Royal Cornwall Hospitals
NHS Trust

# Procalcitonin Guided Antibiotic Stewardship on Respiratory Tract Infections Clinical Guideline

## V2.0

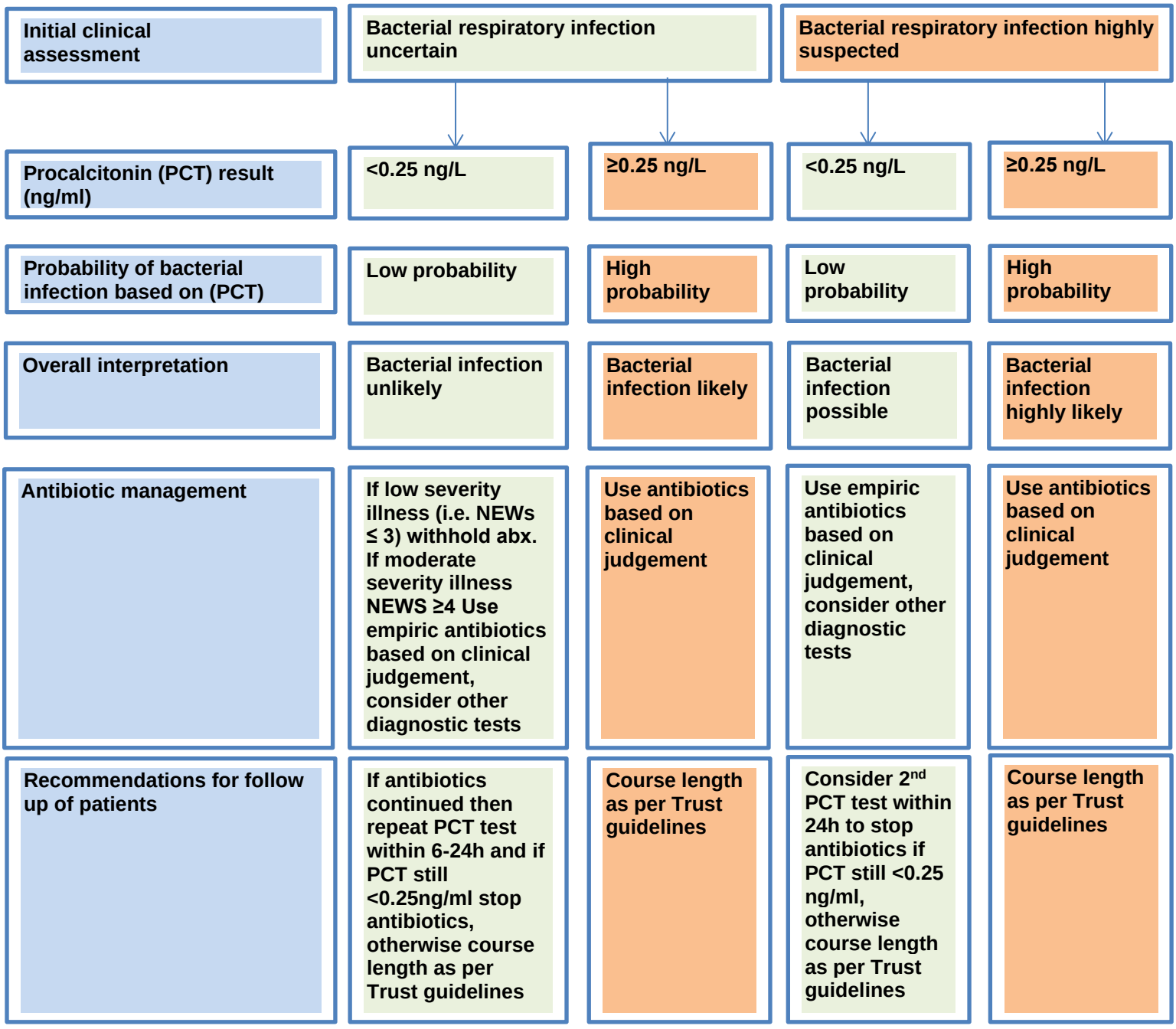
## September 2023

# Summary

### Patients with mild to moderate illness outside critical care

PCT needs to be interpreted taking into consideration both the severity of illness and probability of bacterial infection and should never override clinical judgement. The evidence supports PCT-guided antibiotic stewardship for the following infections and therefore this guidance supports PCT guided antibiotic