ThermoFisher SCIENTIFIC

Procalcitonin (PCT)

Safely reduce antibiotic exposure

B·R·A·H·M·S PCT:
An effective tool for antibiotic stewardship

B·R·A·H·M·S PCT PROVEN CONFIDENCE

thermo scientific

The challenge

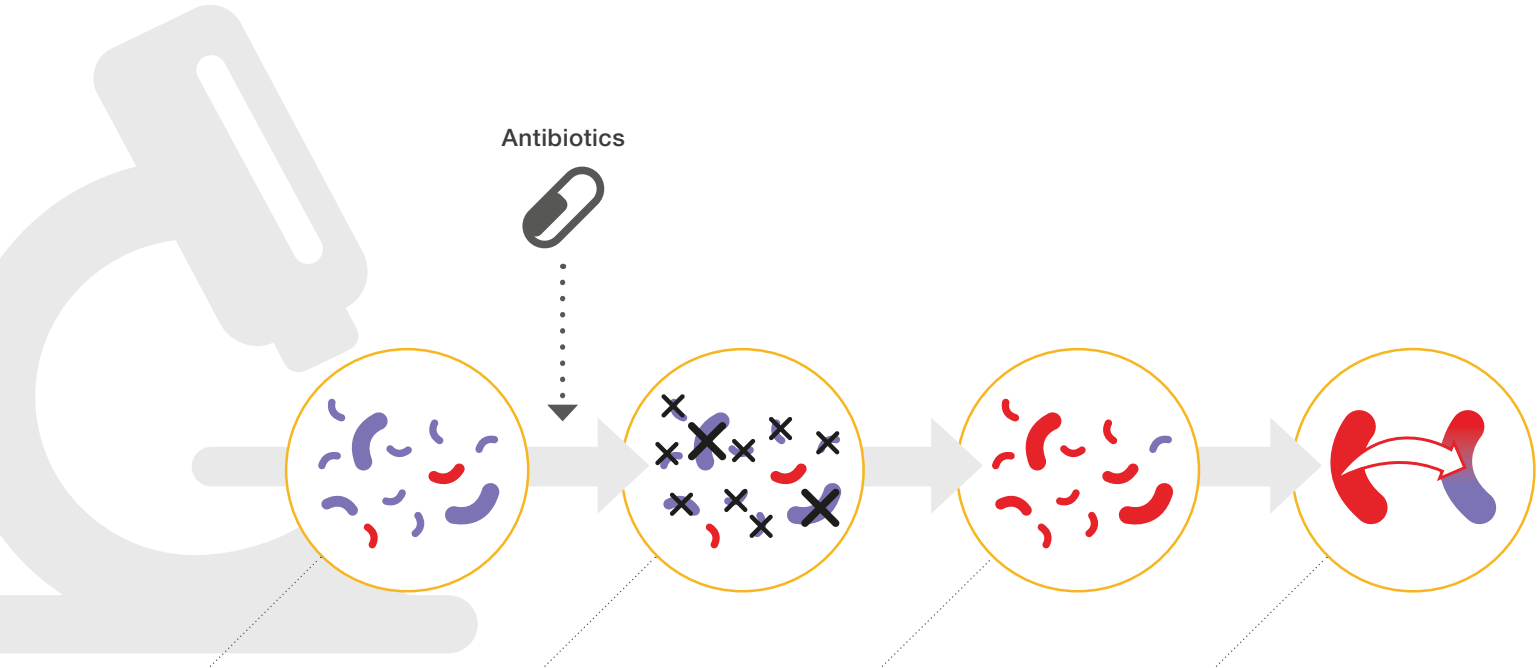
Antibiotic resistance – an increasing threat to public health

Antibiotics (ABx) are a limited resource. At the current pace of injudicious use, all antibiotics will soon become ineffective. The **WHO Global Action Plan on Antimicrobial Resistance**, 2015, emphasizes that antimicrobial resistance is a crisis that must be managed with the utmost urgency.[1]

The **Interagency Coordination Group (IACG) on Antimicrobial Resistance** reported in 2019 that, "unless the world acts urgently, antimicrobial resistance will have disastrous impact within a generation." Deaths due to drug-resistant diseases "could increase to 10 million deaths globally per year by 2050."[2]

1/3 antibiotic prescriptions are unnecessary[3]

How does resistance to antibiotics develop?



A potential for change

Thermo Scientific™ B·R·A·H·M·S PCT™ supports responsible use of antibiotics to prolong their effectiveness

"For adults with an initial diagnosis of sepsis or septic shock and adequate source control where optimal duration of therapy is unclear, we suggest **using procalcitonin AND clinical evaluation to decide when to discontinue antimicrobials** over clinical evaluation alone."

