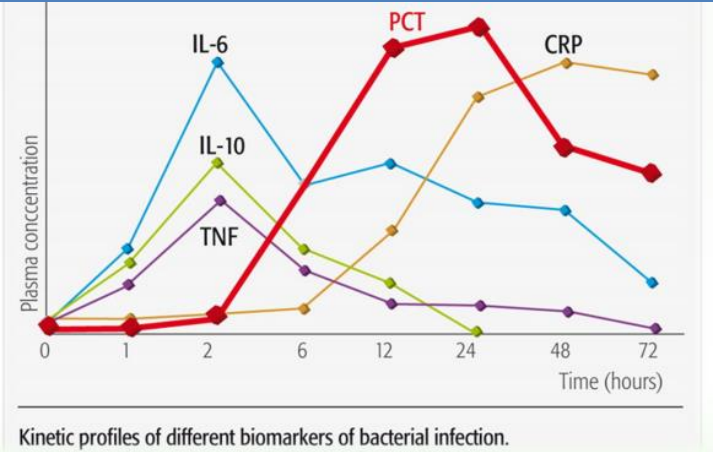


Kinetic profiles of different biomarkers of bacterial infection.

Meisner, M. 2000. *Procalcitonine. A new innovative infection parameter. Biochemical and clinical aspects.* Georg Thieme Verlag, Stuttgart.

Reductie antibioticaduur door gebruik van PCT?

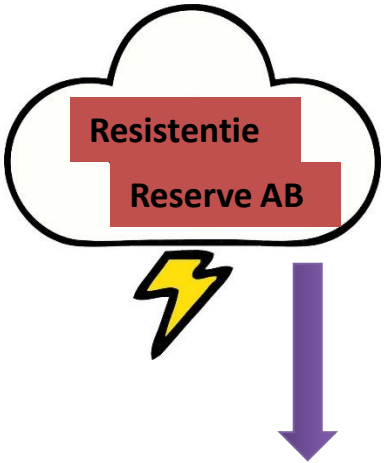
Laurien Oosterwijk

Journal Club 19 mei ’25

Antibioticabeleid bij kinderen

Vaak start empirisch

- Non-specifieke presentatie van infectie
- Urgentie van AB bij zuigeling/jonge kind
- Gebrek aan accurate snelle test die de diagnostische onzekerheid reduceert



Reductie duur
Zsm versmallen

CRP

Leuco's

Kweken

Beeldvorming

Procalcitonin-guided decision making for duration of antibiotic therapy in neonates with suspected early-onset sepsis: a multicentre, randomised controlled trial (NeoPIns)

Martin Stocker*, Wendy van Herk*, Salhab el Helou, Sourabh Dutta, Matteo S Fontana, Frank A B A Schuerman, Rita K van den Tooren-de Groot, Jantien W Wieringa, Jan Janota, Laura H van der Meer-Kappelle, Rob Moonen, Sintha D Sie, Esther de Vries, Albertine E Donker, Urs Zimmerman, Luregn J Schlapbach, Amerik C de Mol, Angelique Hoffman-Haringsma, Madan Roy, Maren Tomaske, René F Kornelisse, Juliette van Gijsel, Eline G Visser, Sten P Willemsen, Annemarie M C van Rossum, r
NeoPInS Study Group†

ARTICLES · Volume 375, Issue 9713, P463-474, February 06, 2010

Use of procalcitonin to reduce patients' exposure to antibiotics in intensive care units (PRORATA trial): a multicentre randomised controlled trial

Lila Bouadma, MD [a] · Charles-Edouard Luyt, MD [e] · Florence Tubach, MD [b] · Christophe Cracco, MD [f] · Antonio Alvarez, MD [g] · Carole Schwebel, MD [h] · et al. Show more