stewardship for these infections **ONLY**; acute bronchitis, exacerbation of COPD, exacerbation of asthma, suspected LRTI but weak signs and symptoms, and patients with sepsis but no source identified. In those with a confirmed HAP, VAP, or CAP (i.e., signs and symptoms in keeping with pneumonia and radiographic evidence of pneumonia) then low PCT can facilitate an early cessation of antibiotics at 3 days,

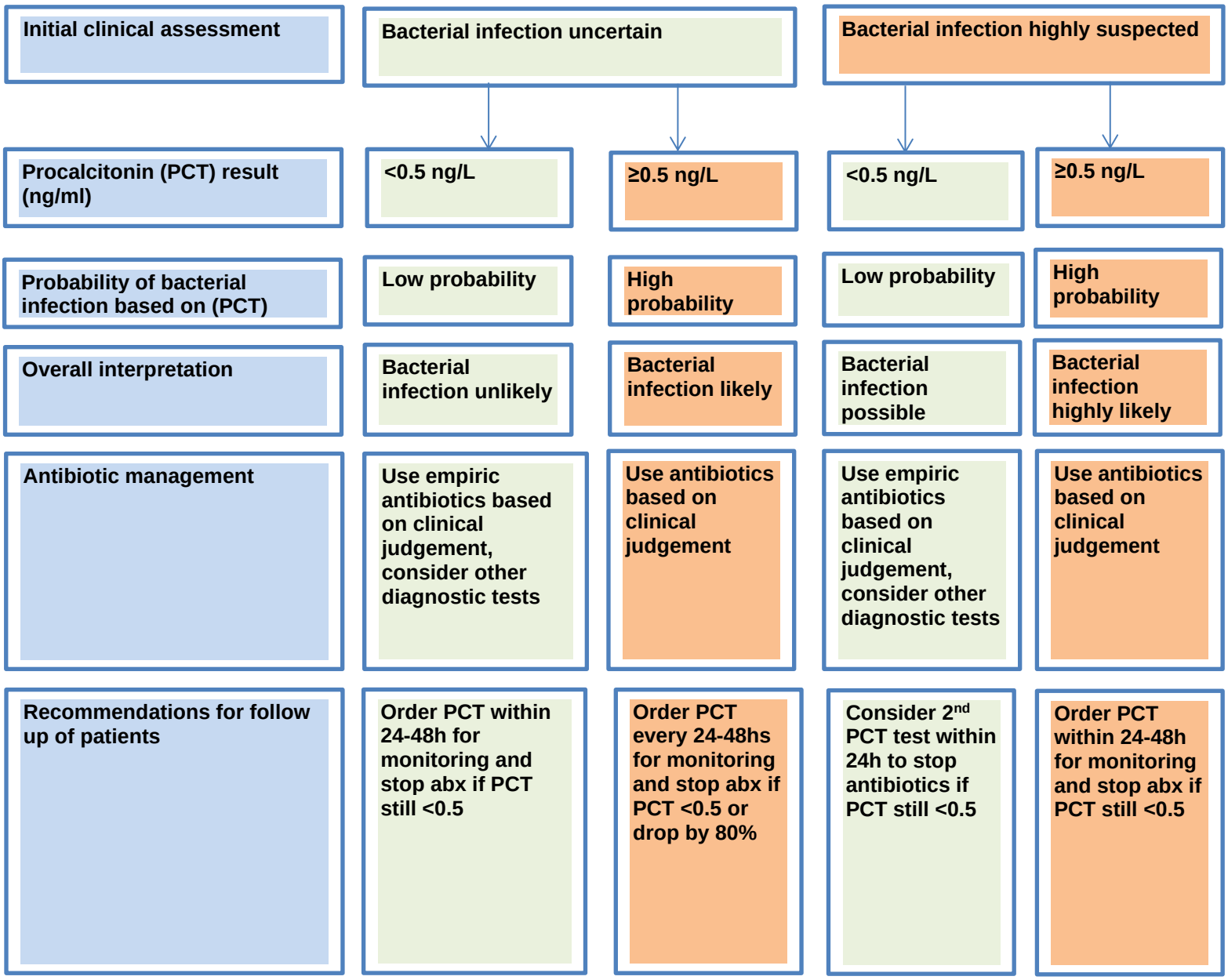
Do not use to guide antibiotic therapy in **Bronchiectasis, Interstitial Lung Disease, Lung Cancer** and **Pleural Infection.**



