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Imaging features for the prediction of clinical endpoints in chronic liver disease - a scoping review

Data charting proforma completion guidance

Guidance overview

1. What is a scoping review?
2. Prognostic vs diagnostic studies?
3. Retrospective vs prospective prognostic studies?
4. What do we mean by recruitment setting?
5. How to determine the prognostic study phase?
6. Sample sizes vs sub-cohort sample sizes
7. Development, internal validation and external validation samples – what do these all mean?
8. Sample sizes vs endpoint sample sizes – what's the difference?
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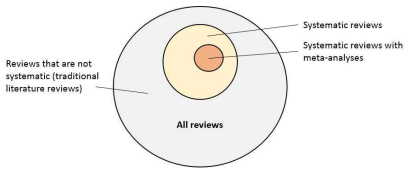
10. Anatomical features: themes vs detailed listing
11. Statistical analysis methods
12. The developed prognostic model – variables, presentation and usability

1. What is a scoping review?

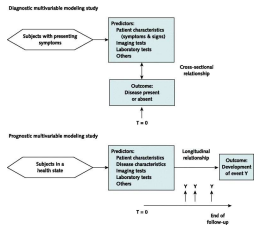


1. What is a scoping review?

Scoping Review	Systematic Review
Identify the types of available evidences in a given field	Uncover international evidence
Clarify key concepts/definitions in the literature	Confirm current practices/address variation in practices/identify new practices
Examine how research is conducted on a certain topic or field	Identify and investigate conflicting results
Identify key characteristics or factors related to a concept	Produce statements to guide decision-making
Identify and analyze knowledge gaps	Identify and inform areas for future research
Precursor to a systematic review	A systematic review!

(taken from https://medium.com/knowledgenudge/to-scope-or-not-to-scope-d4651bdfd75a)

2. Prognostic vs diagnostic studies



(Collins et al. 2015, BMC Med 13, 1)

2. Prognostic vs diagnostic studies

Can be very similar!

- Binary outcome (disease present/absent vs future occurrence yes/no)
- Key interest in generating probability of outcome
- Same approaches to generating multivariable models – predictor selection, model building methods
- Same dangers of overfitting
- Same measures for assessing model performance

(Collins et al. 2015, BMC Med 13, 1)

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2. Prognostic vs diagnostic studies

Key differentiators:

	Diagnostic	Prognostic
Explanatory variables		
Comparator	- Reference standard test - Disease verification	- Event definition - Future event occurrence on follow-up
Outcomes	Disease presence/absence	Event occurrence yes/no
Missing outcomes	Partial verification	Loss to follow-up

(adapted from Collins et al. 2015, BMC Med 13, 1)

3. Retrospective vs prospective prognostic studies?

Relationship between recruitment time and the event/endpoint:

- Retrospective – event/endpoint has already taken place at the time when a patient is recruited into the study
  - Explanatory variables measured before the event/endpoint are then studied
- Prospective – patients recruited into the study are followed-up until they develop the event/endpoint at a future date
  - Selected explanatory variables are measured at recruitment/before the event/endpoint develops

4. What do we mean by recruitment setting?

- Outpatient/community recruitment
  (e.g. stable cirrhotics seen in hepatology OPD; primary care recruitment of patients with a coded diagnosis of NAFLD)
- Inpatient recruitment
  (e.g. patients admitted to hospital with an acute variceal bleed)
- Patient registries - specialist databases to recruit patients from a specific disease cohort
  (e.g. the UK HCV national register; the European NAFLD registry)

- n.b.: Patients may be recruited as inpatients, with explanatory variables collected retrospectively in the outpatient setting ← (please select "inpatient" for Q8)
  (e.g. evaluation of previous outpatient surveillance US data in acutely decompensated inpatients)

5. How to determine the prognostic study phase

Much like clinical trials:

- Phase I: First in humans
- Phase II: Dose finding
- Phase III: Clinical effectiveness – estimating how useful in clinical practice

(Taken from slides provided by Prof Mallett)

5. How to determine the prognostic study phase

For prognostic studies:

- Phase IA: Development of tool
- Phase IB: Evaluation of tool in new people using registers and databases
- Phase IIA: First prospective use in clinical practice
- Phase IIB: Qualitative studies on experience of using tool in clinical practice
- (Phase III: RCT or observational study of effect in clinical practice)

(Taken from slides provided by Prof Mallett)

5. How to determine the prognostic study phase

For prognostic studies:

- Phase IA: Development of tool
  - National registry data
- Phase IB: Evaluation of tool in new people using registers and databases
  - Validation in external datasets

(Taken from slides provided by Prof Mallett)

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5. How to determine the prognostic study phase

For prognostic studies:

