

# **NICE HealthTech Guidance (HTG386):** *Procalcitonin Testing for Diagnosing and Monitoring Sepsis*

**Paul Dark**

What is NICE HTG386?

How does it apply to my current sepsis care?

How might it change as a result of new NIHR health research evidence from the NHS?

# Funding disclosure

## Professor of Critical Care Medicine

Division of Immunology, Immunity to Infection and Respiratory Medicine,  
Faculty of Biology, Medicine and Health,  
The University of Manchester



## Vice Dean for Health and Care Partnerships

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## Honorary NHS consultant

Critical Care and Major Trauma Services,  
Northern Care Alliance NHS Foundation Trust,  
Greater Manchester



## Academic Director

Health Innovation Manchester,  
Manchester University NHS Foundation Trust,  
Greater Manchester



## NIHR Senior Investigator



# Antimicrobial stewardship and sepsis

Initiation

Review and refinement

Duration



# Political context in UK



## Sepsis: NHS Modern Service Framework (NHS 10-Year plan)

### Prevention & Early Recognition:

Enhancing infection prevention and control (IPC) and community-level identification

### Evidence-Based Care:

Aligning with the latest evidence-based guidance and NICE guidelines

### Data & Technology:

Utilizing improved data to monitor sepsis cases, including AI-enabled early warning tools



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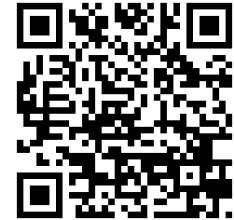


# **NICE** National Institute for Health and Care Excellence

**Suspected sepsis in adults: recognition, assessment and early management**



**Suspected sepsis in children: recognition, diagnosis and early management**



**Procalcitonin testing for diagnosing and monitoring sepsis**



**Tests for rapidly identifying bloodstream bacteria and fungi**



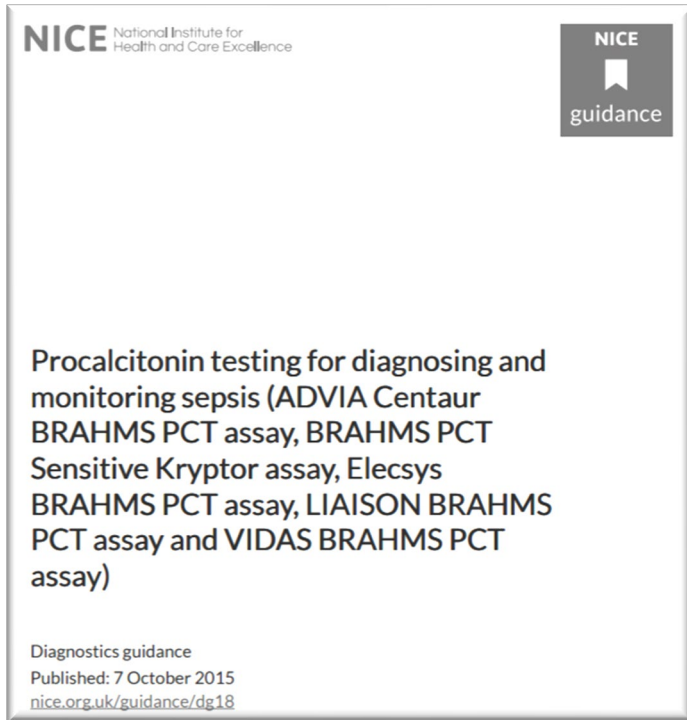
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# Procalcitonin for diagnosing & monitoring sepsis

## PCT-guided treatment duration

- Studies promising internationally, low quality evidence
- Lack of a systematic evidence from the UK
- Uncertainty in current standard NHS clinical practice



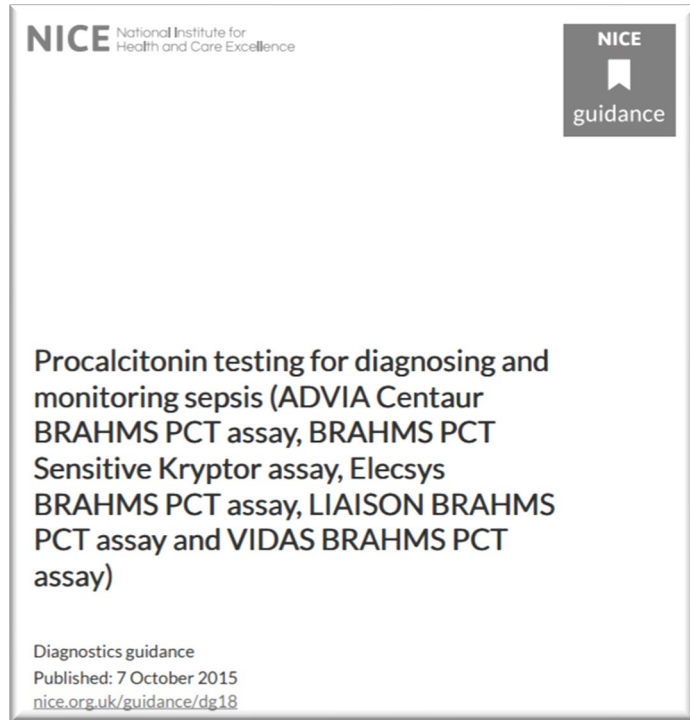
# Procalcitonin for diagnosing & monitoring sepsis