Caution in patients with immune-suppression , autoimmune diseases, cystic fibrosis, pancreatitis, trauma, surgery, pregnancy, high volume transfusion and malaria. Scenarios where clinicians may over-rule the PCT algorithm include; Respiratory or haemodynamic instability, Positive antigen test for Legionella pneumophilia, there is an immediate need for ICU admission, severe illness and Life threatening co-morbidities

**Patients with severe illness in ICU**

PCT needs to be interpreted taking into consideration both the severity of illness and probability of bacterial infection and should never override clinical judgement. The evidence supports PCT guided antibiotic stewardship in critically ill patients with sepsis and septic shock to guide antibiotic course lengths. Trial data show that early PCT guided antibiotic cessation is associated with reduced mortality.




PCT tests needs to be sent within the 24 hours of antibiotics starting. PCT can be added to bloods already in the lab if requested within 8 hours of sending.

# 1. Aim/Purpose of this Guideline

1.1. This guideline will support safe use of procalcitonin to guide antibiotic therapy in medical patients as described below.

1.2. This version supersedes any previous versions of this document.

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Royal Cornwall Hospital Trust rch-tr.infogov@nhs.net

# 2. The Guidance

## 2.1. Background

2.1.1. Procalcitonin (PCT) is a serum peptide biomarker that helps distinguish bacterial infection from other causes of infection or inflammation. Serum procalcitonin is typically undetectable in healthy people. When systemic inflammation is caused by bacterial infection, procalcitonin synthesis is induced in nearly all tissues and released into the blood. Known triggers for PCT synthesis include bacterial toxins, such as endotoxin, and cytokines (TNF-alpha, interleukin-1-beta, and interleukin-6. In contrast, procalcitonin synthesis is not induced in most viral infections. The lack of induction is likely due to cytokines released in viral infections that inhibit TNF-alpha production, such as interferon-gamma. The magnitude of the elevation correlates with the severity of infection and decreasing levels over time correlate with resolution of infection. PCT may not rise if an infection is localized.

2.1.2. Lower respiratory tract infections (LRTIs) are among the most common reasons for antibiotics with many prescriptions unnecessary or inappropriate. This unnecessary prescribing is due to the difficulty with differentiating a viral infection from a bacterial RTI and indeed the difficulty differentiating these from non-infectious mimics of LRTIs (e.g., heart failure) because clinical signs and symptoms are similar.

2.1.3. A Cochrane review looked at data from 26 trials and included 6708 adults with a respiratory tract infection (RTI) in primary care, emergency departments, hospital wards, and intensive care units.

PCT guided antibiotic stewardship, when compared to non-PCT guided control groups significantly reduced mortality in patients with a RTI and sepsis (8.6% in procalcitonin-guided group vs 10.0% in the control groups, and treatment failure was not significantly different between the two groups. Antibiotic exposure in procalcitonin group was lower with a 2.4-day reduction in antibiotic exposure (5.7 versus 8.1 days, 95% CI -2.71 to -2.15, P < 0.001), and there was a lower risk of antibiotic-related side effects (16.3% versus 22.1%, adjusted OR 0.68, 95% CI 0.57 to 0.82, P < 0.001) with no difference in length of hospital stay and intensive care unit stay. The RTIs in this Cochrane review included: community-acquired pneumonia, hospital-acquired pneumonia, ventilator-associated pneumonia, acute bronchitis and exacerbation of asthma and sepsis and suspected acute respiratory tract infection.