Surviving Sepsis Campaign
Guideline 2021[4]

Procalcitonin is the **ONLY recommended biomarker** for antibiotic stewardship in sepsis and LRTI.

World Health Organization
Essential In Vitro Diagnostics List 2019[5]

B·R·A·H·M·S PCT-aided antibiotic therapy has the potential to ...

1

Reduce
initial prescription rates

2

Shorten
treatment durations

3

Save
overall treatment costs

Use of B·R·A·H·M·S PCT reduces antibiotic exposure

Strong evidence supports safe reduction of antibiotics using PCT-aided antibiotic stewardship protocols

- Proven utility across diverse clinical settings
- Reproducible, randomized clinical trials with evidence spanning over 20 years

Proven efficacy:

-16% to -74%

antibiotic exposure

No

adverse impact on outcome

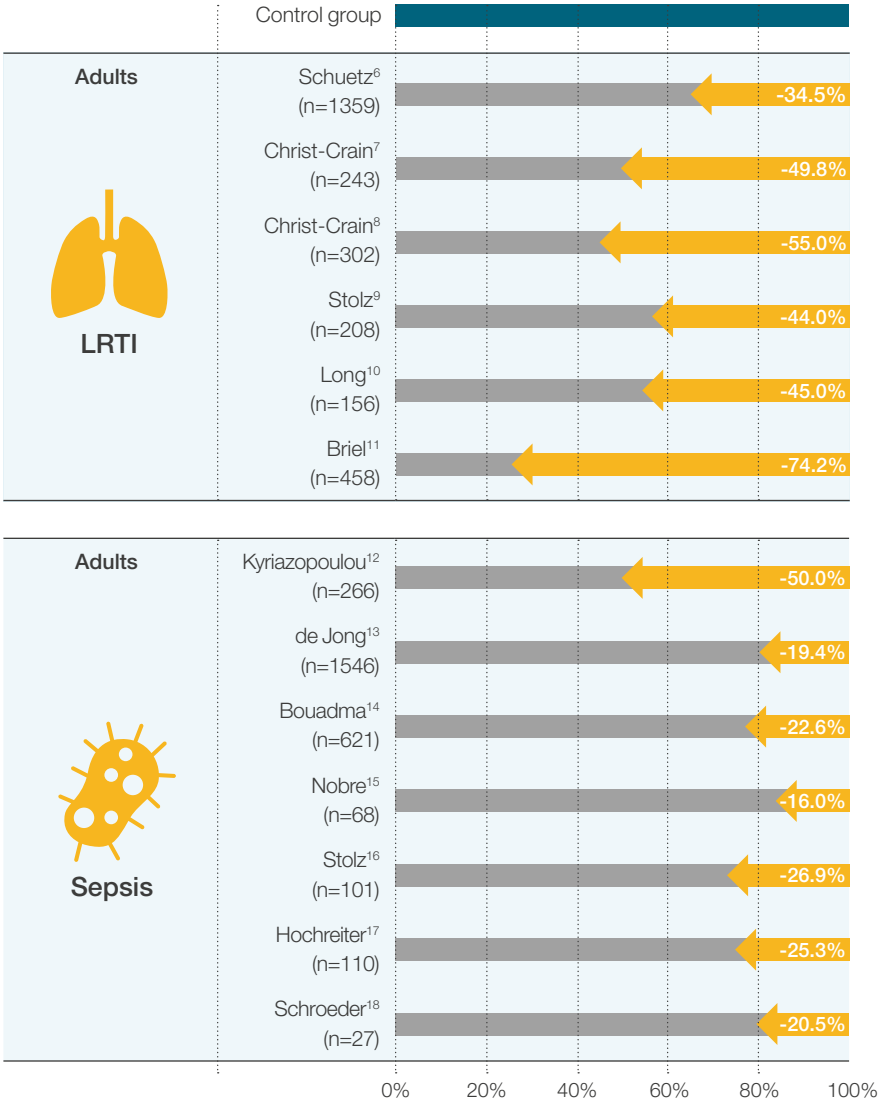
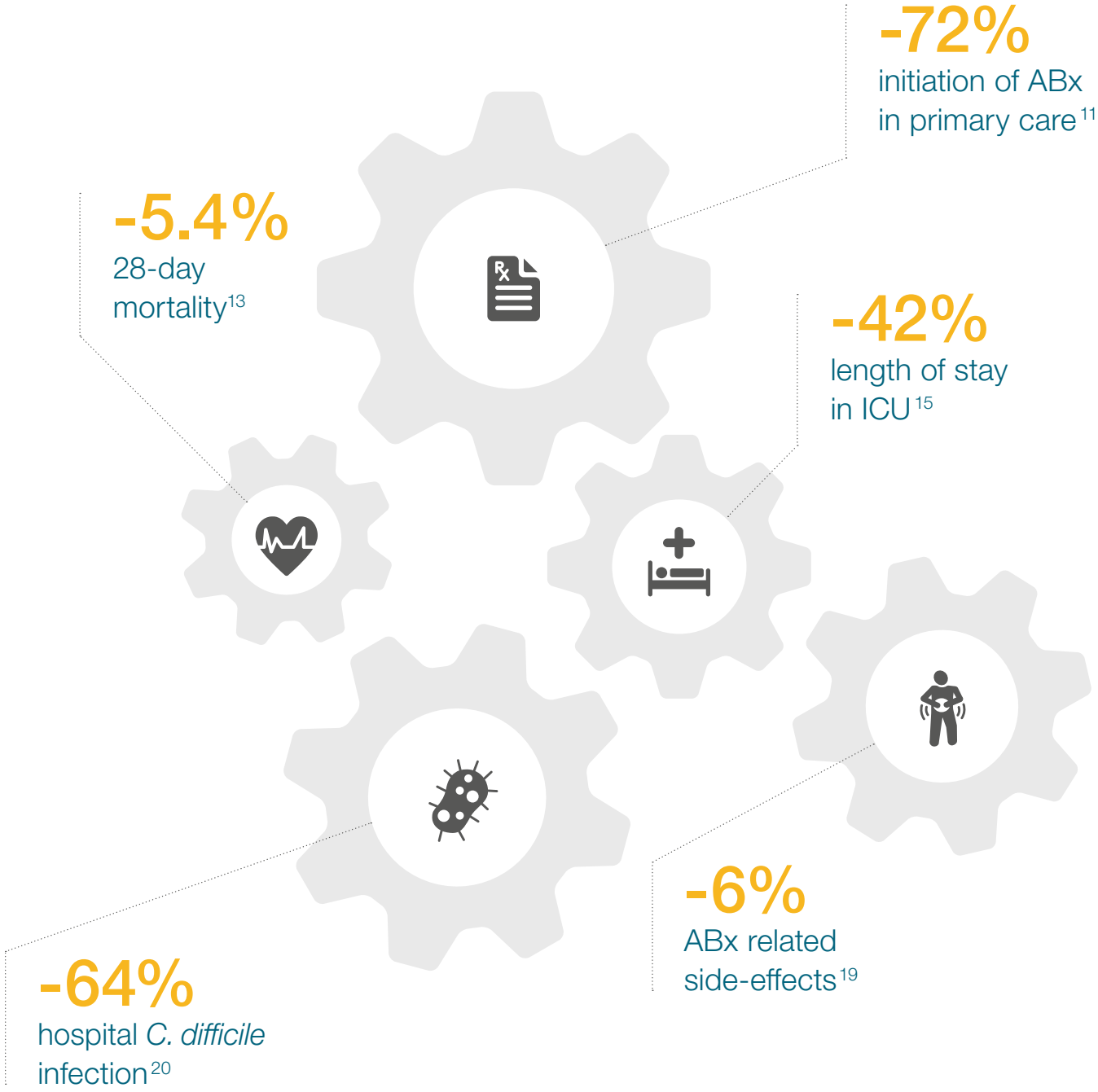