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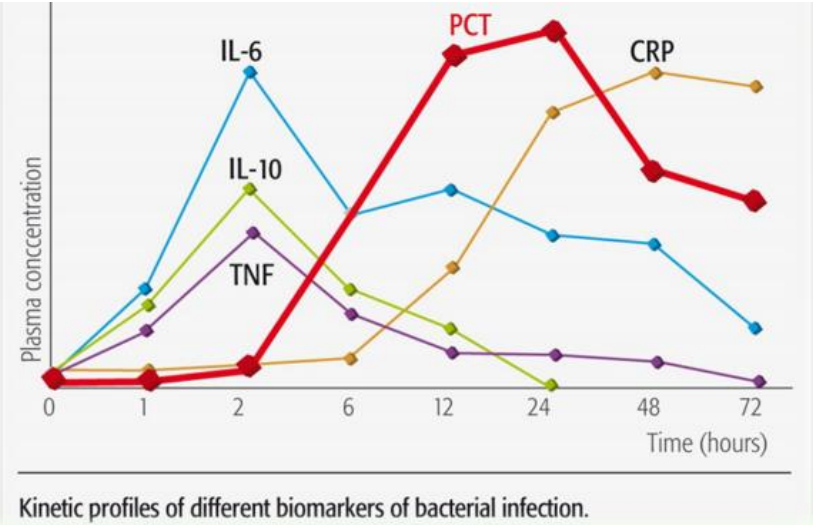
Procalcitonin to stop antibiotics after cardiovascu surgery in a pediatric intensive care unit—The PROSACAB study

Sara Bobillo-Perez, Anna Sole-Ribalta, Monica Balaguer, Elisabeth Esteban, Monica Girona-Alarcon, Lluisa Hernandez-Platero, Susana Segura, Aida Felipe, Francisco Jose Cambra, Cristian Launes, Iolanda Jordan

Published: September 18, 2019 • https://doi.org/10.1371/journal.pone.0220686

Procalcitonine

Peptide precursor van hormoon calcitonine (calcium homeostase)



Kinetic profiles of different biomarkers of bacterial infection.

Meisner, M. 2000. *Procalcitonine. A new innovative infection parameter. Biochemical and clinical aspects.* Georg Thieme Verlag, Stuttgart.

- Schildklier; snel omgezet naar calcitonine (Ca homeostase) Opregulatie bij bacteriele infectie + mediatoren maar geen omzetting.
- Meer specifieke biomarker van gastheerrespons op inflammatoire stimuli bij bacteriële infectie
- Kinetiek sneller dan CRP: vroegere oploop
- Mate van verhoging correleert met ernst en progressie
- Hoge NPV ernstige infectie

BATCH-trial

Lancet Child Adolesc Health
2025; 9: 121–30

Procalcitonin-guided duration of antibiotic treatment in children hospitalised with confirmed or suspected bacterial infection in the UK (BATCH): a pragmatic, multicentre, open-label, two-arm, individually randomised, controlled trial

Cherry-Ann Waldron, Philip Pallmann*, Simon Schoenbuchner, Debbie Harris, Lucy Brookes-Howell, Céu Mateus, Jolanta Bernatoniene, Katrina Cathie, Saul N Faust, Lucy Hinds, Kerenza Hood, Chao Huang, Sarah Jones, Sarah Kotecha, Helen M Nabwera, Sanjay Patel, Stéphane C Paulus, Colin V E Powell, Jenny Preston, Huasheng Xiang, Emma Thomas-Jones†, Enitan D Carrol†, on behalf of the BATCH Trial Team‡*

15 ziekenhuizen England and Wales (6 kinder ZH; afdeling + PICU, 9 algemene ZH)

Superiority (AB-duur reductie) and **non-inferiority** (safety outcomes)

Onderzoeksvraag en uitkomsten

Kan een **procalcitonine-geleid-beslis-algoritme** (I)

bij een **opgenomen** kind met verdenking of bevestigde ‘serious’ **bacteriële** infectie (P)

veilig de **duur** van de antibiotica reduceren (O)

in vergelijking met de **usual care** (C) ?

Superiority

Duur antibiotica iv

Non-inferiority

Veiligheid

+kosteneffectiviteitsanalyse

Studieopzet

2018-2022

Inclusie

- Kinderen van 72u tot 18 jaar oud
- Opname en start AB i.v. voor ~48u bij bewezen of verdenking op bacteriële infectie

Exclusie:

- prematuren <37w gecorrigeerd
- Moribund, Ernstige bacteriele meningitis, endocarditis, hersenabces, gecompl. bot/gewrichtsinfecties
- ernstig immuun gecompromitteerd
- Beperkt beleid
- Inborn NICU kinderen