2.1.4. PCT-guided antibiotic stewardship aims to augment clinical decision making, enabling safe with holding of antibiotics in low severity disease where infection looks unlikely and early antibiotic cessation in patients started on antibiotics but have a low likelihood of infection. In the ICU setting PCT isn't used to guide empiric antibiotic prescribing but used to shorten the treatment course in patients with infection.

## 2.2. **The guidance**

2.2.1. PCT levels should be interpreted in the clinical context taking into consideration both the severity of illness and probability of bacterial infection. The treatment algorithms have been taken from an international consensus paper (Scheutz 2019). This algorithm first asks clinicians to decide on severity of illness (mild, moderate, or severe) and then stratify according to probability of bacterial infection (uncertainty verses bacterial infection highly suspected) and finally the PCT level is added into the assessment of the patient and inform the antibiotic decision making.

2.2.2. For example, patients with mild disease, a low probability of bacterial infection and a low PCT then clinicians are advised against prescribing an antibiotic and further test may be warranted to establish a final (non-infectious) diagnosis. If there are concerns the PCT may be negative due to early stages of infection (PCT starts to rise at 2 hours and peaks at 6 hours) then a second test should be ordered 6-24 hours after the first. If the same patient had moderate severity illness (low PCT and low likelihood of infection) then the advice would be to start antibiotics and to repeat the PCT 6-24 hours later and to stop antibiotics early if the PCT was still low (see algorithm for further scenarios).

2.2.3. While many studies have then measured serial PCTs in individual patients at days 3, 5 and 7 and used these to guide antibiotic cessation we have opted to not measure serial PCTs outside of the ICU. This is because short antibiotic course lengths in patients with a definitive respiratory infection diagnosis are now well evidenced and supported by NICE (recommended antibiotic course lengths for CAP, HAP, infective exacerbation of COPD and bronchitis are all 5 days in non-ICU patients).

2.2.4. Procalcitonin algorithms should never override clinical judgment. In most trials it was permissible to over-rule PCT algorithms using clinical judgment, because PCT should be used as an adjunct to clinical judgment and not a replacement.

2.2.5. Scenarios where clinicians may over-rule the PCT algorithm include:

- respiratory or haemodynamic instability.
- positive antigen test for Legionella pneumophilia.
- immediate need for ICU admission.
- Severe illness.
- Life threatening co-morbidities.

2.2.6. Caution is recommended for patients with immunosuppression (procalcitonin production is not impaired in immunocompromised states such as neutropenia, corticosteroids, bone marrow or solid organ transplantation, and HIV however few trials have included these patients). PCT levels are difficult to interpret in patients with, autoimmune diseases, cystic fibrosis, pancreatitis, trauma, surgery, pregnancy, high volume transfusion and malaria and so not recommended in these patients.

2.2.7. The algorithm is proposed for use in acute respiratory presentations (namely CAP, HAP, infective exacerbation of COPD, infective exacerbation of asthma and bronchitis) and patients with an undefined source of infection as part of differential diagnosis. Procalcitonin may not rise sufficiently in contained localised infections such as tonsillitis, sinusitis, cystitis, uncomplicated skin/soft tissue infections, abscesses, or empyemas or patients with chronic infections such as endocarditis and osteomyelitis and therefore not to be used in these indications.

2.2.8. False negatives can also occur if procalcitonin is drawn too early in the course of infection.

## 2.3. Special patient groups

### 2.3.1. Renal impairment

It is unclear how to interpret procalcitonin levels in patients with renal impairment. Persons with chronic kidney disease (CKD) have higher baseline levels of procalcitonin, believed to be due to higher levels of circulating inflammatory cytokines. Despite higher baseline levels, procalcitonin **does** rise in the setting of infection in patients with CKD. However, the rate of rise may be slower than in healthy patients. Elimination is marginally prolonged in patients with CKD, with a mean half-life of 28.9 hours in healthy patients compared with 33 hours in patients with creatinine clearance <30 mL/minute.