Figure 1. Relative reduction in ABx exposure with PCT-aided therapy
ABx exposure in control group is normalized to 100, shown by a blue bar at the top. The gray bar depicts the relative exposure in PCT group and the orange bar shows the relative ABx exposure reduction. All studies reported significant reduction in ABx exposure.

- ABx exposure in control group (normalized to 100)
- Relative ABx exposure in PCT-aided group
- Relative ABx reduction

Benefits of reduced ABx exposure achieved by PCT-aided antibiotic therapy

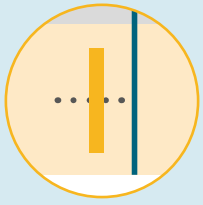


PCT-aided antibiotic therapy led to a reduction in overall treatment costs: 26% in sepsis patients and 18% in LRTI patients[21]

Safe approach

B·R·A·H·M·S PCT-aided reduction in antibiotic exposure has no negative impact on survival

		PCT use is associated with **lower mortality**				PCT use is associated with **higher mortality**		
Subgroups by sepsis 3 definition	**Odds ratio**	0.1	0.2	0.5	1	2	5	10
Meeting sepsis 3 definition	0.86							
Not meeting sepsis 3 definition	0.96							
Subgroups by type of infection								
Respiratory	0.92							
Urinary	0.59							
Abdominal	0.87							
Skin/soft tissue	0.94							
Central Nervous System	0.61							
Overall	**0.89**							



