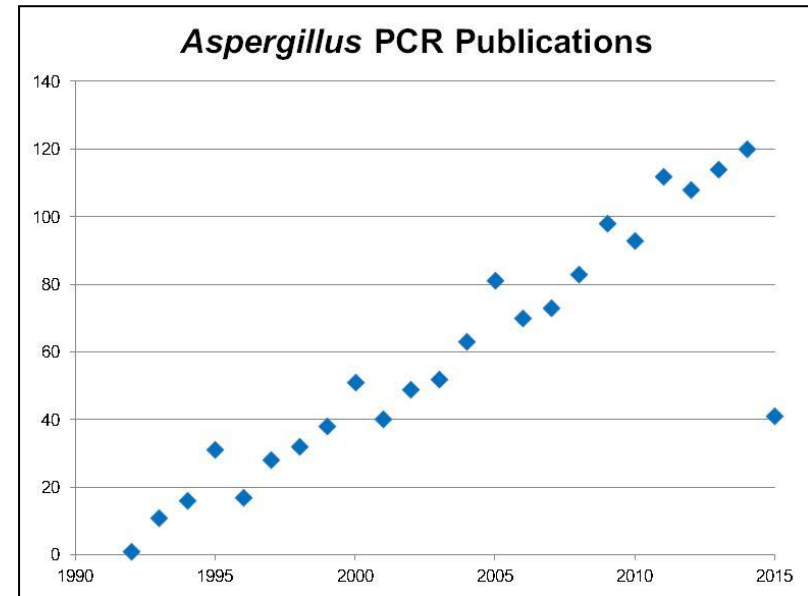


# **Systematic reviews of *Aspergillus* PCR - Cochrane and other.**

**Oliver Morton  
University of Western Sydney**

**EAPCRI Laboratory Working Party**

- 20 Years of *Aspergillus* PCR



- Does it work?

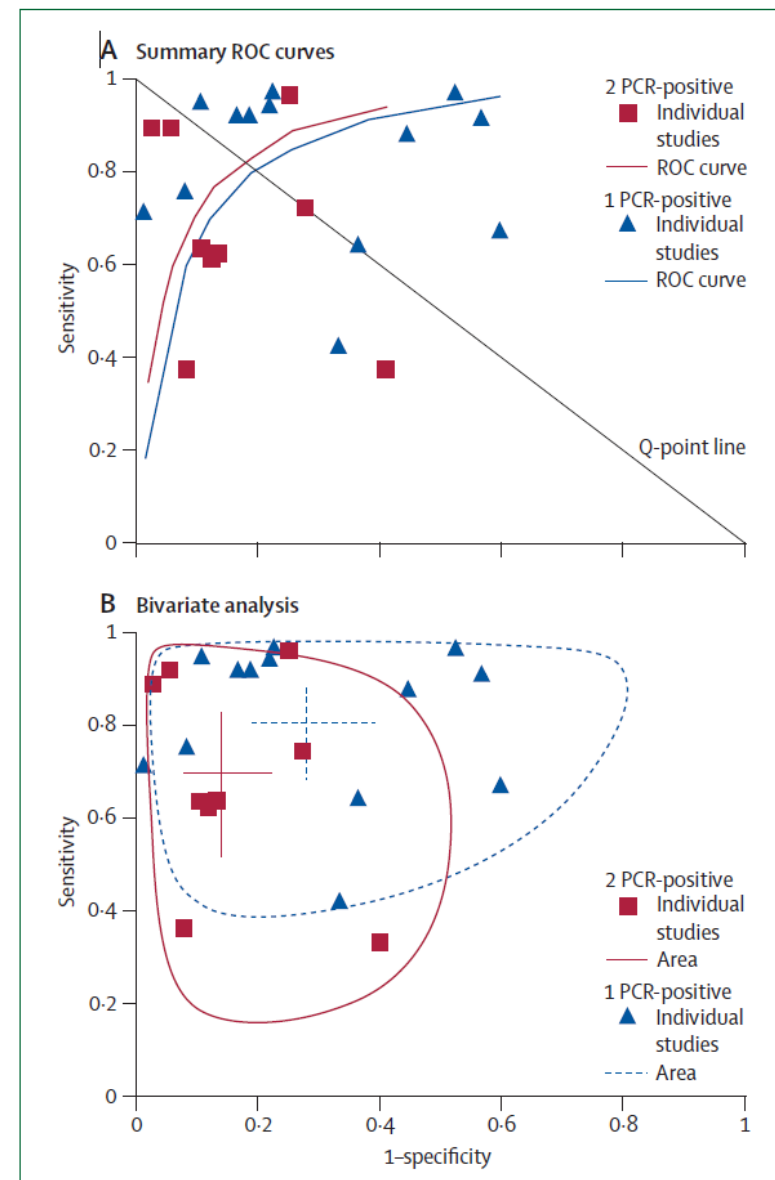
- What have clinical studies shown?