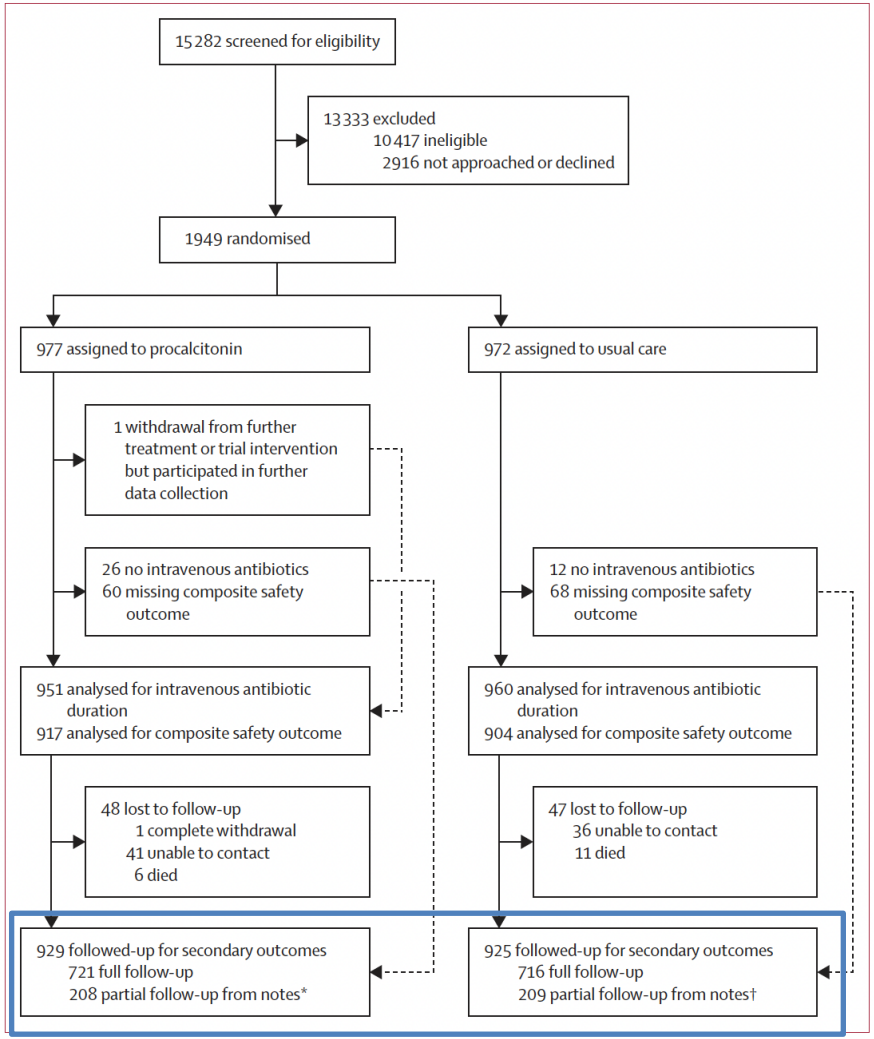
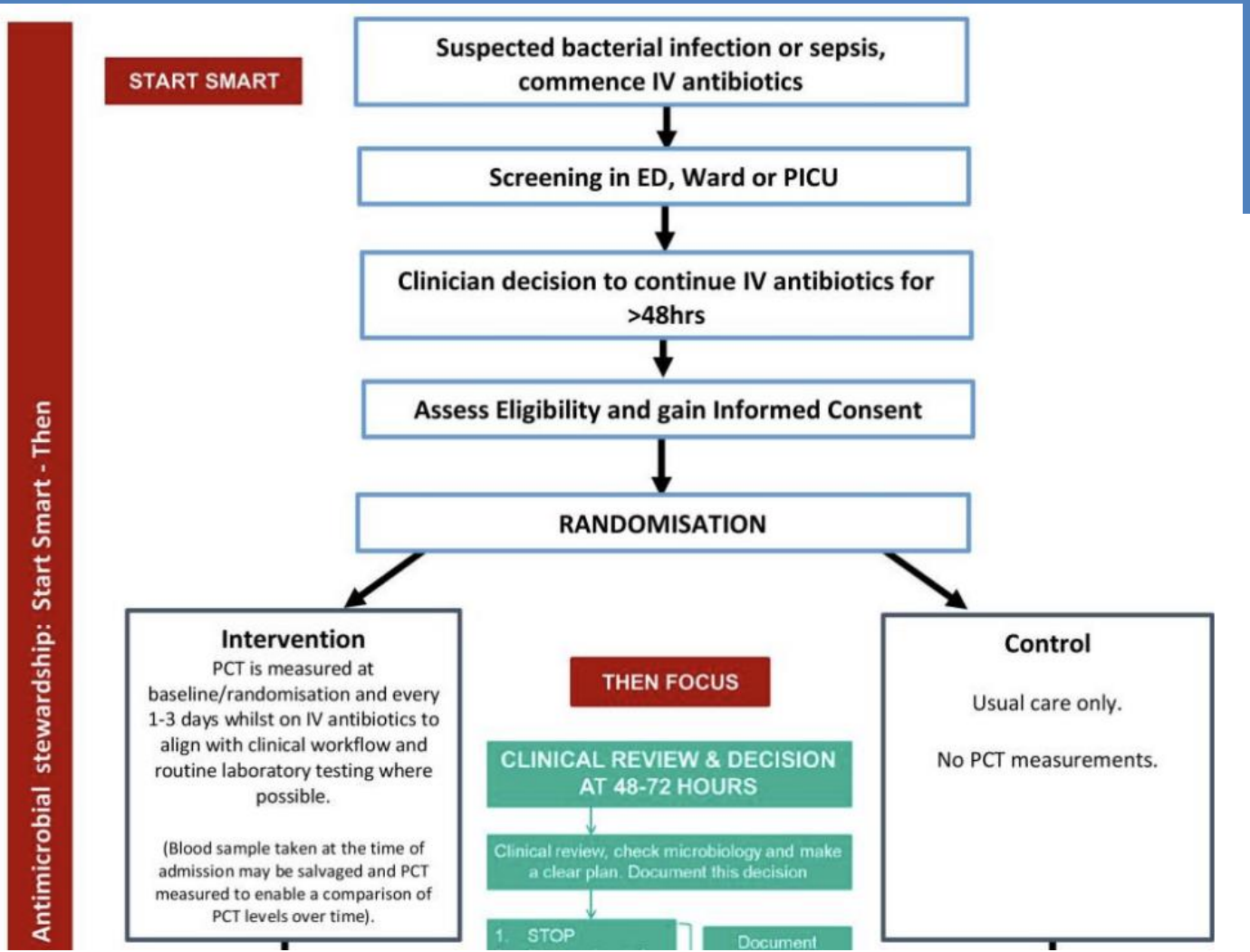