## PCT-guided treatment monitoring

- Studies promising internationally, low quality evidence
- Lack of a systematic evidence from the UK
- Uncertainty in current standard NHS clinical practice

## Recommendations

- Definitive UK research
- Centres running PCT are encouraged to take part in RCTs
- Is there a role for CRP monitoring?
- Children and adults



# Applied health research responding to NICE identified evidence gaps

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Department  
of Health &  
Social Care

## GUIDELINES

# Surviving sepsis campaign: international guidelines for management of sepsis and septic shock



# When to start antibiotics

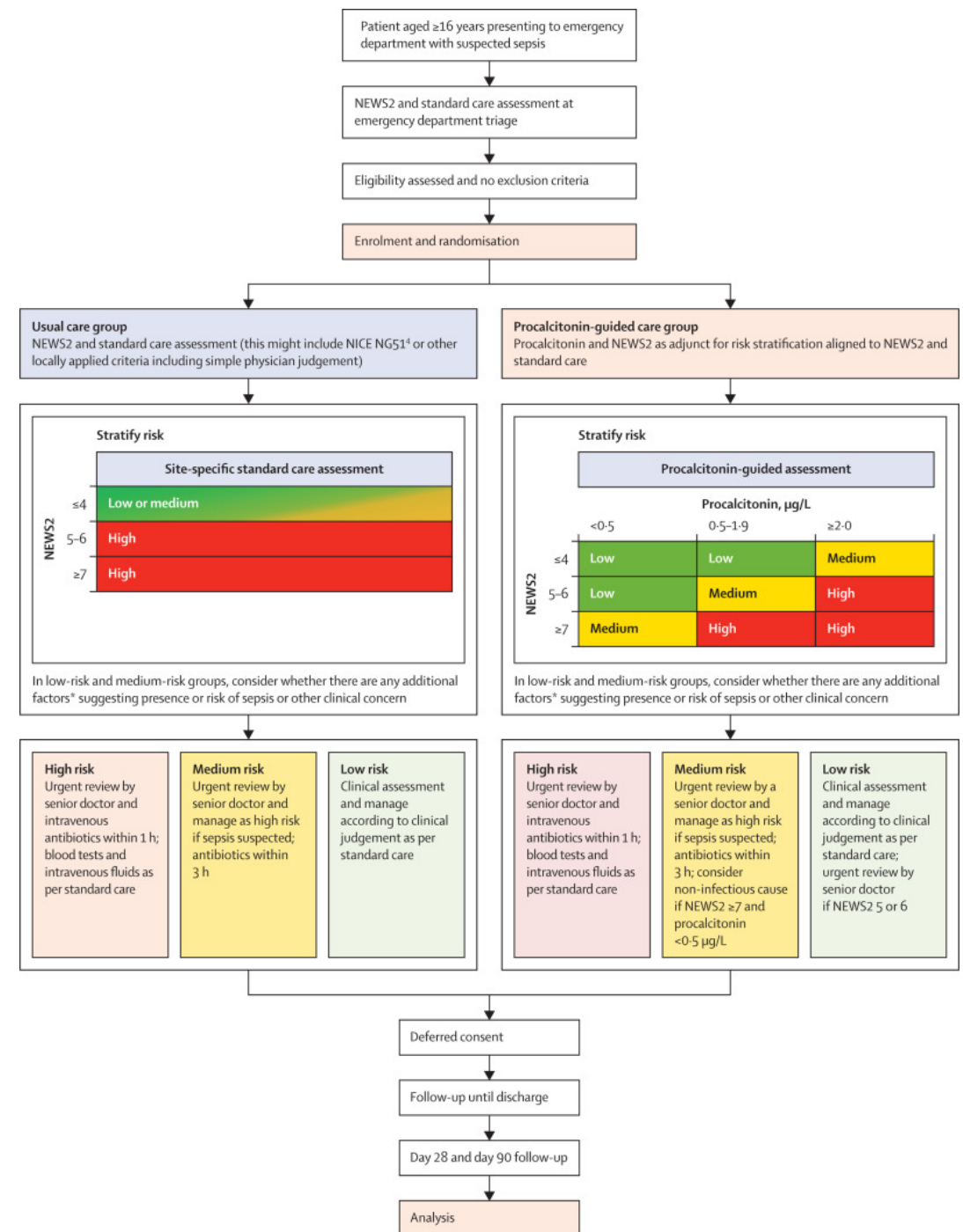
## GUIDELINES

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock



	Shock is <b>present</b>	Shock is <b>absent</b>
Sepsis is <b>definite</b> or <b>probable</b>	<p>✔ ✔</p> <p>Administer antimicrobial therapy <b>immediately</b>, ideally within 1 hour of recognition.</p>	<p>✔ ✔</p> <p>Administer antimicrobial therapy <b>immediately</b>, ideally within 1 hour of recognition.</p>
Sepsis is <b>possible</b>		<p>✔</p> <p>Rapid assessment* of infection vs noninfectious causes of acute illness.</p> <p>Administer antimicrobial therapy <b>within 3 hours</b> if concern for infection persists.</p>

# When to start antibiotics (biomarker decision support)



**PRONTO**

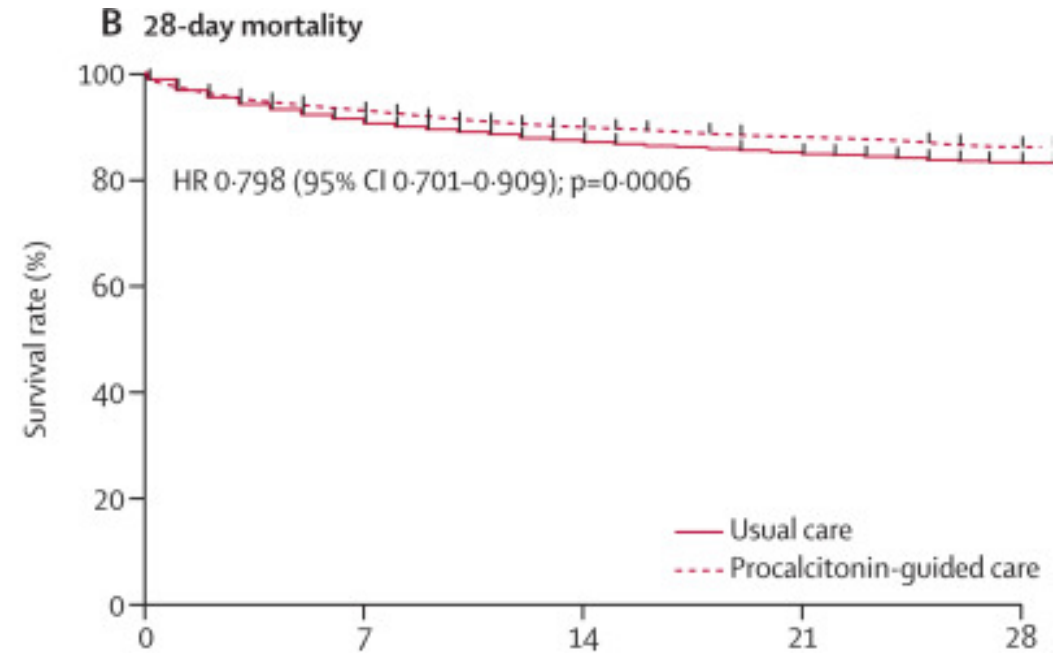
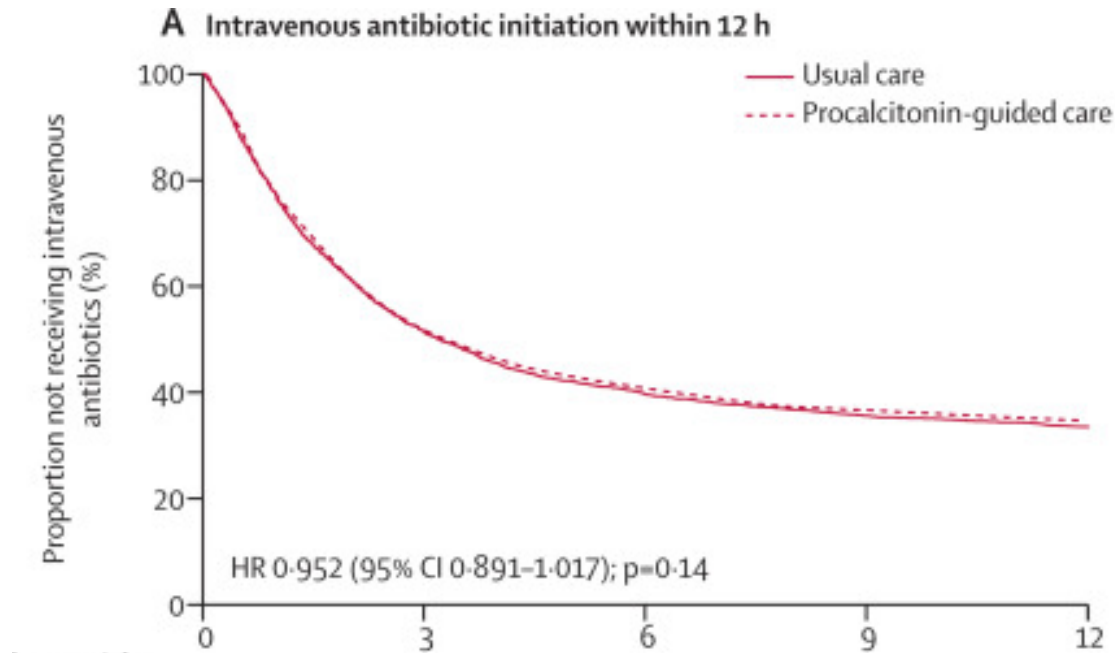
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# When to start antibiotics (biomarker decision support)