- Where do we go from here?

# Mengoli *et al.* 2009

## *Aspergillus* PCR in blood samples

- 16 Studies included from 7059
- Single Positive vs Two Positives
- Two positive tests to confirm diagnosis
  - In low prevalence (> 10%) IA can be ruled out if PCR negative
  - Two or more PCR positives can act as mycological confirmation of IA
- High degree of heterogeneity between studies
- Identified lack of standardisation as a factor inhibiting analysis



# Arvanitis *et al.* 2014

## Aspergillus PCR in blood samples

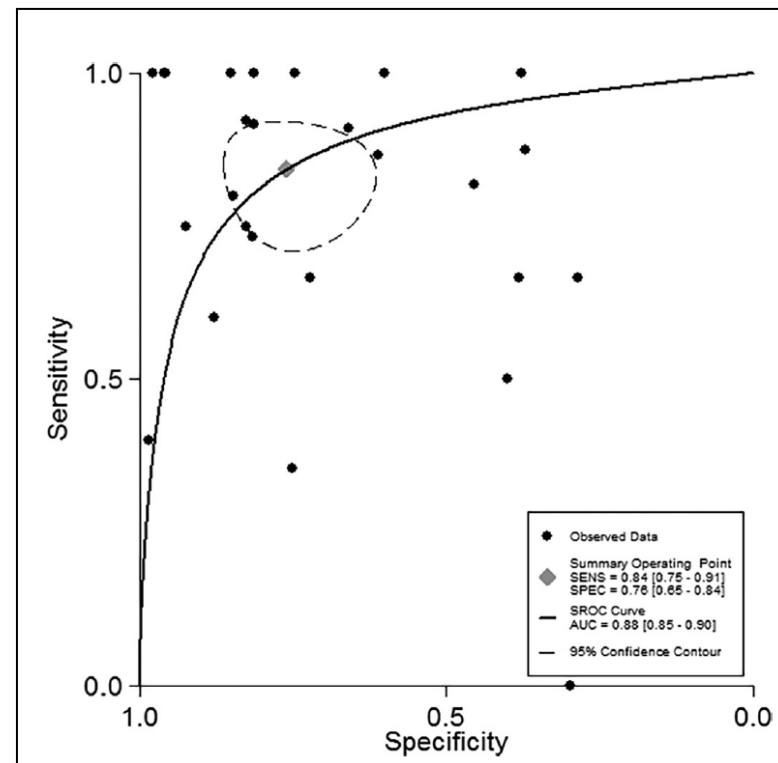
25 Studies included  
(partial inclusion of case-control studies)

### Outcomes:

- Performance of Whole Blood and Serum was not significantly different

- EAPCRI Guideline Compliance was significant

- Two assay positives to define PCR positive case improves positive likelihood ratio