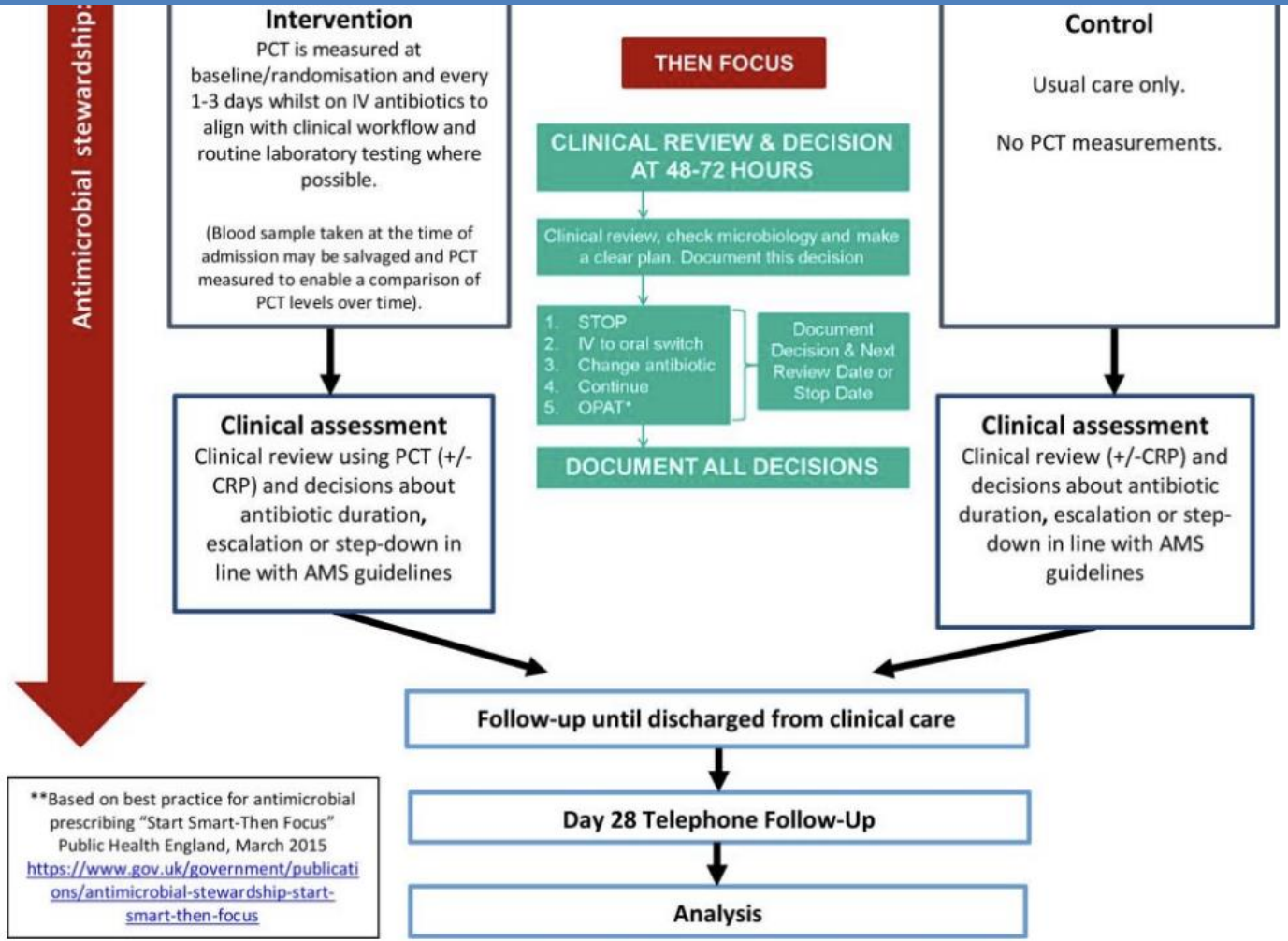