**PRONTO**

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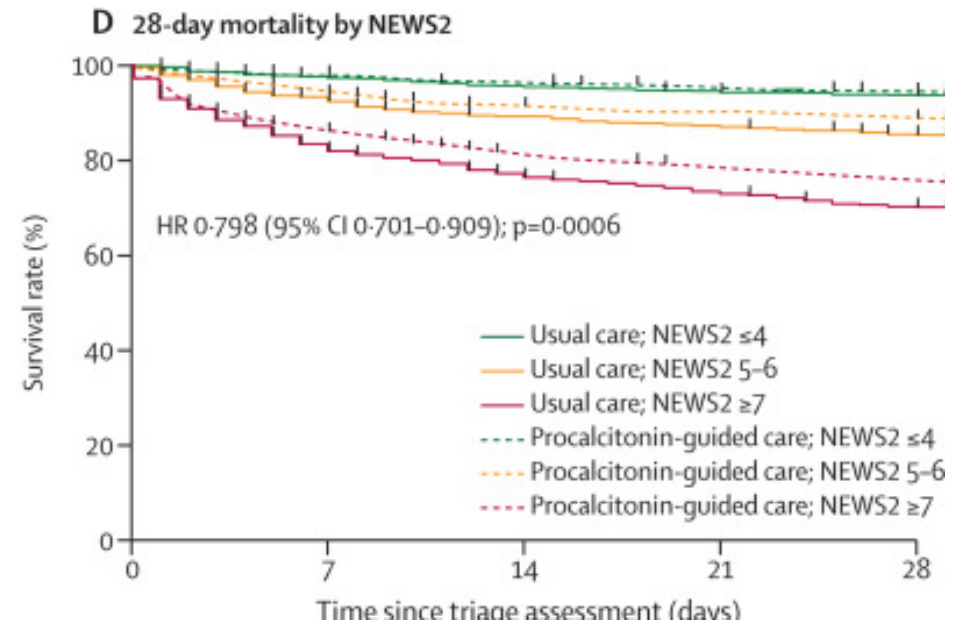
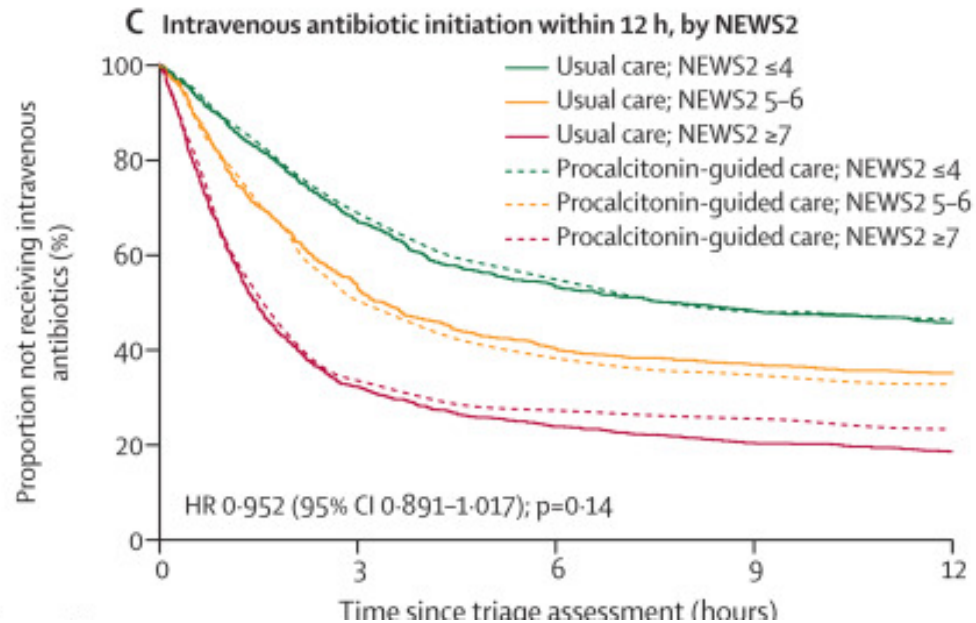
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# When to start antibiotics (biomarker decision support)



