



2018

28-30 JUNE
VIENNA, AUSTRIA

**SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE**

The predictive value of serum biomarkers in the assessment and management of paediatric febrile neutropaenia



MASCC/ISOO

ANNUAL MEETING ON SUPPORTIVE CARE IN CANCER



www.mascc.org/meeting



#MASCC18

2018
28-30 JUNE
VIENNA

MASCC/ISOO
ANNUAL MEETING
SUPPORTIVE CARE IN CANCER



Faculty Disclosure

X	No, nothing to disclose
	Yes, please specify:

Background

- Febrile Neutropaenia (FN) is the second most common reason for presentation to hospital
- Typical paediatric FN episode different to typical adult FN episode:
 - 33-50% upper respiratory tract infections
 - Higher rate of fever of unknown origin
 - Lower mortality (0.2 – 3%)
- Risk stratification rules are not universal in paediatrics



2018

28-30 JUNE
VIENNA, AUSTRIA

SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE



Aims



2018

28-30 JUNE
VIENNA, AUSTRIA

SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE

- Build on two preceding reviews (2012, 2013) to:

1. Evaluate the sensitivity and specificity of biomarkers at predicting adverse outcomes
2. Evaluate the predictive role of biomarkers in guiding management decisions for cessation or early de-escalation of treatment



Results



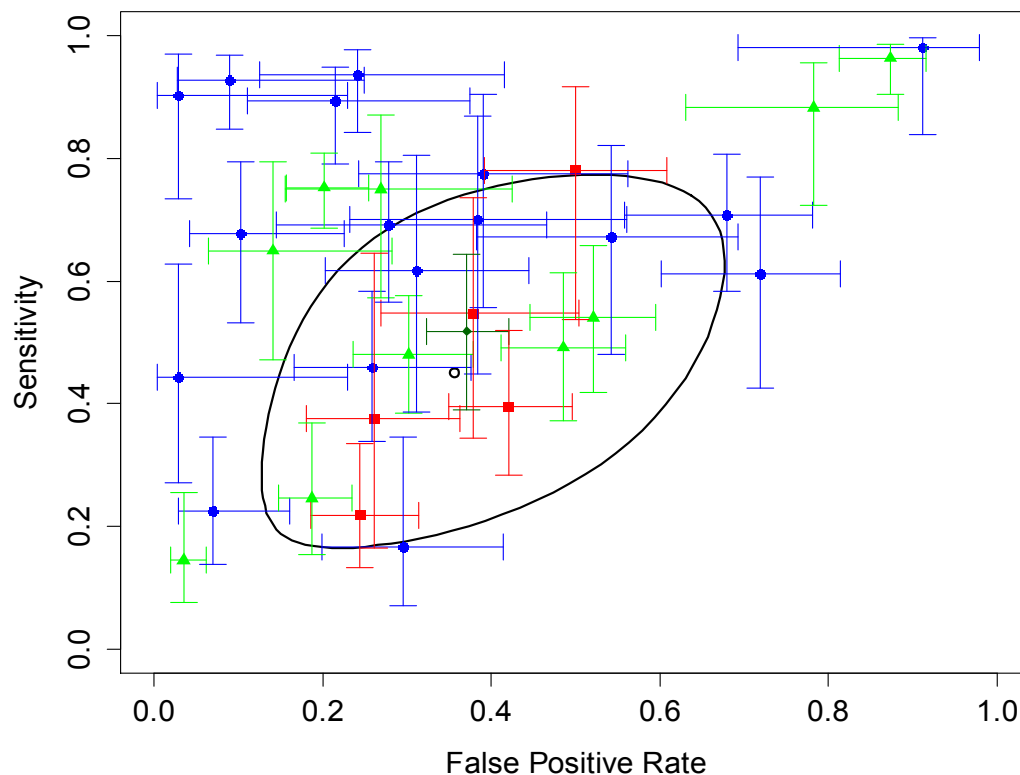
- April 2016
- Overall quality of studies good
- 7676 episodes from 4508 patients from 11 countries evaluating 30 biomarkers

Biomarker	2012 review	2013 review	2017 review	Total studies
C Reactive Protein (CRP)	20	9	11	40
Procalcitonin (PCT)	8	6	7	21
Interleukin 6 (IL-6)	10	2	7	19
Interleukin 8 (IL-8)	10	5	8	13



Biomarkers to predict outcome subgroup

CRP by outcome group



Cross-Hairs plot of CRP to detect adverse outcome

red cross = bacteraemia

blue cross = Clinical bacterial infection

light green cross = Serious bacterial infections

dark green cross = severe sepsis

Length of cross = 95% confidence interval of study specificity and sensitivity.

Small black circle = pooled sensitivity and specificity.