Figure 1: Trial profile

Methode

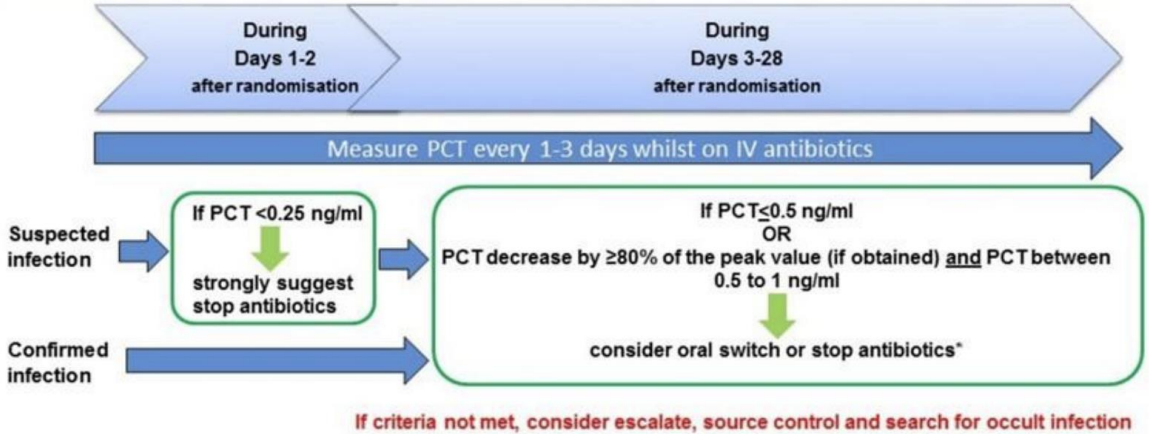

Antimicrobial stewardship: Start Smart - Then
START SMART
Suspected bacterial infection or sepsis, commence IV antibiotics
Screening in ED, Ward or PICU
Clinician decision to continue IV antibiotics for >48hrs
Assess Eligibility and gain Informed Consent
RANDOMISATION
Intervention
PCT is measured at baseline/randomisation and every 1-3 days whilst on IV antibiotics to align with clinical workflow and routine laboratory testing where possible.
(Blood sample taken at the time of admission may be salvaged and PCT measured to enable a comparison of PCT levels over time).
THEN FOCUS
CLINICAL REVIEW & DECISION AT 48-72 HOURS
Clinical review, check microbiology and make a clear plan. Document this decision
1. STOP
Document
Control
Usual care only.
No PCT measurements.

