School for Primary Care Research

Increasing the evidence base for primary care practice

Comparing Methods for Identifying an Intermediate Range of Test Result

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INTRODUCTION

- Diagnostic tests rarely discriminate perfectly between patients with and without a disease, leaving a subset for whom disease status cannot be established
- It is argued that the frequently adopted binary framework for reporting diagnostic accuracy results is inadequate due to its inability to recognise the uncertainty inherent in diagnostic practice[1]
- Despite being recommended in the STARD statement, there is currently no standardised method for identifying an intermediate range of values on a quantitative test scale
- Two existing methods were identified in the literature, both of which have been rarely cited or implemented in diagnostic research

1 Feinstein (1990). *Jnl Cl Epi.*

AIM

To evaluate two existing and one new method for identifying an intermediate range on a quantitative test scale

DATA

- 701 children with suspected serious bacterial infection were consecutively recruited in a UK paediatric assessment unit
- Index tests: white blood cell count (WBC), procalcitonin (PCT) and C-reactive protein (CRP)
- Reference standard: cases of 'serious bacterial infection' were agreed by a panel of clinicians

THE 'GREY ZONE' METHOD

Coste and Pouchot's 'grey zone' method is based on the concept of 'desired' post-test probabilities, applying Bayesian theory to derive likelihood ratio intermediate range limits[2] e.g. to achieve LRs corresponding to PPV=0.9 and NPV=0.1

2 Coste et al. (2003). *Int Jnl Epi.*

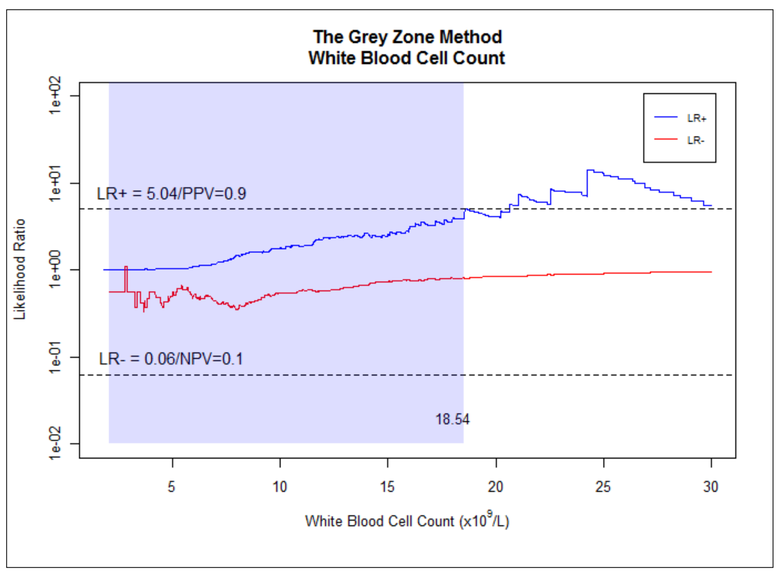
THE TG-ROC METHOD

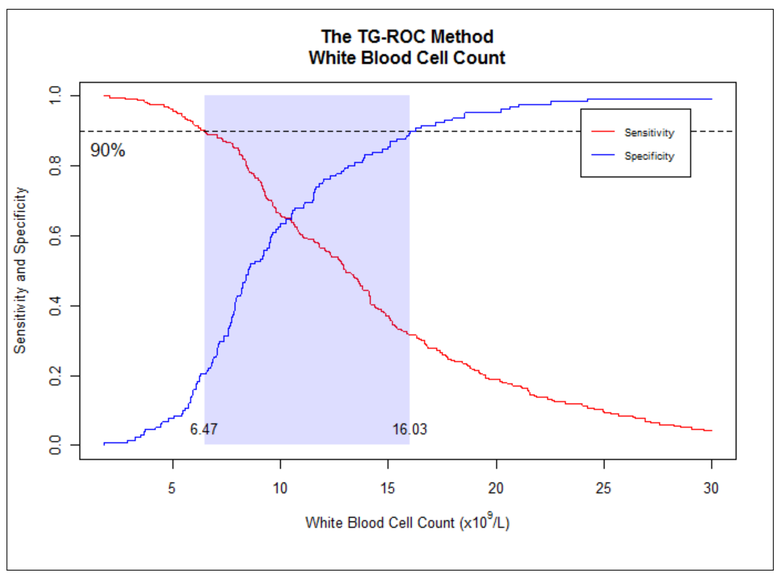
Greiner's 'Two-Graph Receiver Operating Characteristic' (TG-ROC) defines an intermediate range as values which fail to achieve 90% sensitivity and specificity[3]