### Single Positive PCR Result:

Sensitivity 84%

Specificity 76%

### Two or More Positive PCR Results:

Sensitivity 64%

Specificity 95%

# EAPCRI Systematic Review for Cochrane Database

## Inclusion Criteria:

1. Appropriate reference standard, e.g. EORTC/MSG criteria
2. Reports all data for 2x2 analysis
3. Prospective Analysis

## Data Extraction:

2 analysts per article  
QUADAS

## Analysis:

Bivariate Analyses  
HSROC  
Investigate Heterogeneity

# Results

## Article Selection:

Overall number of articles : 1672

Final number: 18

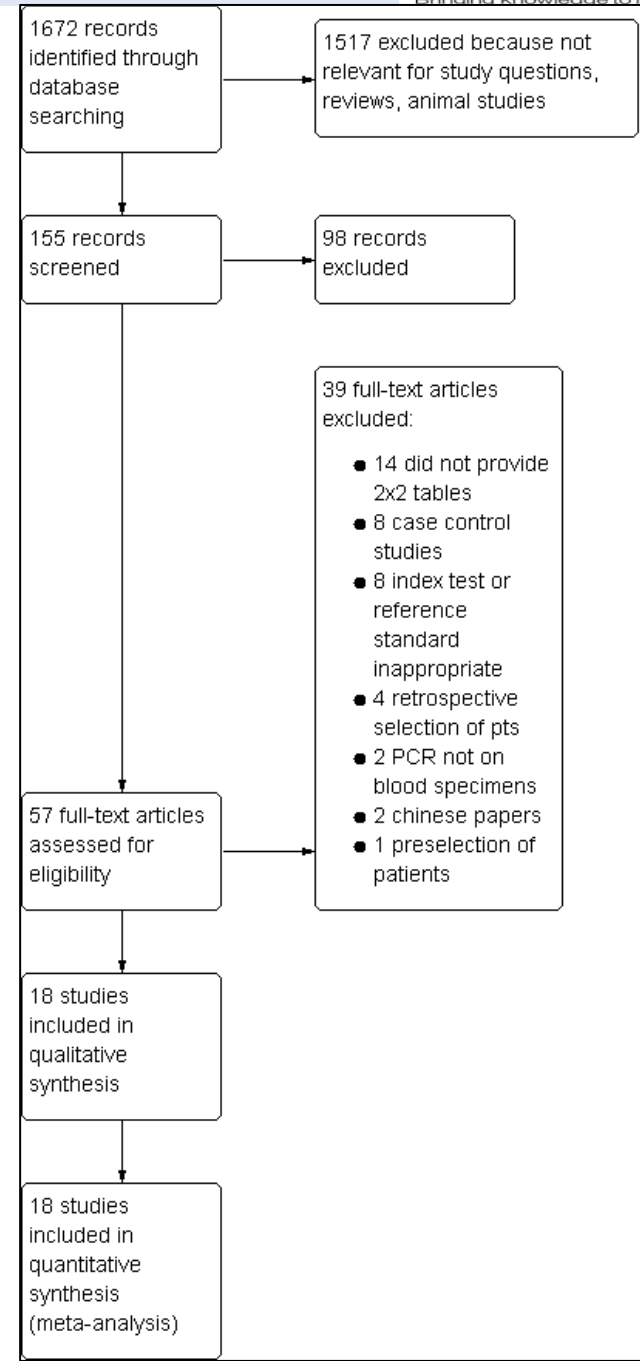
## Overall:

- 154 articles potentially relevant
- 56 articles selected for full review
- 18 articles from period 2000-2013