Methode


Antimicrobial stewardship**
Intervention
PCT is measured at baseline/randomisation and every 1-3 days whilst on IV antibiotics to align with clinical workflow and routine laboratory testing where possible.
(Blood sample taken at the time of admission may be salvaged and PCT measured to enable a comparison of PCT levels over time).
Clinical assessment
Clinical review using PCT (+/-CRP) and decisions about antibiotic duration, escalation or step-down in line with AMS guidelines
THEN FOCUS
CLINICAL REVIEW & DECISION AT 48-72 HOURS
Clinical review, check microbiology and make a clear plan. Document this decision
1. STOP
2. IV to oral switch
3. Change antibiotic
4. Continue
5. OPAT*
Document Decision & Next Review Date or Stop Date
DOCUMENT ALL DECISIONS
Control
Usual care only.
No PCT measurements.
Clinical assessment
Clinical review (+/-CRP) and decisions about antibiotic duration, escalation or step-down in line with AMS guidelines
Follow-up until discharged from clinical care
Day 28 Telephone Follow-Up
Analysis
**Based on best practice for antimicrobial prescribing "Start Smart-Then Focus" Public Health England, March 2015
https://www.gov.uk/government/publications/antimicrobial-stewardship-start-smart-then-focus

Methode

In the standard care group: use clinical response +/- CRP to guide oral switch and discontinuation.
In PCT group: use clinical response (+/- CRP) and PCT to guide oral switch and discontinuation.
Measure PCT at randomisation/baseline and every 1-3 days whilst on IV antibiotics, or up to 28 days, as indicated clinically. If on Outpatient Parenteral Antimicrobial Therapy (OPAT), frequency can be every 7 days or according to local standard care. PCT results will be made available to the clinician.



* For confirmed infections see below:

Evidence from systematic review of antibiotic duration and timing of switch from intravenous to oral route
McMullan, BJ *et al.* 2016 Lancet ID 16(8) e139-e152

Infections that can be safely treated with IV antibiotics for <5 days; pneumonia, pyelonephritis, lymphadenitis, cellulitis, bone and joint infections afebrile and pain improving, mastoiditis, sinusitis, retropharyngeal abscess, empyema (afebrile for >24hrs), pyomyositis.

Infections that usually require ≥5 days of IV antibiotics; bacteraemia, intra-abdominal infections, empyema (still febrile at 96 hrs and chest drain still in), complicated bone and joint infections, discitis, uncomplicated culture negative meningitis.

BATCH

Karakteristieken

	Procalcitonin group (n=977)	Usual care group (n=972)
Age at randomisation, years	3·1 (0·8–8·8)	3·1 (0·7–8·7)
Sex		
Female	427 (44%)	478 (49%)
Male	550 (56%)	494 (51%)
Ethnicity*		
Asian or Asian British	37/939 (4%)	34/923 (4%)
Black, African, Caribbean, or Black British	12/939 (1%)	14/923 (2%)
Mixed or multiple ethnic groups	42/939 (4%)	39/923 (4%)
Other ethnic group	10/939 (1%)	8/923 (1%)
White	838/939 (89%)	828/923 (90%)
Duration of symptoms at admission, h	70 (24–144)	60 (24–120)
Prescribed antibiotic use in past 14 days*	423/972 (44%)	418/970 (43%)
Route of admission*		
Emergency department or acute assessment unit	532/974 (55%)	534/971 (55%)
General practitioner	19/974 (2%)	20/971 (2%)
High dependency unit	34/974 (3%)	29/971 (3%)
Inpatient ward	62/974 (6%)	60/971 (6%)
Other hospital	237/974 (24%)	238/971 (25%)
Paediatric intensive care unit	42/974 (4%)	35/971 (4%)
Operating theatre	48/974 (5%)	55/971 (6%)
Comorbidities*		
None	575/964 (60%)	571/963 (59%)
One	114/964 (12%)	126/963 (13%)
Two or more	275/964 (29%)	266/963 (28%)

Data are median (IQR), n (%), or n/N (%). *Data are not available for all randomly assigned participants.

