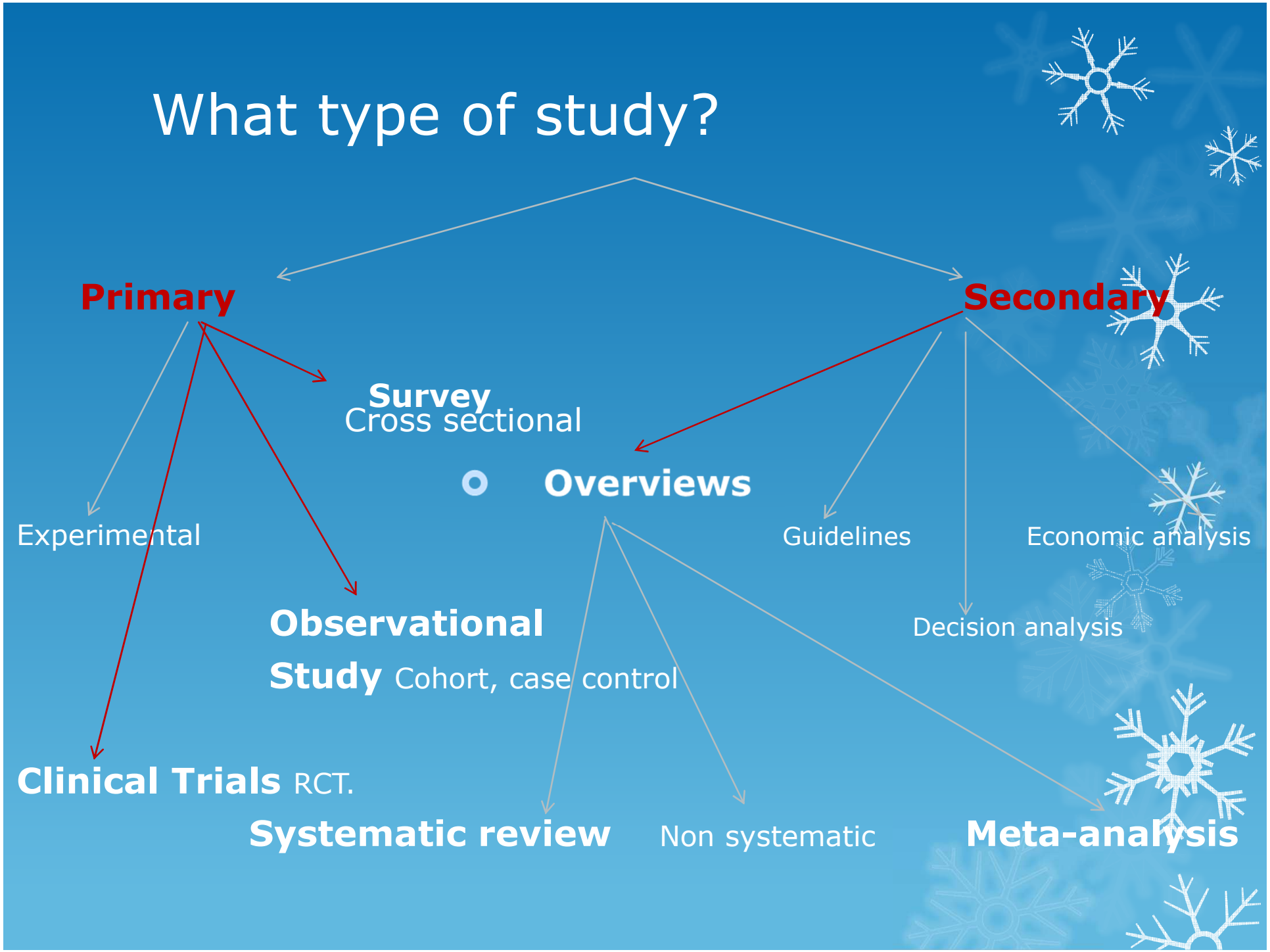
# Journal interpretation

- What is the question to be answered?
- Whom is the study about?
- Type of study
- Was the design appropriate?
- Was systematic bias avoided?
- Statistics and sample size
- Conclusions

# Study population

- Recruitment
- Inclusions
- Exclusions
- Were the subjects studied in real life circumstances

# What type of study?



# Was the study design appropriate?

Hierarchy of evidence

| Research field | Study type |
|---|---|
| Therapy or intervention | RCT |
| Prognosis | Longitudinal cohort study |
| Diagnosis | Cross sectional survey |
| Screening | Cross sectional survey |
| Causation | Cohort, Case control, case reports |

# Systematic review

Overview of primary studies that used explicit and reproducible methods

Cochrane collaboration undertakes systematic reviews

"A systematic review attempts to identify, appraise and synthesize all the empirical evidence that meets pre-specified eligibility criteria to answer a given research question. Researchers conducting systematic reviews use explicit methods aimed at minimizing bias, in order to produce more reliable findings that can be used to inform decision making."