Overall better survival in the PCT group

Odds ratio: 0.89

Figure 2. Effect of PCT-guided antibiotic treatment on clinical outcomes in ICU patients – results of a patient level meta-analysis of 11 randomized trials (2252 PCT group patients, 2230 control group patients)[22]

Lower 28-day mortality

SAPS[13]

Study in the Netherlands, a country with a low average use of antibiotics[23] (1546 sepsis patients)

19%
ABx reduction
Median reduction of treatment duration: 7 to 5 days

5.4%
lower 28-day mortality

44%
compliance to PCT algorithm

PCT-aided ABx stewardship

PROGRESS[12]

Study in Greece, a country with a high average use of antibiotics[23] (266 sepsis patients)

50%
ABx reduction
Median reduction of treatment duration: 10 to 5 days

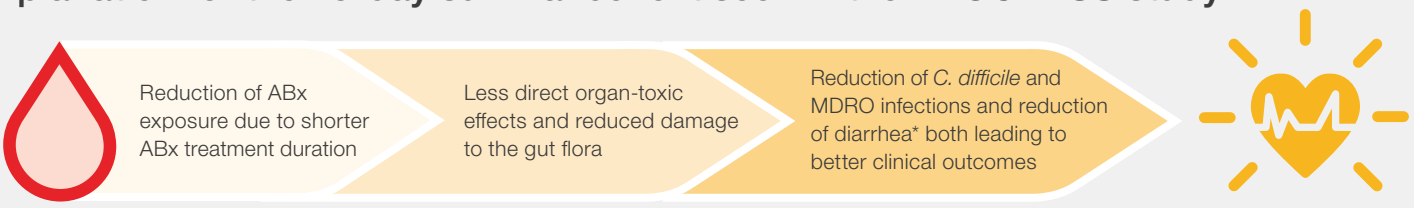
53%
adverse events reduction

46%
lower 28-day mortality

77%
compliance to PCT algorithm

PCT-aided ABx therapy contributes to improved clinical outcomes

Explanation for the 28-day survival benefit seen in the PROGRESS study[12]