Table 1: **Baseline characteristics of the randomised participants**

Karakteristieken

	Procalcitonin group (n=977)	Usual care group (n=972)
Bone, joint, or muscle infection	86 (9%)	99 (10%)
CNS infection*	5 (1%)	5 (1%)
Fever alone	30 (3%)	28 (3%)
Influenza-like illness	2 (<1%)	8 (1%)
Gastrointestinal or abdominal infection	147 (15%)	128 (13%)
Inflammatory syndrome	3 (<1%)	13 (1%)
Lower respiratory tract infection	213 (22%)	221 (23%)
None	5 (1%)	4 (<1%)
Other	143 (15%)	142 (15%)
Otitis media	5 (1%)	2 (<1%)
Syndromes caused by defined pathogen†	0	2 (<1%)
Sepsis syndrome	129 (13%)	130 (13%)
Soft tissue infection	135 (14%)	113 (12%)
Tonsillitis or pharyngitis	16 (2%)	15 (2%)
Unknown	25 (3%)	32 (3%)
Urinary tract infection	89 (9%)	94 (10%)
Upper respiratory tract infection (other)	38 (4%)	35 (4%)

Data are n (%). Each patient could have zero, one, or multiple initial diagnoses.
*Eg, central line infection, line sepsis, culture negative meningitis, enterovirus meningitis, meningococcal meningitis, viral meningitis, and meningoencephalitis.
†Eg, measles, varicella, and scarlet fever.

Table 2: **Initial diagnoses by study group**

Resultaten

	Procalcitonin group (n=951)	Usual care group (n=960)	Treatment effect
Median intravenous antibiotic duration, h (IQR)	96·0 (59·5–155·5)	99·7 (61·2–153·8)	HR 0·96 (95% CI 0·87–1·05)
Composite safety outcome	78/917 (9%)	85/904 (9%)	RD –0·81% (95% CI upper bound 1·11); RR 0·90 (95% CI upper bound 1·15)

Data are n/N (%) unless otherwise stated. 95% CIs for the composite safety outcome are one-sided, with no lower bound. Covariates in all models: centre as a random effect and age as a fixed effect. HR=hazard ratio. RD=risk difference. RR=risk ratio.

Table 3: **Coprimary endpoint analysis**

Niet-inferieur

'Composite safety outcome' (non-inferiority)

- ongeplande opname of heropname op de PICU, ongeplande heropname in ZH, <7 dagen na stoppen AB iv
- Herstart i.v. antibiotica binnen 7 dagen na stoppen
- Mortaliteit (alle redenen) in 28d na randomisatie