- Phase IIA: First prospective use alongside clinical practice
  - Does it identify the right patients compared to normal practice?
- Phase IIB: Qualitative studies on using tool in clinical practice
  - Is it usable?
  - Would it be used?
- Phase III: RCT or other comparative study design of using tool vs current practice

(Taken from slides provided by Prof Mallett)

6. Sample sizes vs sub-cohort sample sizes

- All studies should state the overall number of patients involved in the study
- When recording overall sample size (Q10), record the sample size that actually participated in the study rather than the sample size that was screened
  (e.g. 23000 patient records were screened for prospective inclusion into the study, from those 13000 were excluded because of incomplete records and a further 9000 were excluded because they did not have any imaging and 500 cases were lost to follow-up → overall sample size = 1000)

6. Sample sizes vs sub-cohort sample sizes

Regarding the non-liver disease sub-cohort questions:

- Study designs may include a non-liver disease sub-cohort
- These would be either healthy volunteers/non-liver disease patients:
  (e.g. survival (months), recorded after US in patients undergoing HCC surveillance was compared with survival in age-matched patients undergoing US for non-hepatic causes)

6. Sample sizes vs sub-cohort sample sizes

Regarding the liver disease sub-cohort questions:

- Example:
  patients were recruited from hepatology OPD, with viral hepatitis (n=85), ALD (n=75) and NAFLD (n=100) ← (please record the combined total of the liver disease aetiologies recruited, i.e. "liver disease sub-cohort size =260")
- Please also tick the relevant disease aetiologies studied (Q14)

7. Development, internal validation and external validation samples – what do these all mean?

- Phase IA studies contain only development samples
  (i.e. all the data collected is used to build the model)
- Phase IB studies include either internal or external validation sample

7. Development, internal validation and external validation samples – what do these all mean?

- Internal validation:
  - The original data collected is split into a separate "development" sub-cohort and a "test/validation" cohort ← please record the sizes of each of these cohorts in Qs15-16
  - The method by which the data is split between cohorts is important to study quality:
    - Randomly? Re-sampling the data? Temporal separation? Geographic separation?

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7. Development, internal validation and external validation samples – what do these all mean?

- External validation:
  - A separately recruited sample is used to test/validate the previously derived model
  - How the test/validation sample is defined is important to study quality:
    - Disease-based separation? Temporal separation? Geographic separation?
- 'Phase IIA' vs 'Phase IB externally validated study'?
  - Phase IIA must be "external" (often separately published study) and must be prospective

8. Sample sizes vs endpoint sample sizes – what's the difference?

- Prognostic studies are interested studying the development of a clinical endpoint/event
- Not all recruited patients will experience the clinical endpoint/event
- The size of the sample that goes on to experience the endpoint is important to the overall study quality and statistical power
  (e.g. a study proposes development of a model for predicting mortality in patients with NAFLD. The recruited sample size is 500, but after 5 years only ten patients die)

8. Sample sizes vs endpoint sample sizes – what's the difference?

- Record the clinical endpoints/events being studied
- Record the number of subjects that experiences each endpoint
  (regardless of which liver disease/non-liver disease sub-cohort they are from)
- Occasionally, there may be studies where most of the cohort experiences the event
  (e.g. a retrospective survival study with recruitment based on patients with hepatic encephalopathy recorded as a cause of death) ← in this situation, for Q21, state this and record the size of the smaller event cohort (such as age-matched controls without hepatic encephalopathy)

9. Follow-up interval – what do we mean?

- All prognostic studies have an interval between experiencing the event and measurement of explanatory variables
- This should be clearly stated(!)
- This interval could be fixed (e.g. in a prospective study) or maybe variable (e.g. interval between scan and death)
- The way the interval is recorded tends to be mean±SD, but there are variations (Qs23-26)

10. Anatomical features: themes vs detailed listing

- Thematic groups will be used for theme-based analysis, but the more important question is the specific detailed listing (Q29)
- Please include all variables studied (even if these do not end up getting used in the final proposed model)
- Please specify variable type and unit (i.e. length, volume, area, relative area, presence, categorical variables)
- Please specify those that are linked with endpoints (Q31)

11. Statistical analysis methods

- Refers to the method used to develop the model
- Important because will define which studies can provide useful data that can potentially be used in a meta-analysis

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12. The developed prognostic model – variables, presentation and usability

- Variables:
  How many do the authors propose as having prognostic value?
- Presentation:
  - Do the authors provide an explicit statement of the model they've developed?
  - What form does the proposed model take?

12. The developed prognostic model – variables, presentation and usability

- Usability:
  - How do they propose their model will work?
  - Does the model categorise patients?
  - Does the model estimate time to an endpoint?
  - Do the authors provide any clinical guidance for how the model should be used?