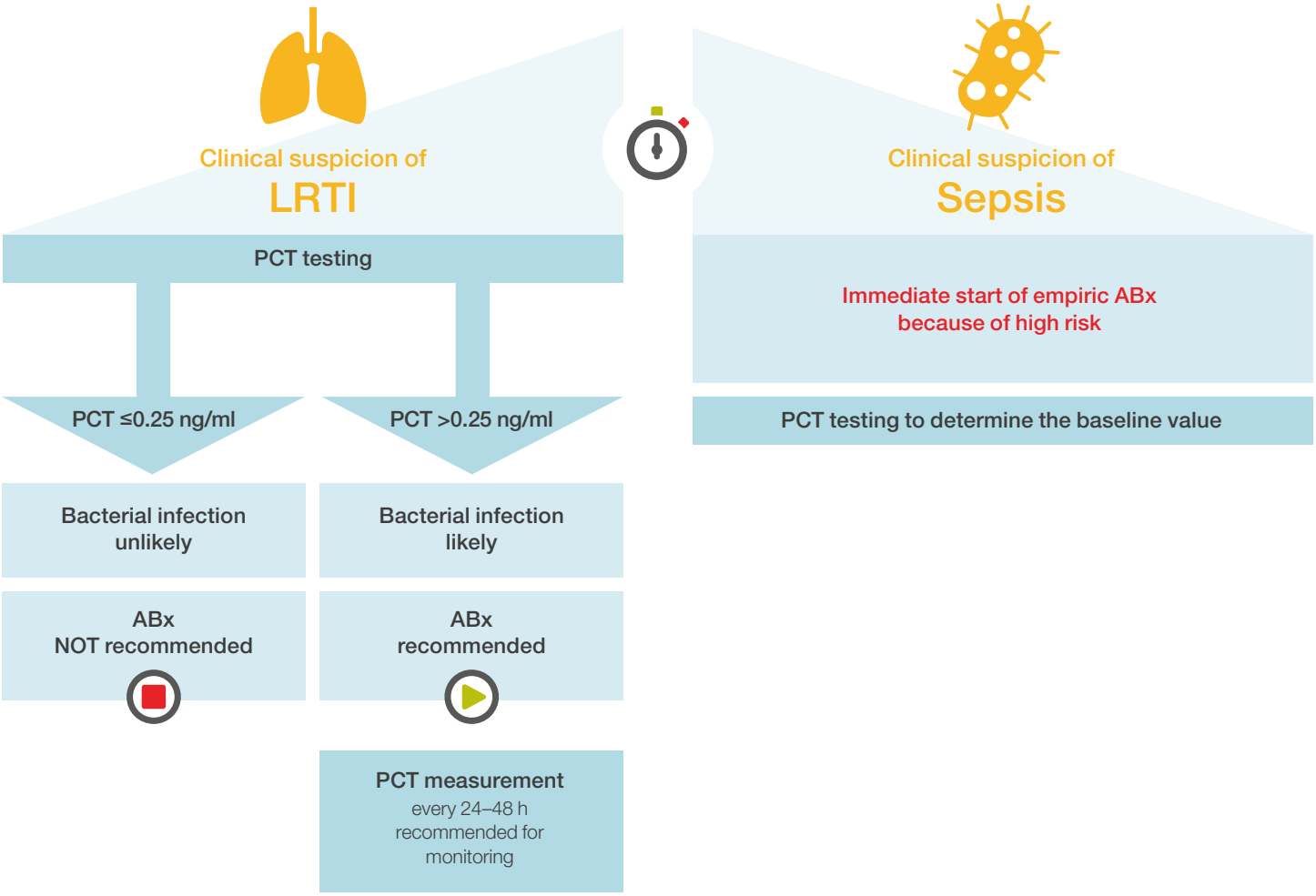


PCT-aided ABx stewardship

Reduction of mortality

* Reduction of diarrhea leads to lower incidence of severe and life-threatening consequences like electrolyte disturbances, dehydration, cardiovascular instability, and acute kidney injury.
MDRO Multidrug-resistant organisms

When to start antibiotics?



PCT values should always be interpreted in context of the patient's clinical condition.

PCT levels increase 3–6 hours after bacterial challenge and return to normal as the infection is resolved (Figure 3)[24,25,26]

- High specificity and sensitivity for bacterial infection
- Indicator for disease severity and treatment response