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Respiratory Medicine

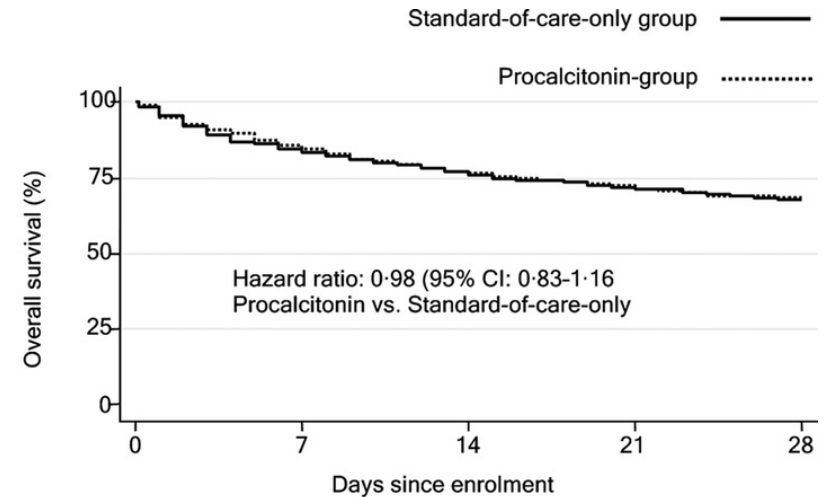


# Daily review and refinement – a warning

## Procalcitonin-guided interventions against infections to increase early appropriate antibiotics and improve survival in the intensive care unit: A randomized trial

Jens-Ulrich Jensen and colleagues

*“Procalcitonin-guided antimicrobial escalation in the intensive care unit did not improve survival but did lead to organ-related harm and prolonged admission to the intensive care unit.”*



Number at risk:					
Procalcitonin	604	518	466	436	414
Standard-of-care	596	505	458	429	405



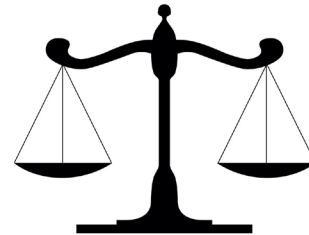
# When to stop antibiotics

Daily clinical assessment

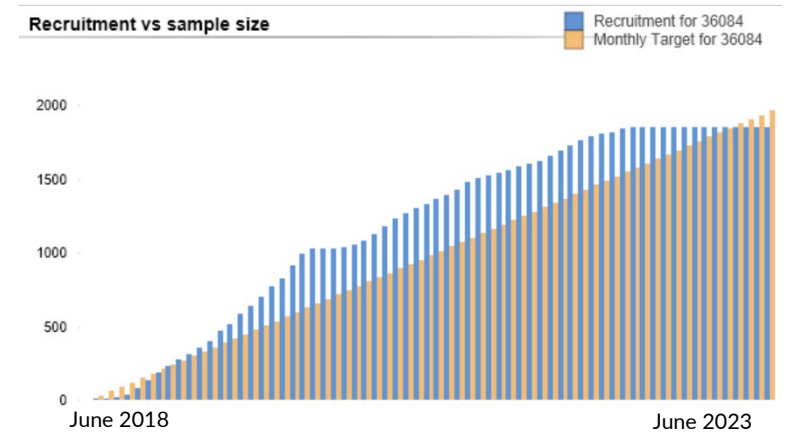
Adequate source control/line removal

Aim for shorter antimicrobial treatment duration

Ideally personalised



# When to stop antibiotics (biomarker decision support)



## BATCH

Biomarker-guided duration of Antibiotic Treatment in Children Hospitalised with confirmed or suspected bacterial infection