Because of these dynamics, a higher procalcitonin threshold may be more useful for patients with renal dysfunction. Single procalcitonin levels may be unreliable in patients with CKD and trends in procalcitonin levels are more useful. Additional studies are needed to determine how to best use procalcitonin in this population and whether use is associated with reduction in unnecessary antibiotic prescription.

### 2.3.2. **Immunocompromised patients**

Have generally been excluded from trials evaluating procalcitonin efficacy but observational studies suggest that procalcitonin levels correlate with the presence of bacterial infection and the severity of infection in this population. Because morbidity from bacterial infections can be high in this population, and because immunocompromised patients may require longer durations of antibiotics in general procalcitonin guided antibiotic discontinuation in immunocompromised individuals is not recommended.

### 2.3.3. **Surgery and trauma**

Severe physiologic stressors such as surgery, trauma, or burns can lead to procalcitonin elevations. Aggregated data from small studies suggest that procalcitonin has moderate diagnostic accuracy for sepsis in surgical and trauma patients but further study is needed to inform practice.

### 2.3.4. **Practicalities**

Blood should be sent in a yellow-top tube to Clinical Chemistry. PCT testing will be carried out at RCHT24 hours a day. Turn-around time is expected to be within 3 hours. The request for PCT may be able to be ‘added-on’ to samples taken within 8 hours dependent upon laboratory capacity. Tests cost £10 each and therefore it is important patients meet the criteria defined above.

# 3. Monitoring compliance and effectiveness

| Information Category | Detail of process and methodology for monitoring compliance |
|---|---|
| **Element to be monitored** | 1) Compliance with the procalcitonin algorithm.<br>2) pre-72 hour stop rates. |
| **Lead** | Neil Powell. |
| **Tool** | ARK audit tool. |
| **Frequency** | Daily (Monday to Friday) for first three months. |
| **Reporting arrangements** | ASMC.<br>MPC. |
| **Acting on recommendations and Lead(s)** | ASMC on behalf of MPC. |
| **Change in practice and lessons to be shared** | Required changes to practice will be identified and actioned within a week. A lead member of the team will be identified to take each change forward where appropriate. Lessons will be shared with all the relevant stakeholders via specialty governance meetings. |

# 4. Equality and Diversity

4.1. This document complies with the Royal Cornwall Hospitals NHS Trust service Equality and Diversity statement which can be found in the Equality Diversity And Inclusion Policy or the Equality and Diversity website.

4.2. Equality Impact Assessment

The Initial Equality Impact Assessment Screening Form is at Appendix 2.

# Appendix 1. Governance Information

| Information Category | Detailed Information |
|---|---|
| **Document Title:** | Procalcitonin Guided Antibiotic Stewardship on Respiratory Tract Infections Clinical Guideline V2.0 |
| **This document replaces (exact title of previous version):** | Procalcitonin Guided Antibiotic Stewardship on Respiratory Tract Infections Clinical Guideline V1.0 |
| **Date Issued/Approved:** | Friday 15 September 2023 |
| **Date Valid From:** | September 2023 |
| **Date Valid To:** | September 2026 |
| **Directorate / Department responsible (author/owner):** | Neil Powell, Consultant Antimicrobial Pharmacist. |
| **Contact details:** | 01872 252593. |
| **Brief summary of contents:** | Appropriate use of Procalcitonin test within RCHT. |
| **Suggested Keywords:** | Procalcitonin and PCT. |
| **Target Audience:** | **RCHT:** Yes<br>**CFT:** No<br>**CIOS ICB:** No |
| **Executive Director responsible for Policy:** | Chief Medical Officer. |
| **Approval route for consultation and ratification:** | Medication Practice Committee.<br>Pathology Governance Group. |
| **Manager confirming approval processes:** | Richard Andrzejuk. |
| **Name of Governance Lead confirming consultation and ratification:** | Kevin Wright. |
| **Links to key external standards:** | Cochrane review on Procalcitonin. |
| **Related Documents:** | **References**<br>Up to date accessed via hospital intranet March 2020 https://www.uptodate.com/contents/search.<br>Huang et al. Procalcitonin-Guided Use of Antibiotics for Lower Respiratory Tract Infection. NEJM 2018. |