Resultaten

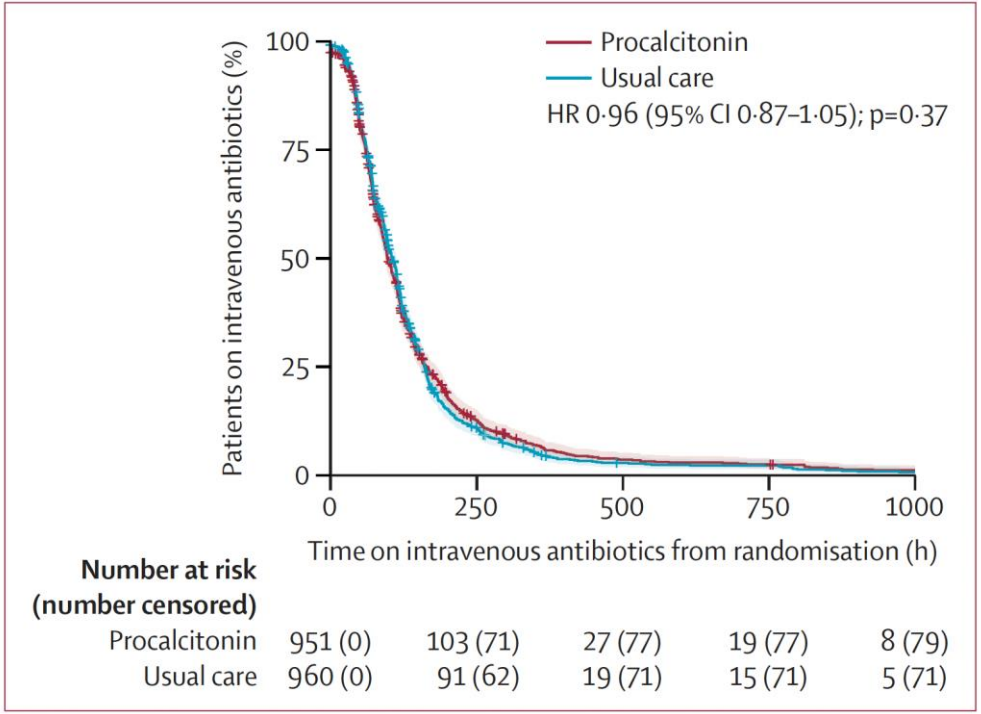


Figure 2: **Kaplan–Meier estimates of the duration of intravenous antibiotic use**
Censored observations shown by + symbols.

Tevens geen effect op secundaire uitkomstmaten

- Losse 3 componenten ‘composite safety outcome’
- Bijwerkingen medicatie
- Hospital-acquired infectie tot 28d
- Totale duur antibiotica (IV en oraal)
- Tijd tot ontslag uit ziekenhuis
- Tijd tot switch breed > smal spectrum

- Kosten-effectiviteitsanalyse

Interventie niet kosten-effectief

Resultaten

Geen relevante reductie in i.v. antibiotica duur, niet-inferieur m.b.t. veiligheid, niet kosten-effectief

Slechts 24% (PCT) strikt volgens het protocol behandeld
> bij 1/3 PCT uitslag niet in overweging genomen
> bij 1/3 geen resultaten beschikbaar op moment van heroverwegen

In die groep mediane iv AB duur was **77,3u (IQR 50,0-132,0)**

Per-protocol analyse (PCT beschikbaar en 'overwogen'):
HR 0.82 (95% 0.56-1.22) voor AB duur PCT-groep

→ Proces kent mogelijk obstakels om te implementeren

→ '**pragmatic study**'; routine klinische praktijk in diverse settings; realiteit vs protocol?

Discussie

Conclusie **inconsistent** met eerdere RCT's

- NeoPins: reductie AB-duur bij neonaten verdenking EOS (Proven sepsis uitgesloten!)
- PRORATA: reductie antibiotica exposure bij acuut zieke volwassene
- PROSACAB: reductie antibiotica en meer de-escalatie bij kinderen na cardiovasculaire chirurgie

Mogelijk **verklarend**:

- Heterogene groep
- Nu geen uitspraak over effect subgroepen
- Beperkte groep volledig conform protocol
- Delay in beschikbaar zijn PCT resultaten bij implementatie; mogelijk van invloed
- Onderschat gezien nog leereffect van artsen?
- Over all lage AB duur en goede antimicrobial stewarship programms

Implicaties voor de PICU WKZ

- **Is het resultaat van de studie relevant voor PICU WKZ?**
  - Nu geen directe implicaties voor werkvloer
  - Vervolg literatuur

PCT wordt niet gebruikt

Klein % PICU populatie

PICU-subgroepen wel effect?

Tissières *et al. Annals of Intensive Care* (2025) 15:55
https://doi.org/10.1186/s13613-025-01470-y

Annals of Intensive Care

REVIEW Open Access

Use of procalcitonin in therapeutic decisions in the pediatric intensive care unit

Pierre Tissières[1*], Elisabeth Esteban Torné[2], Johannes Hübner[3], Adrienne G. Randolph[4], Corsino Rey Galán[5] and Scott L. Weiss[6]

Expert review
> Refereert oa naar Batch
> Stelt algoritme voor

ORIGINAL CLINICAL REPORT

OPEN

Procalcitonin-Guided Management and Duration of Antibiotic Therapy in Critically Ill Cancer Patients With Sepsis (Pro-Can Study): A Randomized Controlled Trial

Lama H. Nazer, PharmD, BCPS, FCCM[1]

OBJECTIVES: To evaluate the effect of procalcitonin-guided management on the