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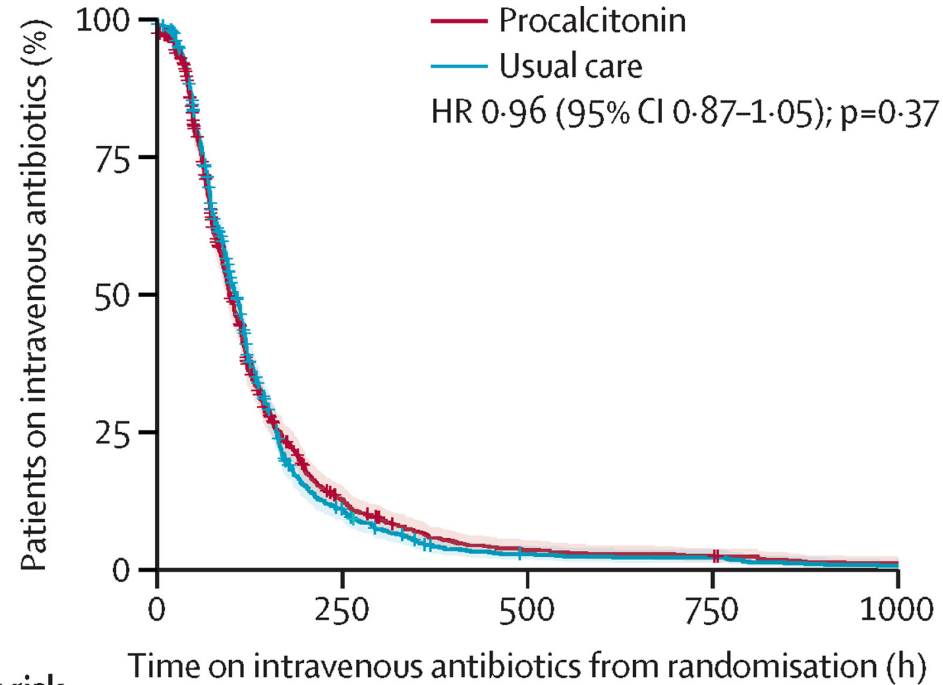
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# When to stop antibiotics (biomarker decision support)



	Number at risk (number censored)				
	0	250	500	750	1000
Procalcitonin	951 (0)	103 (71)	27 (77)	19 (77)	8 (79)
Usual care	960 (0)	91 (62)	19 (71)	15 (71)	5 (71)



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# When to stop antibiotics (biomarker decision support)

*“In a wide range of critically ill hospitalised medical and surgical adult NHS patients with sepsis, there is a significant safe reduction of, on average, **10%** in the total antibiotic days when a **daily PCT** protocol is administered compared with standard care. A **daily CRP** protocol does not reduce the total duration of antibiotics.”*

