The validation of qualitative test methods

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Types of result

- Qualitative
  - Binary (0/1) = absent/present, fail/pass
  - Ordinal, eg low, moderate, high
- Semi-quantitative
  - <1, 1-10, >1, . . .
- Quantitative
  - Measure of concentration on a continuous scale

Issues for validating qualitative tests

- The is very little information in one binary result
- Different statistical methods are needed for dealing with such data
- Study design
  - Types and numbers of samples?
- Reporting
  - What to report and how to analyse?

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Types and numbers of responses

Actual	Observed		
	Negative	Positive	
Negative	TN	FP	Ntot
Positive	FN	TP	Ptot

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Reliability measures

False positive rate = FP/Ntot
Specificity = TN/Ntot = 1 – False positive rate

False negative rate = FN/Ptot
Sensitivity = TP/Ptot = 1 – False negative rate

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Reliability measures – some comments

The overall 'accuracy' on any population of samples

accuracy = p × sensitivity + (1 – p) × specificity

depends on the proportion p of actual positives in the population. Need to know both specificity and sensitivity in order to generalise.

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Reliability measures – some comments

- Both sensitivity and specificity may depend on sample type and the presence of interferents
- Sensitivity will usually depend on the amount of analyte present in the sample. This has implications for
  - study design
  - interpreting 'average' sensitivity from a study

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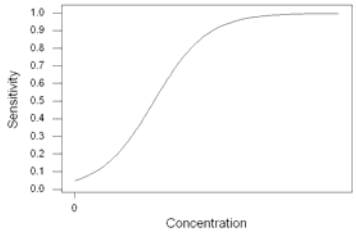
Sensitivity as a function of concentration



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Study design – choice of samples

- Aim to provide estimates of specificity, and sensitivity at a range of analyte concentrations
  - Desirable to include a blank sample
  - Concentration should be known for positives
  - Do not just use 'easy' samples
  - Use ongoing studies to build up a picture of the sensitivity curve

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Study design – numbers of replicates

- Need substantial numbers of replicates to establish a sensitivity with and degree of precision
- For example, the 95% confidence limits for a true proportion when we observe 4 successes out of 5 are (0.41, 0.98), for 16 out of 20 they become (0.60, 0.93).

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Reporting

- Report numbers of positive and negative results for each sample
- If relevant report the concentration for each positive sample
- Fine to invent scoring rules – tailor to the specific context

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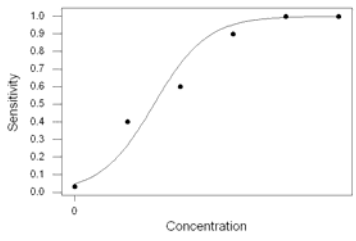
Modelling sensitivity as a function of concentration – logistic or probit regression



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Conclusions

- The validation of qualitative test methods needs special approaches
- These need not be complicated – in fact the simpler the better
- A reference

  S.L.R. Ellison and T. Fearn, Trends in Analytical Chemistry, 24, 468-476, 2005.