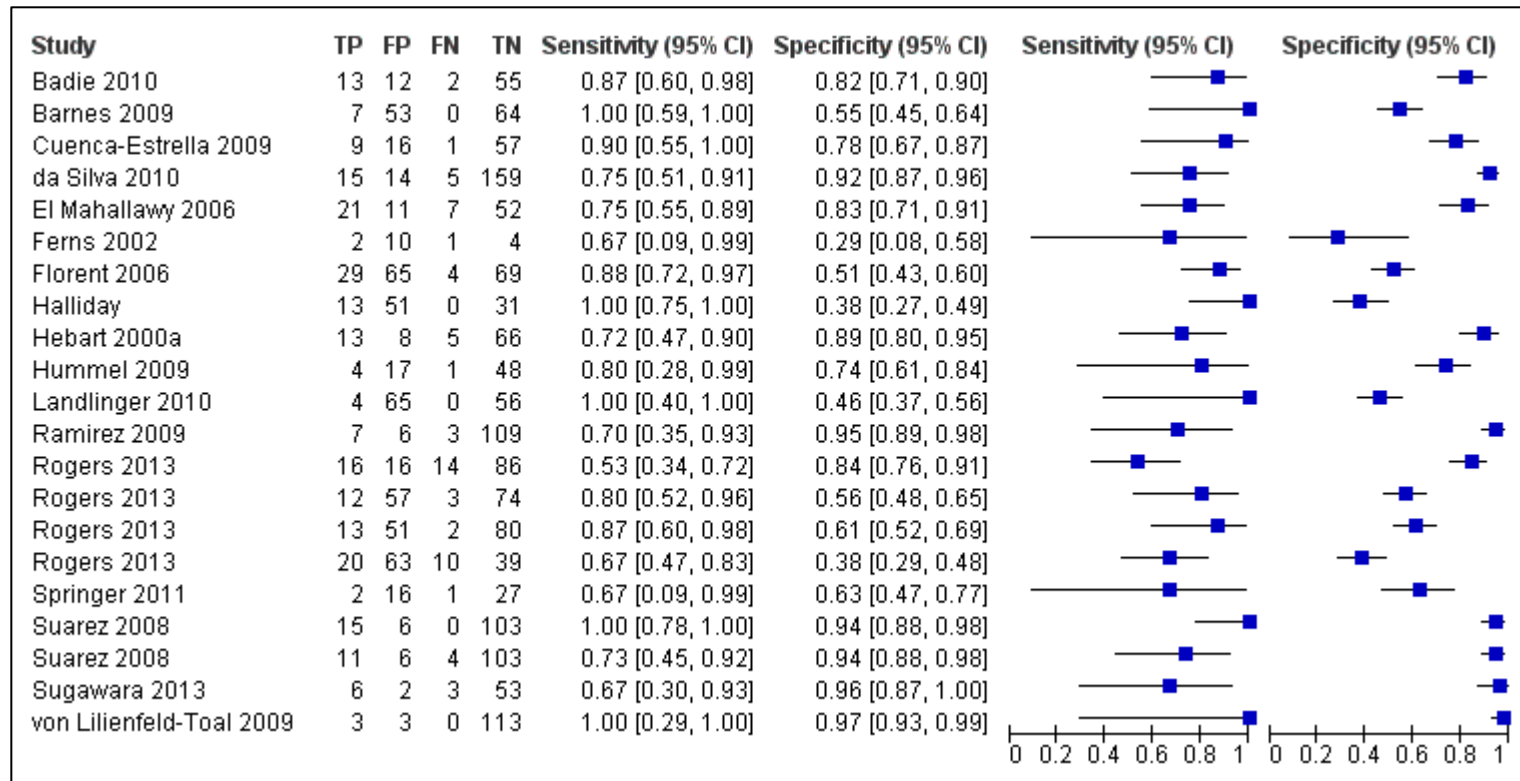
Incidence of IA: 13%

Tested 17 studies for single positive result

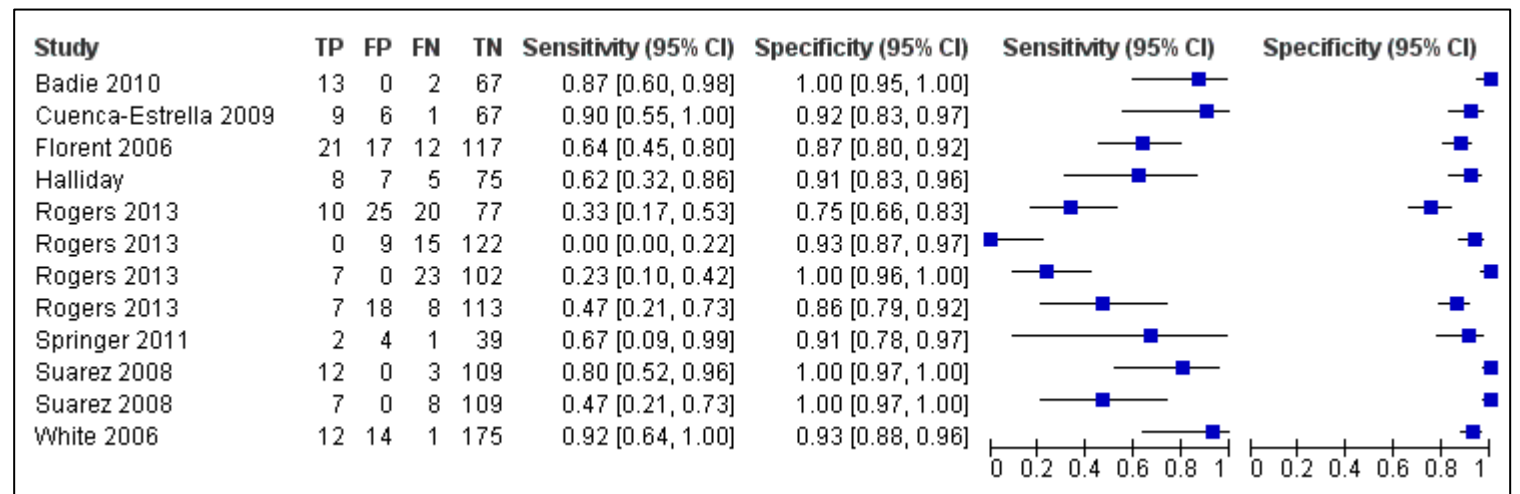
Tested 8 studies for 2 or more positive results