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JAMA

Dark P, Hossain A, McAuley DF, et al; for the  
ADAPT-Sepsis Collaborators

**Biomarker-Guided Antibiotic  
Duration for Hospitalized  
Patients With Suspected Sepsis**

The ADAPT-Sepsis Randomized Clinical Trial



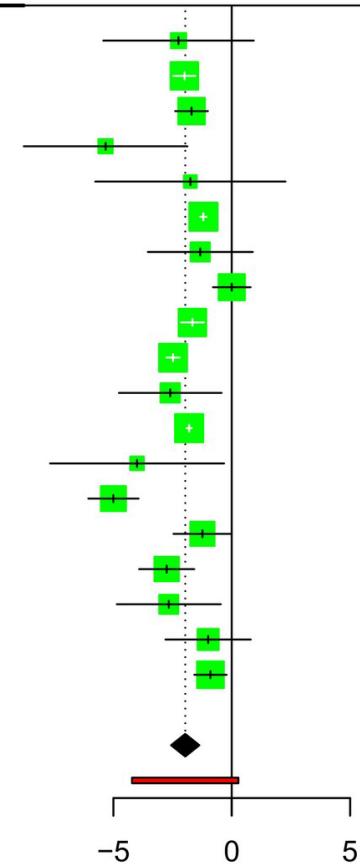
sepsis  
**adapt**

Biomarker-guided antibiotic duration for sepsis

# When to stop antibiotics (biomarker decision support)

19 eligible randomised PCT clinical trials in last 10 years, n=6382 patients

Study	Experimental		Control		Mean Difference		Weight	Mean Difference IV, Random, 95% CI
	Mean	SD	Mean	SD	IV, Random, 95% CI	IV, Random, 95% CI		
Nobre et al. [43]*	11.75	7.222	39	14.00	7.188	40	2.3%	-2.25 (-5.43 to 0.93)
Hochreiter et al. [45]	5.90	1.700	57	7.90	0.500	53	7.5%	-2.00 (-2.46 to -1.54)
Schroeder et al. [44]	6.60	1.100	14	8.30	0.700	13	7.0%	-1.70 (-2.39 to -1.01)
Stolz et al. [46]*	10.67	7.630	51	16.00	9.920	50	2.0%	-5.33 (-8.79 to -1.87)
Deliberato et al. [47]*	15.50	8.274	42	17.25	10.017	39	1.6%	-1.75 (-5.77 to 2.27)
Liu et al. [48]	8.10	0.300	42	9.30	0.300	40	7.8%	-1.20 (-1.33 to -1.07)
Shehabi et al. [49]*	11.67	10.460	196	13.00	11.950	198	3.6%	-1.33 (-3.55 to 0.89)
Bloos et al. [50]*	7.33	6.690	552	7.33	6.690	537	6.8%	0.00 (-0.79 to 0.79)
de Jong et al. [51]*	5.67	4.460	761	7.33	5.200	785	7.5%	-1.66 (-2.14 to -1.18)
Liu et al. [59]	7.74	0.610	49	10.22	0.780	49	7.7%	-2.48 (-2.76 to -2.20)
Mahmutaj et al. [52]	10.60	6.600	50	13.20	4.200	50	3.7%	-2.60 (-4.77 to -0.43)
Xu et al. [53]	8.30	0.300	79	10.10	0.400	77	7.9%	-1.80 (-1.91 to -1.69)
Jeon et al. [54]*	10.67	4.740	23	14.67	8.580	29	1.8%	-4.00 (-7.67 to -0.33)
Kyriazopoulou et al. [57]*	5.67	1.500	125	10.67	6.000	131	6.2%	-5.00 (-6.06 to -3.94)
Mazlan et al. [55]	10.28	2.680	43	11.52	3.060	42	5.8%	-1.24 (-2.46 to -0.02)
Vishalashi et al. [56]	4.98	2.560	45	7.73	3.060	45	5.9%	-2.75 (-3.92 to -1.58)
Shukeri et al. [15]*	6.17	1.540	40	8.83	6.920	40	3.6%	-2.66 (-4.86 to -0.46)
Nazer et al. [58]*	7.67	5.290	77	8.67	6.050	76	4.4%	-1.00 (-2.80 to 0.80)
Dark et al. [14]	9.80	7.200	898	10.70	7.600	905	7.1%	-0.90 (-1.58 to -0.22)
<b>Total (95% CI)</b>			<b>3183</b>			<b>3199</b>	<b>100.0%</b>	<b>-2.0 (-2.6 to -1.4)</b>
<b>Prediction interval</b>								<b>(-4.2 to 0.3)</b>



Days Abx saving



Heterogeneity:  $\tau^2 = 1.0591$ ;  $\chi^2 = 161.22$ ,  $df = 18$  ( $P < 0.0001$ );  $I^2 = 88.8\%$