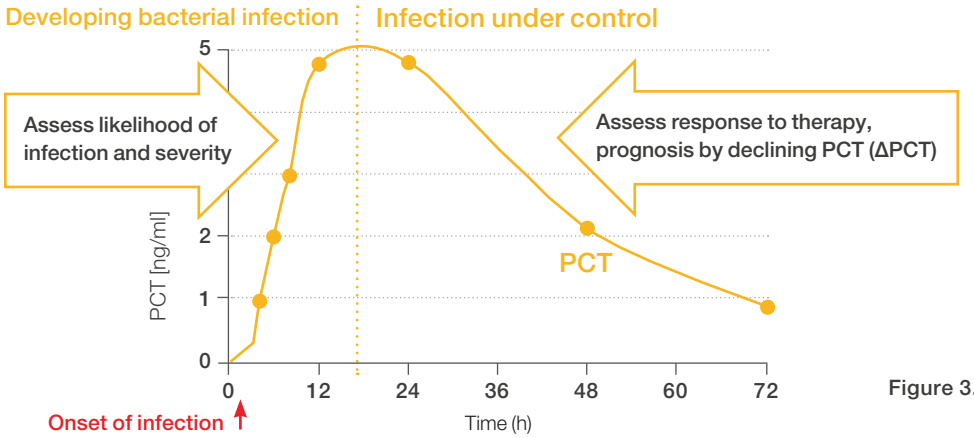
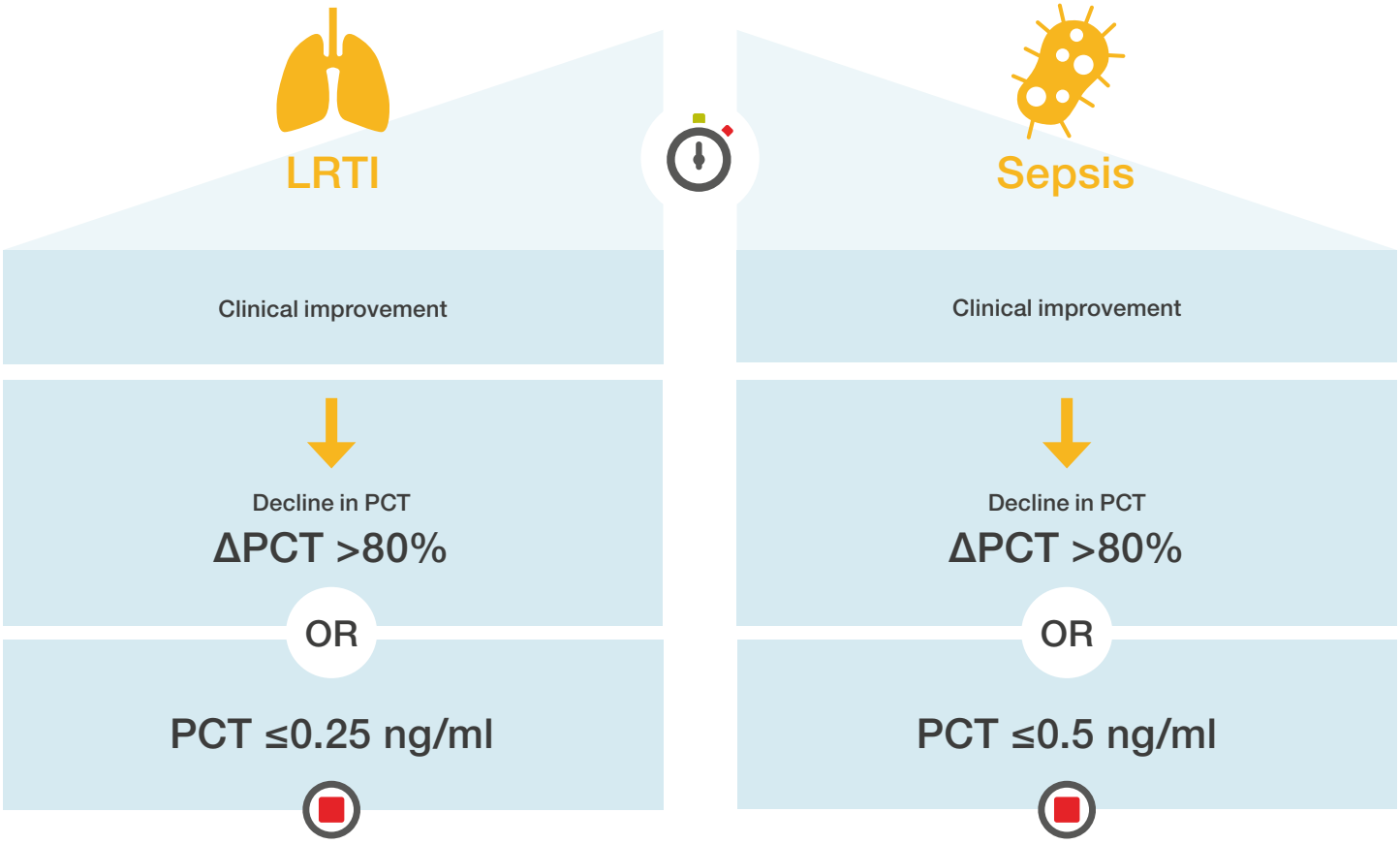


Figure 3. Kinetics of PCT[24,25]

When to stop antibiotics?



PCT values should always be interpreted in context of the patient's clinical condition.

Daily monitoring of PCT course allows for **customized ABx treatment duration, hence reduced ABx exposure**

Ensure using the quality assay for SAFE clinical decision making

PCT cut-offs and clinical algorithms were established by use of the global reference standard Thermo Scientific B·R·A·H·M·S PCT sensitive KRYPTOR™ assay and are valid solely for B·R·A·H·M·S PCT assays.

Efficacy of PCT in adults with LRTI symptoms

Patients in the ED
Is it bacterial infection?

As much as 75% of all antibiotic doses are prescribed for acute respiratory tract infections, despite their mainly viral cause.[7] PCT-aided therapy in such patients allows reduction in ABx exposure without any adverse impact on outcome.[6]

-14%
initiation of ABx[6]

Up to
-35%
ABx exposure[6,*]

-30%
adverse effects from ABx[6]

Data from: Effect of Procalcitonin-Based Guidelines vs Standard Guidelines on Antibiotic Use in Lower Respiratory Tract Infections (ProHOSP)[6]
Largest prospective, multicenter, randomized controlled trial with PCT in LRTI patients presenting to EDs:
• 1359 LRTI patients, 6 centers • PCT group (n=671), control group (n=688)

* % reduction related to non PCT-aided group

0.25 ng/ml
B·R·A·H·M·S PCT
LRTI cut-off

Community-acquired pneumonia (CAP)

Tailor the treatment duration in hospitalized patients

Up to
-40%
ABx exposure[27]