Black ellipse = 95% confidence region of pooled sensitivity and specificity

Pooled sensitivity 45% (95% CI 15-75%)

Pooled specificity 65% (95% CI 30-85%)



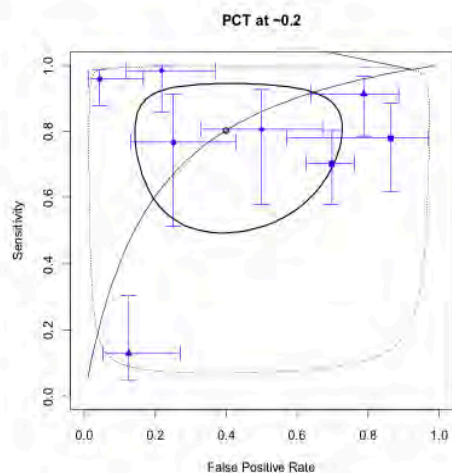
Biomarker predictive ability at different thresholds



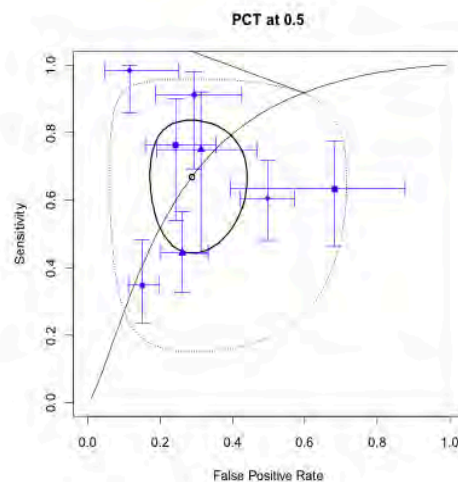
2018

28-30 JUNE
VIENNA, AUSTRIA

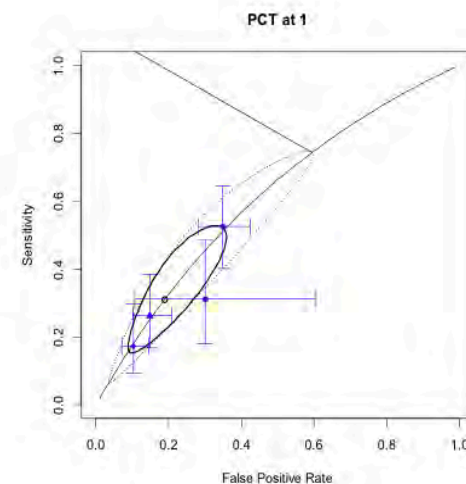
SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE



Pooled sensitivity 80% (95% CI 50-90%)
Pooled specificity 60% (95% CI 25-85%)

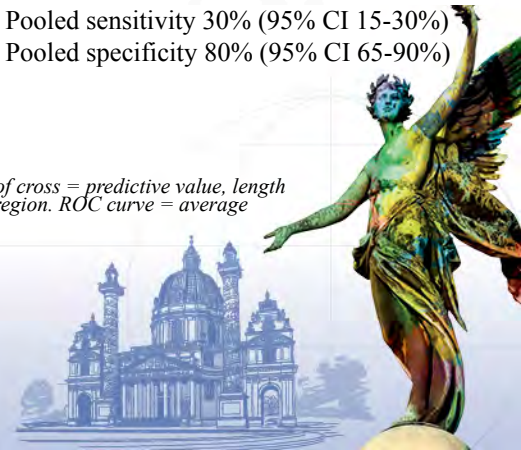


Pooled sensitivity 70% (95% CI 45-85%)
Pooled specificity 70% (95% CI 55-85%)



Pooled sensitivity 30% (95% CI 15-30%)
Pooled specificity 80% (95% CI 65-90%)

Cross-Hairs ROC plot showing relationship of sensitivity and specificity of PCT at different cut off levels. Crosses = individual studies; centre of cross = predictive value, length of cross = CIs within the study. Small circle = pooled predictive value of marker; solid ellipse 95% confidence region, dashed ellipse 95% prediction region. ROC curve = average pooled data in population, distance of cross from ROC curve = variance from average.



Serial Biomarkers

- 10 studies in updated review (6 in previous)
- Meta-analyses not possible
- CRP values more discriminatory after 2 days than at admission
- Serial PCT more discriminatory over time (rises and falls)
- IL-6 and IL-8; no benefit in serial testing



2018

28-30 JUNE
VIENNA, AUSTRIA

SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE



Conclusions

- No recommendations for single point use of biomarkers to guide de-escalation or cessation treatment
- Serial biomarkers have promising predictive ability
- Bacteraemia and severe sepsis can be reliably predicted by CRP, PCT, IL-6 and IL-8
- The ideal threshold cut-off biomarker; PCT value of 0.5ng/ml may be most useful



2018

28-30 JUNE
VIENNA, AUSTRIA

SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE



Acknowledgements



Dr Bob Phillips



Centre for Reviews and Dissemination



2018

28-30 JUNE
VIENNA, AUSTRIA

SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE