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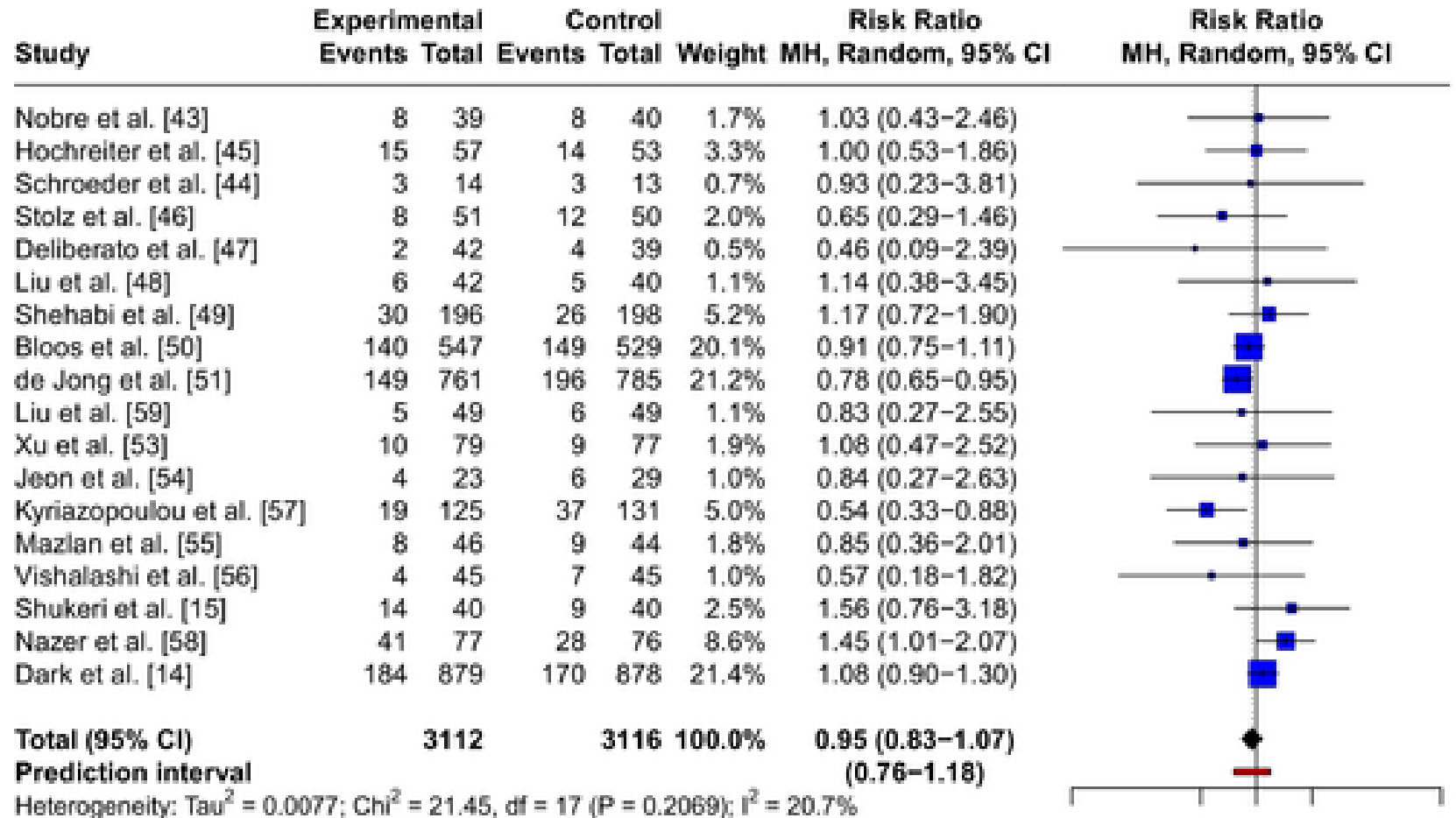
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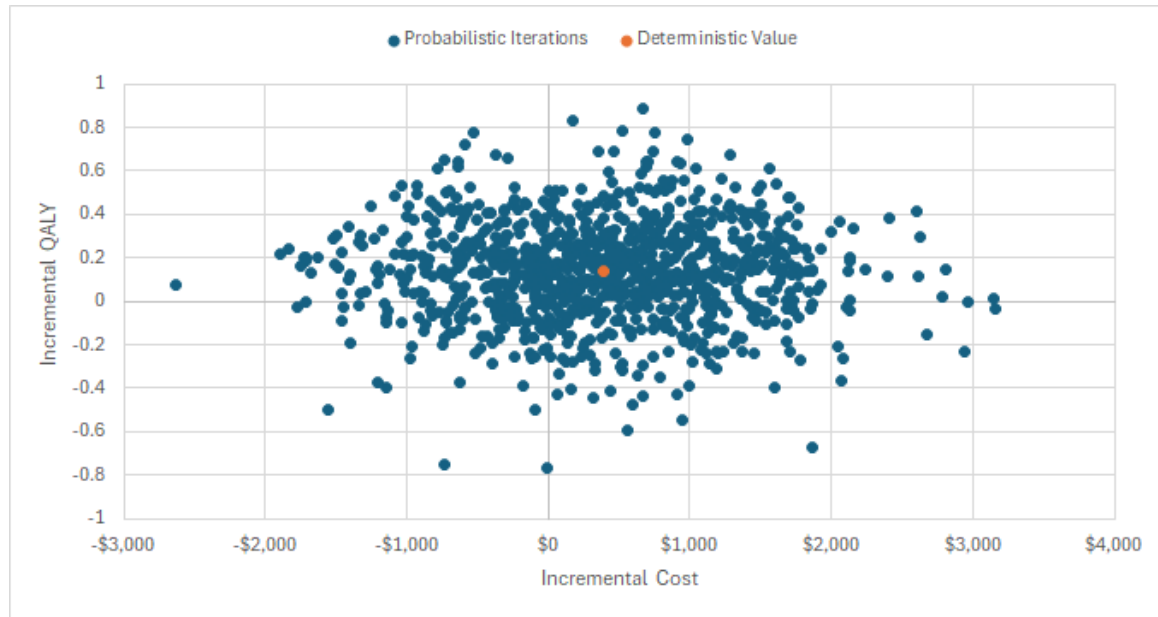
19 eligible randomised PCT clinical trials in last 10 years, n=6382 patients



Safety: risk of death



# When to stop antibiotics (biomarker decision support)



## Introducing NHS PCT-protocol

Cost per QALY = £2053

Probability of being cost effective = 0.73



# NICE guidance for biomarkers in sepsis: a 2026 update

## Procalcitonin for diagnosing and monitoring sepsis

*New evidence has become available that could have a material effect on the recommendations.*

*In **March 2026**, the NICE Prioritisation Board agreed that updated guidance on the use of procalcitonin tests in sepsis would be valuable.*