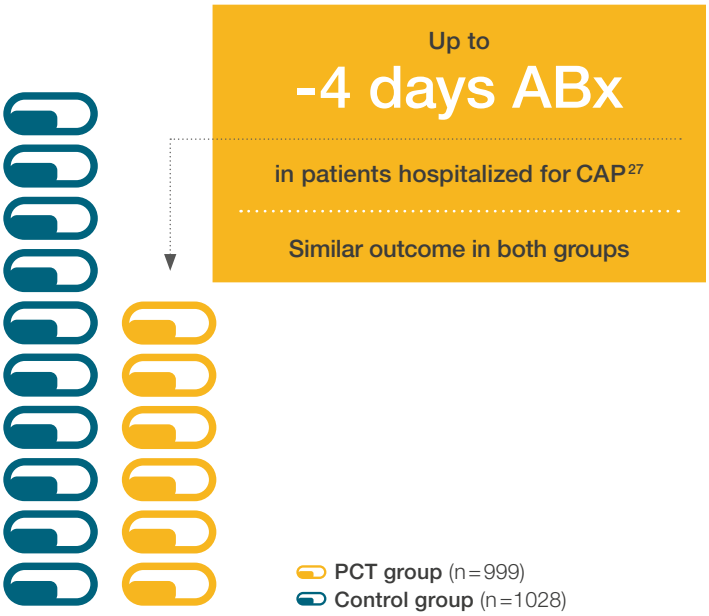


Figure 4. Meta-analysis data for 2027 patients hospitalized for CAP, total exposure of ABx in median days: PCT group = 6 days, control group = 10 days[27]

Acute COPD exacerbations

Does every exacerbation require ABx?

- Significant sustained reduction in total antibiotic exposure for up to 6 months[9]
- No decrease in mean time to next exacerbation[9]
- No increase in lung function decline[9]

Up to
-44%
ABx exposure
at index exacerbation[9]

If it is viral, antibiotics will not help. PCT testing can aid in decision making on antibiotic therapy.

Efficacy of PCT in adults in Intensive Care Units

How to know the appropriateness of an empiric antibiotic?

Effective antibiotic treatment is reflected by declining PCT values,[28] consistent with its half-life time of about 20–24 hours.[25] Serial determinations of PCT can be used to monitor the course of infection in sepsis patients. Appropriate empiric antibiotic therapy is associated with a significant decline in PCT.[28]

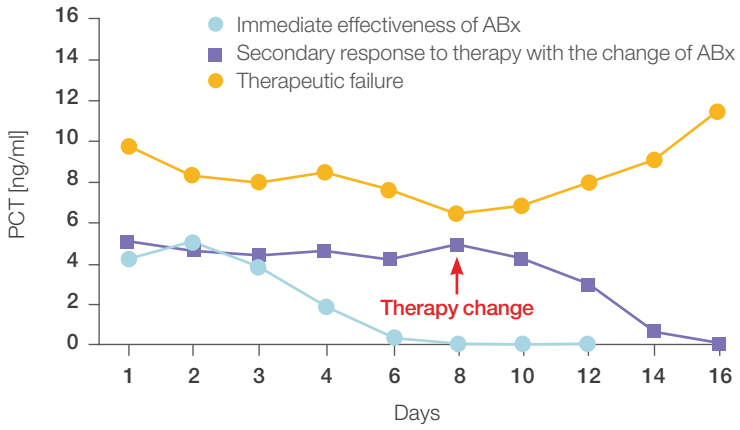


Figure 5. Typical course of PCT serum level according to patient's response to antibiotic treatment (n=109)[29]

Efficacy and safety in critically ill patients

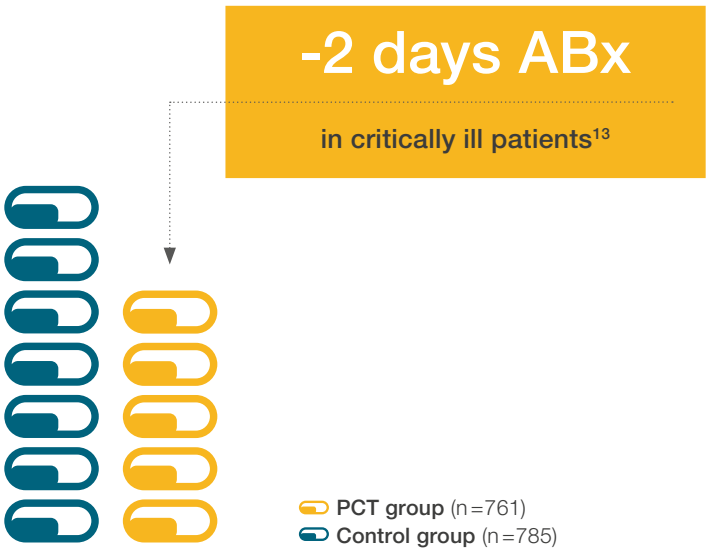


Figure 6. Median duration of ABx treatment in PCT-guided group = 5 days, in control group = 7 days[13]