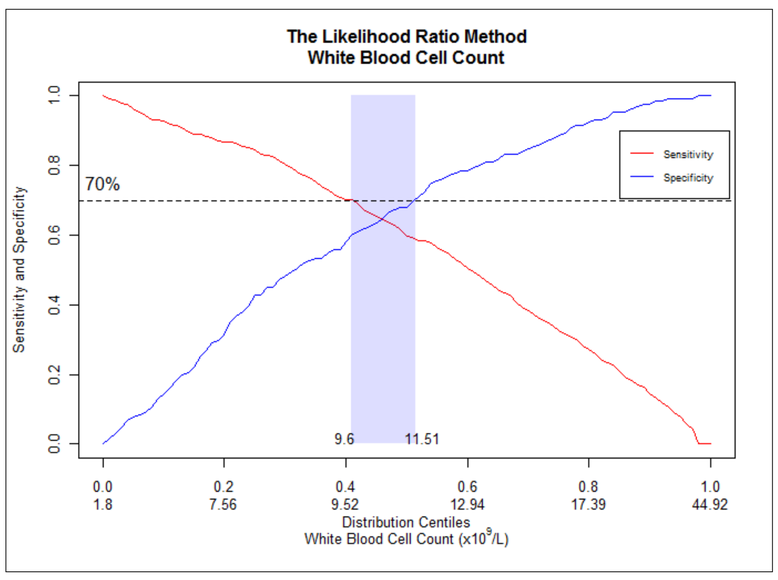
3 Greiner (1995). *Jnl Immun Methods.*

THE LIKELIHOOD RATIO METHOD

We define intermediate results as those which hold very little diagnostic information: test values with LR- greater than 0.5 and a LR+ less than 2.
Results are plotted on a modified version of the TG-ROC, using centiles of the sample distribution to enable comparability.







Grey Zone: PPV= 0.9 and NPV = 0.1

Test	Lower limit	Upper limit	% Neg	% in IR	% Pos
WBC	No solution	18.54	0.0%	83.0%	17.0%
PCT	No solution	0.44	0.0%	70.5%	29.5%
CRP	No solution	105	0.0%	74.9%	25.1%

EVALUATION

- No solution if 'desired' accuracy level is beyond the discriminatory capacity of the test
- Likelihood ratio curves very unstable and non-monotonic due to the sparseness of the data

TG-ROC: Sensitivity and Specificity = 90%

Test	Lower limit	Upper limit	% Neg	% in IR	% Pos
WBC	6.47	16.03	14.0%	62.5%	23.8%
PCT	0.12	0.42	14.8%	55.0%	30.2%
CRP	8	99	9.7%	64.1%	26.3%

EVALUATION

- Method will always find IR limits, unless single threshold exceeds 90% Se and Sp.
- The TG-ROC curves are smooth, making it easy to interpret

LR - ≥ 0.5 and LR + ≤ 2

Test	Lower limit	Upper limit	% Neg	% in IR	% Pos
WBC	9.6	11.51	40.8%	10.7%	48.5%
PCT	0.16	0.28	25.5%	26.8%	47.7%
CRP	No Solution	49	0.0%	54.4%	45.6%

EVALUATION

- IRs encompass a reasonable % of the patients
- Problem of unstable LR curves overcome
- Still will not always provide a solution (although this will happen less frequently)

The National Institute for Health Research School for Primary Care Research is a partnership between the Universities of Birmingham, Bristol, Keele, Manchester, Nottingham, Oxford, Southampton and UCL.

This poster summarises independent research funded by the National Institute for Health Research. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

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