Grading and the GRADE instrument

G-I-N meeting

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Professional good intentions and plausible theories are insufficient for selecting policies and practices for protecting, promoting and restoring health.

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How can we judge the extent of our confidence that adherence to a recommendation will do more good than harm?

GRADE

Grades of Recommendation Assessment, Development and Evaluation

Why bother about grading?

- People draw conclusions about the
  - **quality of evidence**
  - **strength of recommendations**
- Systematic and explicit approaches can help
  - protect against errors
  - resolve disagreements
  - facilitate critical appraisal
  - communicate information
- However, there is wide variation in currently used approaches

Confused?

Recommendation for use of oral anticoagulation in patients with atrial fibrillation and rheumatic mitral valve disease

Evidence	Recommendation	Organization
B	Class I	AHA
C+	1	ACCP
IV	C	SIGN

Guideline development process

Quality of evidence

The extent to which one can be confident that an estimate of effect or association is correct.

It depends on the:

- **study design** (e.g. RCT, cohort study)
- **study quality/limitations** (protection against bias; e.g. concealment of allocation, blinding, follow-up)
- **consistency of results**
- **directness of the evidence** including the
  - **populations** (those of interest versus similar; for example, older, sicker or more co-morbidity)
  - **interventions** (those of interest versus similar; for example, drugs within the same class)
  - **outcomes** (important versus surrogate outcomes)
  - **comparison** (A - C versus A - B & C - B)

Quality of evidence

The quality of the evidence (i.e. our confidence) may also be REDUCED when there is:

- ↓ Sparse or imprecise data
- ↓ Reporting bias

The quality of the evidence (i.e. our confidence) may be INCREASED when there is:

- ↑ A strong association
- ↑ A dose response relationship
- ↑ All plausible confounders would have reduced the observed effect
- ↑ All plausible biases would have increased the observed lack of effect

Quality assessment criteria

Quality of evidence	Study design	Lower if	Higher if
High	Randomised trial	**Study quality**: -1 Serious limitations -2 Very serious limitations -1 Important **inconsistency** **Directness**: -1 Some uncertainty -2 Major uncertainty -1 **Sparse or imprecise data** -1 High probability of **reporting bias**	**Strong association:** +1 Strong, no plausible confounders +2 Very strong, no major threats to validity +1 Evidence of a **Dose response gradient** +1 All plausible **confounders** would have reduced the effect
Moderate			
Low	Observational study		
Very low	Any other evidence		

Categories of quality

- **High**: Further research is very unlikely to change our confidence in the estimate of effect. ⨁⨁⨁⨁
- **Moderate**: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. ⨁⨁⨁◯
- **Low**: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. ⨁⨁◯◯
- **Very low**: Any estimate of effect is very uncertain. ⨁◯◯◯

Judgements about the overall quality of evidence

- most systems just use evidence about primary benefit/outcome
- but what about other outcomes (downsides)?
- options:
  - ignore all but primary outcome
  - base it on the evidence for benefits
  - some blended approach
  - having separate grades for benefits and harms
  - weakest of any outcome

Strength of recommendation

The extent to which one can be confident that adherence to a recommendation will do more good than harm.

- **trade-offs** (the relative value attached to the expected benefits, harms and costs)
- **quality of the evidence**
- **translation of the evidence** into practice in a specific setting
- **uncertainty about baseline risk**

Judgements about the balance between benefits and harms

- Before considering cost and making a recommendation
- For a specified setting, taking into account issues of translation into practice

Clarity of the trade-offs between benefits and the harms

- the estimated size of the effect for each main outcome
- the precision of these estimates
- the relative value attached to the expected benefits and harms
- important factors that could be expected to modify the size of the expected effects in specific settings; e.g. proximity to a hospital

Balance between benefits and harm

- **Net benefits:** The intervention does more good than harm.
- **Trade-offs:** There are important trade-offs between the benefits and harms.
- **Uncertain net benefits:** It is not clear whether the intervention does more good than harm.
- **Not net benefits:** The intervention does not do more good than harm.

Judgements about recommendations

This should include considerations of costs; i.e. "Is the net gain (benefits-harms) worth the costs?"

- Do it
- Probably do it

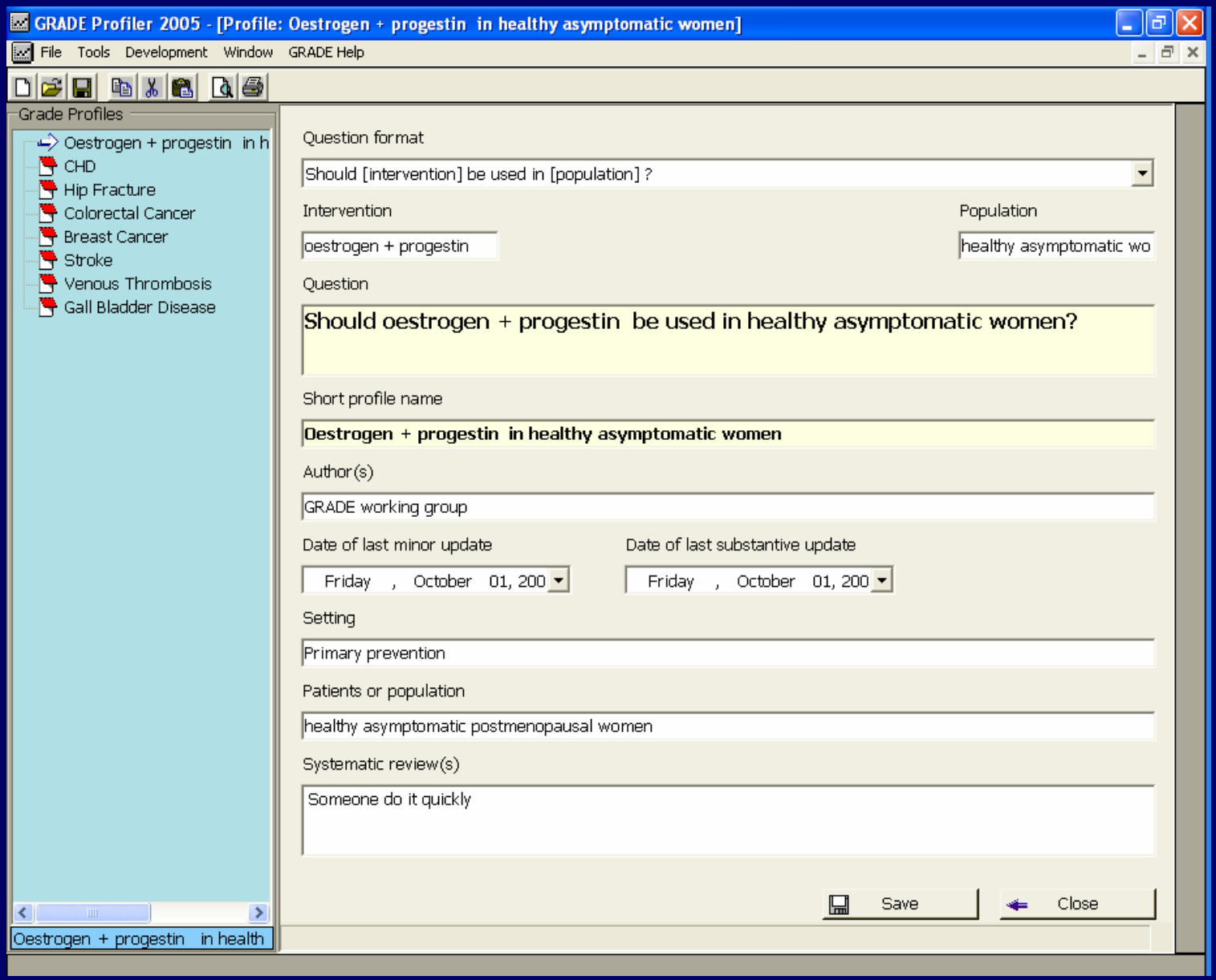
No recommendation

- Probably don't do it
- Don't do it

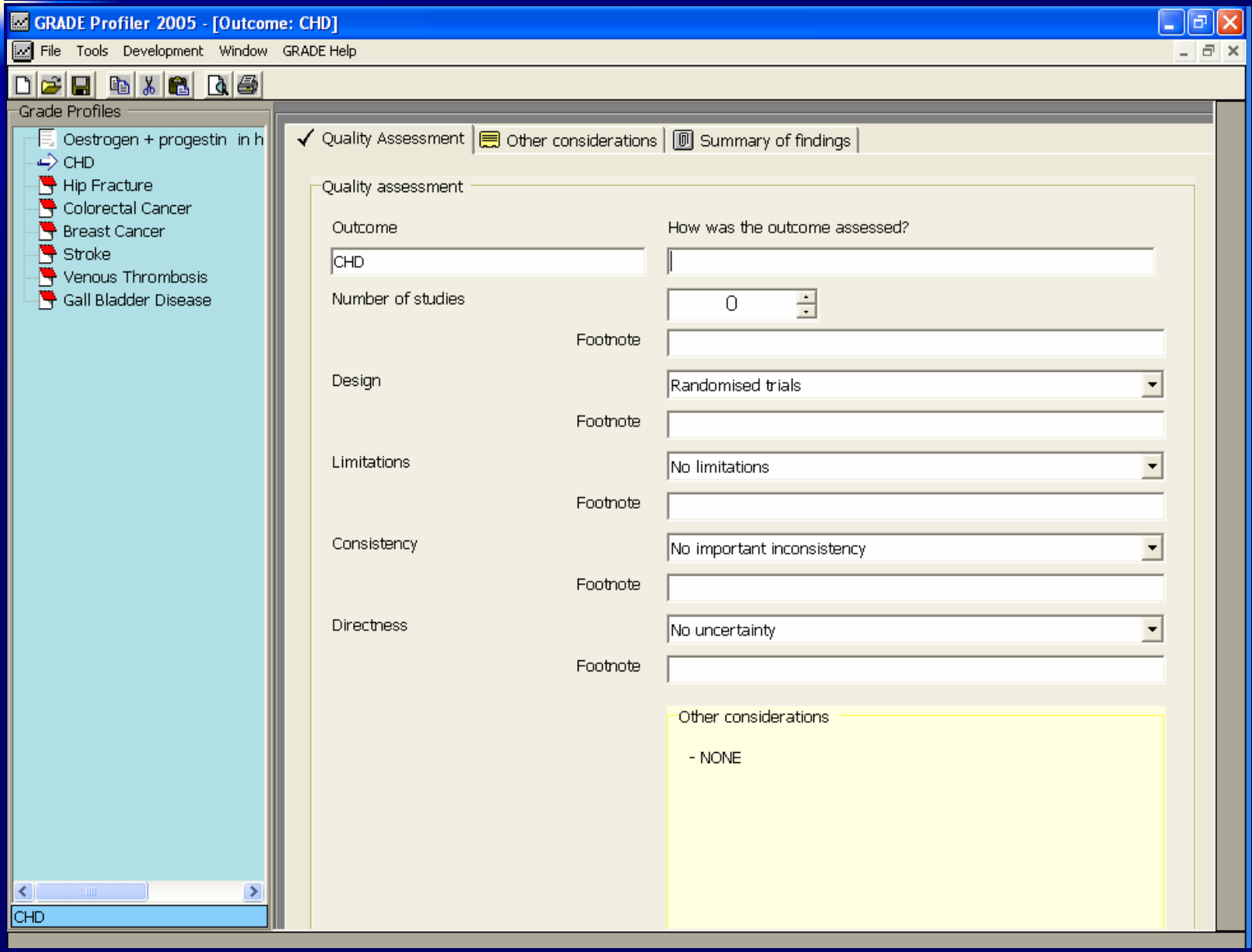
GRADE for diagnostic tests

Quality of evidence	Study design	Lower if *
High	Cross-sectional (or cohort) studies of patients with diagnostic uncertainty with direct comparison	**Study limitations** (including representativeness of population, choice of gold standard, incomplete performance of tests, independence of test interpretation) -1 Serious limitations -2 Very serious limitations -1 **Important inconsistency** **Directness** -1-Some uncertainty -2-Major uncertainty -1 **Sparse or imprecise data** -1 **High probability of reporting bias**
Moderate		
Low	Anything else	
Very low		

GRADE profiler (GRADEpro)



Separation by outcomes



Work in groups of two

- take a pencil (and paper)
- write down the most important issues/questions you have about GRADE

Small group sessions

- find a group
- select spokes person
- take 30 minutes to complete the task
- be prepared to criticise

Summary

What is good about GRADE?

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What is most challenging?

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What do we need to do next?

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