# Meta-analysis

A statistical method of combining the results of several studies that address a set of similar research hypotheses, to estimate the true " effect size" of an intervention with greater statistical power than that available from a single study.

It is a mathematical synthesis of the results of 2 or more primary studies that addressed the same hypothesis in the same way

## EVALUATING a SYSTEMATIC REVIEW

- Was a thorough search done of literature?
  - Medline, Cochrane, other databases
  - Grey literature
  - Foreign language literature
  - References listed in primary sources
  - Contacting experts to find unpublished literature
- Was methodological quality assessed and the trial weighted accordingly?
- Methodological quality – the extent to which systematic bias is prevented (inclusion/exclusion clearly defined criteria , length of follow up, sample size, withdrawals)
- Precision – likelihood of random errors (depicted as width of CI)
- External validity – extent to which results are generalisable or applicable to a target population
- How sensitive are the results to the way the review has been done?
- Are the studies homogenous?
- What are the results?

# Advantages of systematic reviews

- Explicit methods limit bias
- Conclusions more reliable and accurate because of methods used
- Large amounts of information can be assimilated and quickly
- Comparison of different studies
- Reasons for heterogeneity can be compared
- Meta- analysis

  - increases precision of overall result
  - Increased statistical power
  - Generalisation of results across those recruited to a range of studies, rather than those eligible for a single study.

# Problems

- Inability to control for problems in the underlying studies (a good meta-analysis of bad studies will produce a bad result).
- Publication bias ("file drawer problem") – studies with positive outcomes are more likely to be published, those with negative outcomes to be filed away.
- Selection of trials for inclusion (objective or subjective?).
- Variation between studies in definition and/or measurement of effect size.
- Personal or agenda-driven bias.

# Statistics and results

| Study | Sample size Total | Cases | Follow-up period (years) | Risk ratio (95% CI) |
|---|---|---|---|---|
| ESTHER | 9083 | 1338 | 11.0 | 1.51 (1.26 to 1.80) |
| Tromsø | 4406 | 1141 | 14.2 | 1.21 (1.00 to 1.46) |
| MONICA-KORA | 939 | 366 | 15.9 | 1.35 (0.96 to 1.90) |
| SENECA | 661 | 270 | 8.3 | 2.13 (1.39 to 3.26) |
| HAPIEE CZ | 2029 | 453 | 7.9 | 2.08 (1.46 to 2.96) |
| HAPIEE Pol | 1700 | 411 | 7.0 | 1.56 (1.09 to 2.24) |
| HAPIEE Lit | 1574 | 368 | 4.2 | 2.32 (1.59 to 3.38) |
| NHANES | 5626 | 2348 | 12.3 | 1.42 (1.24 to 1.63) |
| Summary | 26 018 | 6695 | — | 1.57 (1.36 to 1.81) |

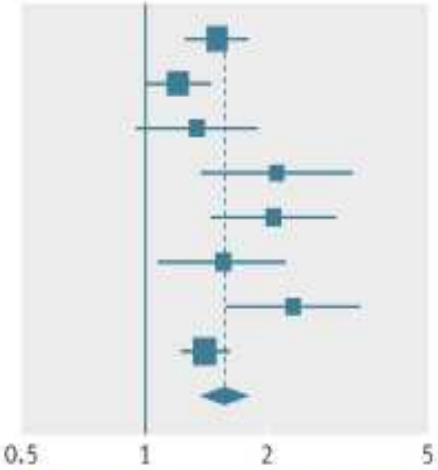



**Fig 1** Risk ratios of all-cause mortality for bottom versus top quintiles of 25-hydroxyvitamin D concentration in eight cohorts (meta-analysis of individual participant data)

# Meta- analysis Results

- Tabulated – inclusion criteria, sample size, baseline characteristics, withdrawal rate and results with primary and secondary end-points.
- Standardised by computer software e.g. Metaview
- Forest Plot
- Studies represented by squares ; the size of the square reflects the weight of study
- Horizontal line 95% confidence interval of risk ratio
- Vertical line corresponds to “no effect” line; RR of 1
- When the confidence interval inlcudes 1 it indicates the result is not significant
- Diamond is the pooled risk ratio

# Heterogeneity

- Homogeneity is when results between studies are mathematically compatible
- Can be assessed by "eye ball" test:

→Look for overlap of confidence intervals

→If the vertical dotted line that runs through the combined RR crosses all the confidence intervals the studies are homogenous

- Formal tests include: Cochran Q test (Cochran chi-square)

→If Cochran Q test statistically significant there is heterogeneity