Up to
-6%
mortality at 1 year[13]

Data from: The Stop Antibiotics on Procalcitonin Guidance Study[13]

- Largest prospective, multicenter, randomized, controlled, open-label intervention trial with PCT in critically ill patients
- Conducted in the Netherlands – a healthcare system with comparatively low use of ABx[23]
- 1575 critically ill patients, 15 centers

Multi-disciplinary approach to PCT-aided ABS

Several recent studies have emphasized the importance of a multi-disciplinary approach for successfully leveraging the benefit of PCT.[30,31,32] A pharmacist led PCT-protocol implementation study showed not only a reduction in days of ABx therapy from 9 days to 6 days but also improved significantly the appropriate ordering of PCT tests, subsequently resulting in higher antibiotic discontinuation rates (Figure 7).[32]

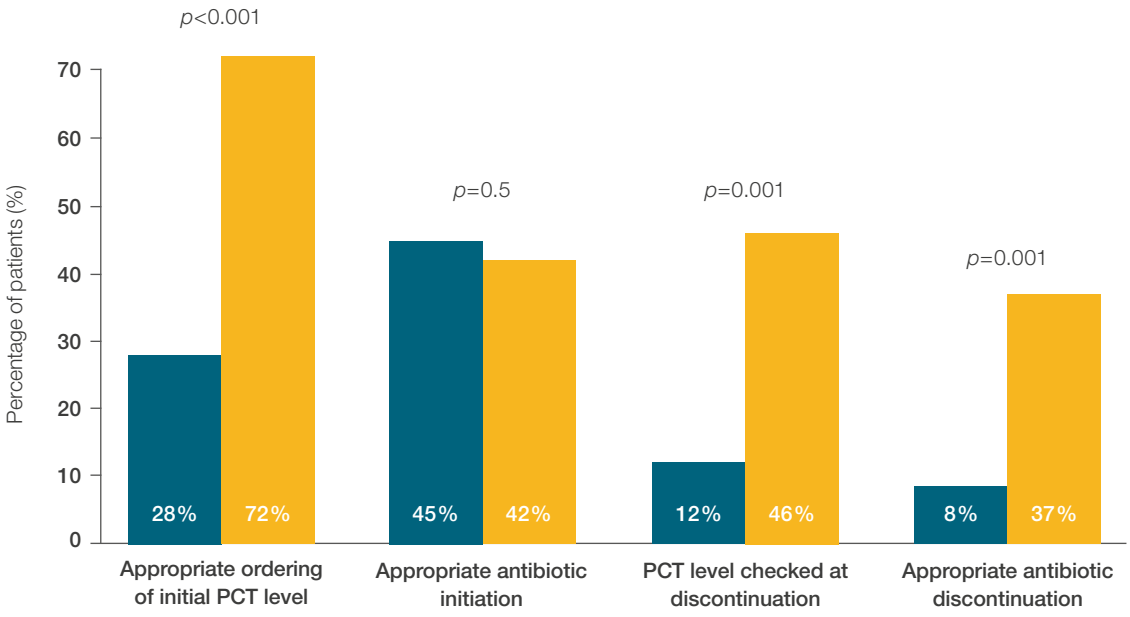


Figure 7. Impact of pharmacist-led PCT protocol on appropriateness of ordering of PCT levels and its impact on antibiotic prescriptions[32]

B·R·A·H·M·S

PCT

PCT-aided antibiotic stewardship protocols lead to

Reduced initial ABx prescription rates

Shortened ABx treatment duration

Decreased average LOS

Less ABx resistance

Reduced overall treatment costs

-26% in sepsis patients[21]

-18% in LRTI patients[21]

The economic impact of PCT-guided treatment has been studied through health economic modeling in various settings:

- Sepsis patients – ICU[33]
- Acute Respiratory Infections – inpatient, ICU, outpatient[34]
- COPD exacerbation – inpatient[35]

Treatment cost reductions ranging from 9% to 49% have been demonstrated across various countries.[21,33,36,37]

The cost of testing for PCT is more than offset by downstream cost savings.

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Secured clinical decision making independent of platform

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BIOMÉRIEUX	VIDAS® B·R·A·H·M·S PCT
DiaSorin	LIAISON® B·R·A·H·M·S PCT II GEN
FUJIREBIO Diagnostics, Inc.	Lumipulse® G B·R·A·H·M·S PCT
LSI Medience	PATHFAST™ B·R·A·H·M·S PCT
QuidelOrtho™	VITROS® B·R·A·H·M·S PCT
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