## Single Positive PCR Result



## >1 Positive PCR Result



# 1 Positive or 2?

**1 positive** assay result

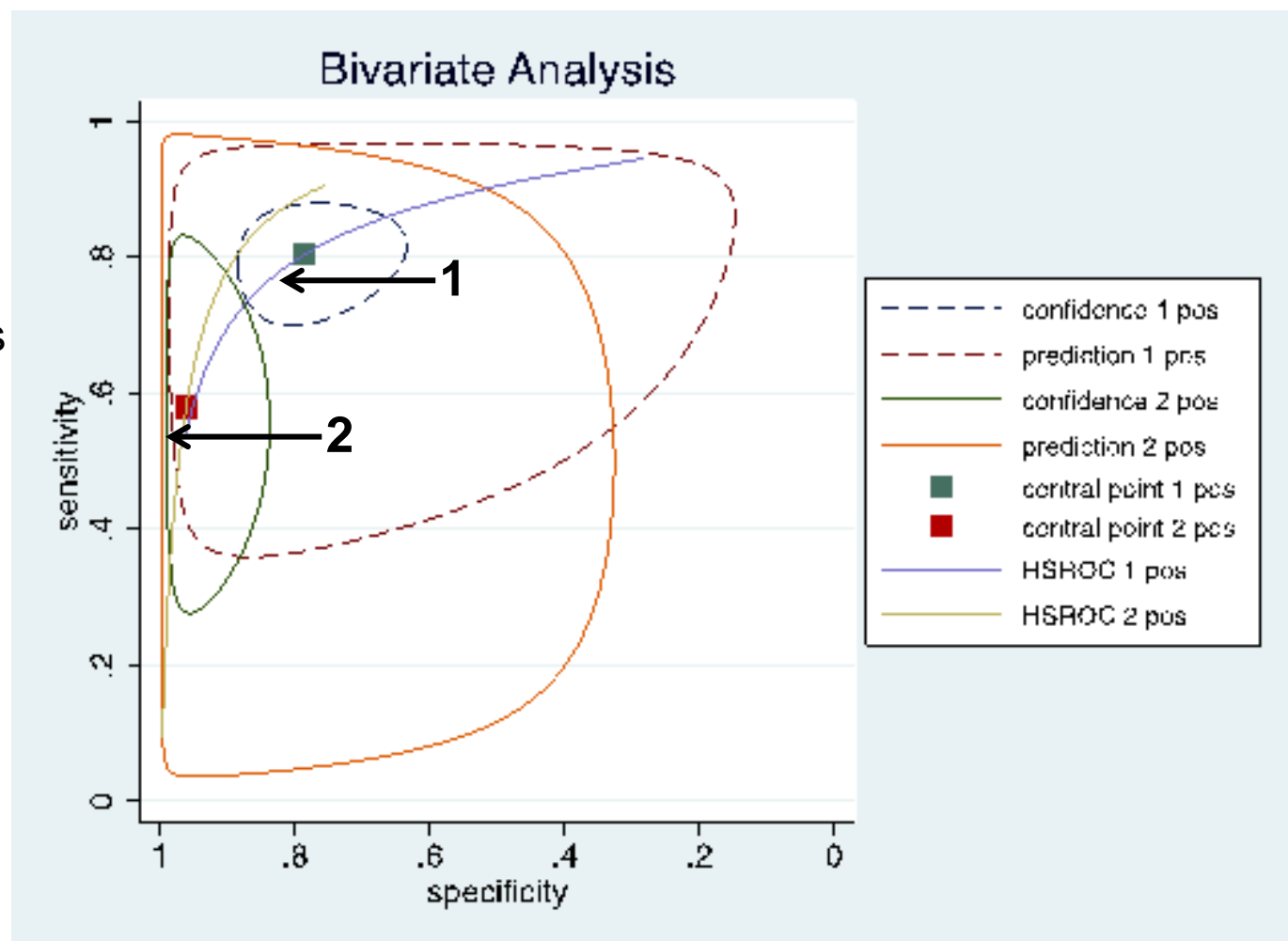
Sens: 80.5%

Spec: 78.5%

**2 positive** assay results

Sens: 57.9%

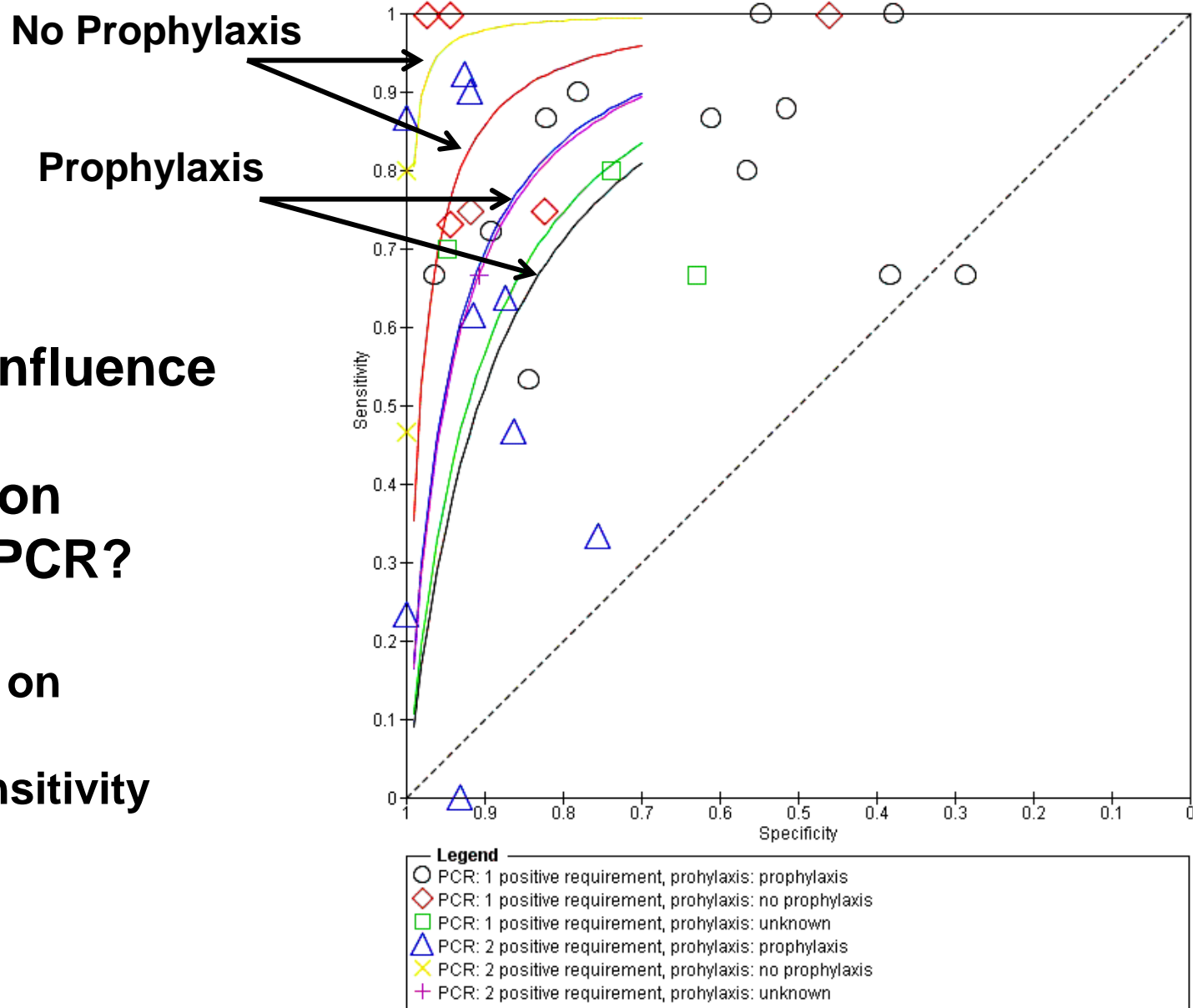
Spec: 96.2%



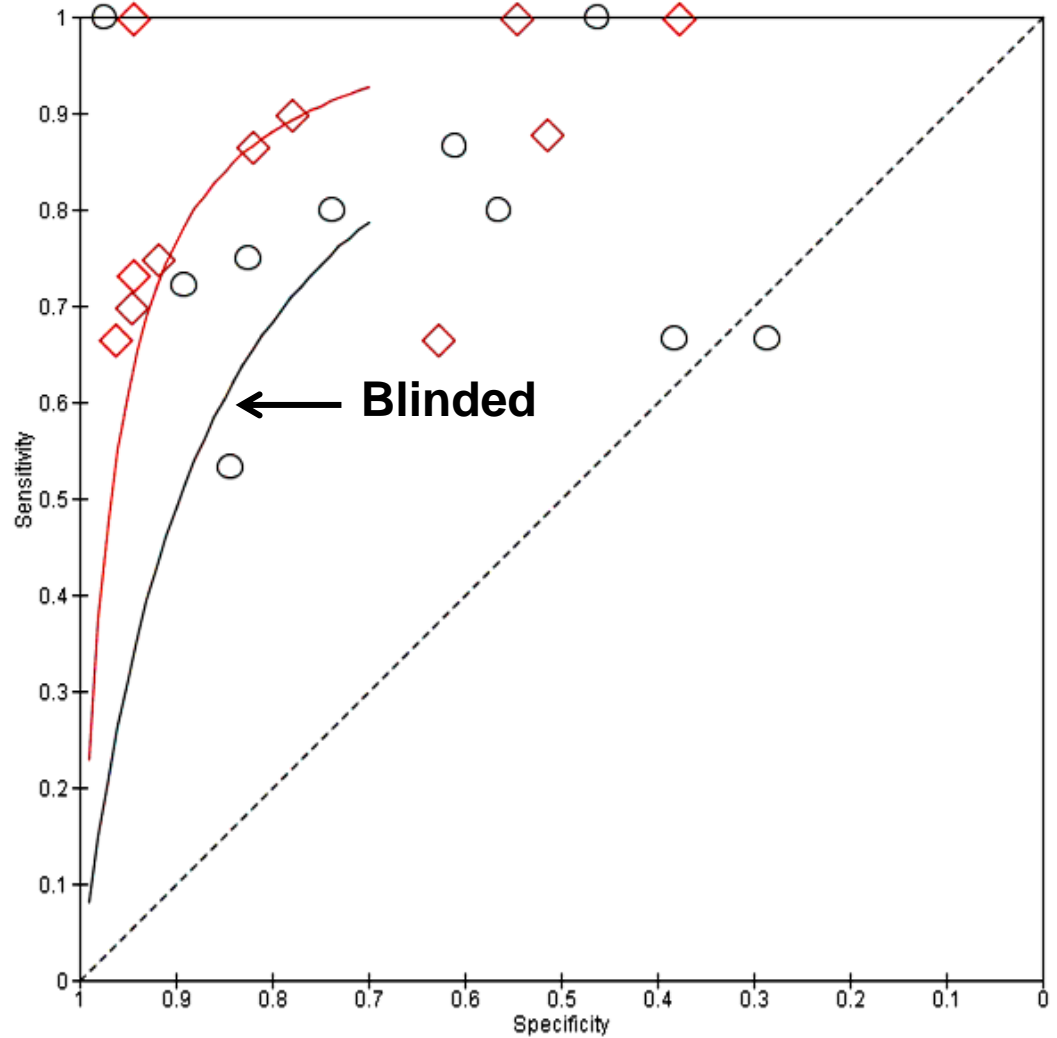


## What is the influence of antifungal prophylaxis on *Aspergillus* PCR?

- Large effect on Specificity
- Less for Sensitivity



# What is the impact of blinding the index or reference tests?



# Questions

1. How should positive PCR results be interpreted?
2. Areas for improvement: sample type, technology?
3. Standardisation of PCR assays?
4. Comparability of studies; minimum information required for analysis?
5. What will PCR be used for? Diagnosis or Screening
6. What are the exact effects of antifungals on PCR?

# Acknowledgements:

- European *Aspergillus* PCR Initiative
- Our Sponsors