| Information Category | Detailed Information |
|---|---|
| | Schuetz P *et al.* Procalcitonin to initiate or discontinue antibiotics in acute.<br>respiratory tract infections (Review). Cochrane library 2017. |
| **Training Need Identified?** | Yes |
| **Publication Location (refer to Policy on Policies – Approvals and Ratification):** | Internet and Intranet |
| **Document Library Folder/Sub Folder:** | Clinical / Pharmacy |

**Version Control Table**

| Date | Version Number | Summary of Changes | Changes Made by |
|---|---|---|---|
| May 2020 | V1.0 | Initial issue | Neil Powell, Consultant Antimicrobial Pharmacist |
| September 2023 | V2.0 | Minor edits of the text, no changes to the clinical guidelines. | Neil Powell, Consultant Antimicrobial Pharmacist |

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**All Policies, Strategies and Operating Procedures, including Business Plans, are to be kept for the lifetime of the organisation plus 6 years.**

**This document is only valid on the day of printing.**

**Controlled Document.**

This document has been created following the Royal Cornwall Hospitals NHS Trust The Policy on Policies (Development and Management of Knowledge Procedural and Web Documents Policy). It should not be altered in any way without the express permission of the author or their Line Manager.

# Appendix 2. Equality Impact Assessment

## Section 1: Equality Impact Assessment (EIA) Form

The EIA process allows the Trust to identify where a policy or service may have a negative impact on an individual or particular group of people.

For guidance please refer to the Equality Impact Assessment Policy (available from the document library) or contact the Equality, Diversity, and Inclusion Team rcht.inclusion@nhs.net

| Information Category | Detailed Information |
|---|---|
| **Name of the strategy / policy / proposal / service function to be assessed:** | Procalcitonin Guided Antibiotic Stewardship on Respiratory Tract Infections Clinical Guideline V2.0 |
| **Directorate and service area:** | Pathology, Clinical Support |
| **Is this a new or existing Policy?** | Existing |
| **Name of individual completing EIA** (Should be completed by an individual with a good understanding of the Service/Policy): | Neil Powell, Consultant Antimicrobial Pharmacist |
| **Contact details:** | 01872 252593 |

| Information Category | Detailed Information |
|---|---|
| **1. Policy Aim - Who is the Policy aimed at?** (The Policy is the Strategy, Policy, Proposal or Service Change to be assessed) | Optimise antibiotic use in patients with suspected respiratory tract infections. |
| **2. Policy Objectives** | Safe with holding, or early cessation, of antibiotics in with low severity illness and low likelihood of bacterial infection. |
| **3. Policy Intended Outcomes** | Reduced antibiotic use in medical specialties through increased pre-72 hour antibiotic stop rates. |
| **4. How will you measure each outcome?** | Quarterly ARK audits. |
| **5. Who is intended to benefit from the policy?** | Medical patients. |

| Information Category | Detailed Information |
|---|---|
| **6a. Who did you consult with?**<br>(Please select Yes or No for each category) | • Workforce: Yes<br>• Patients/ visitors: No<br>• Local groups/ system partners: No<br>• External organisations: No<br>• Other: No |
| **6b. Please list the individuals/groups who have been consulted about this policy.** | **Please record specific names of individuals/ groups:**<br>Medication Practice Committee.<br>Pathology.<br>All Medical Specialties. |
| **6c. What was the outcome of the consultation?** | Agreed |
| **6d. Have you used any of the following to assist your assessment?** | **National or local statistics, audits, activity reports, process maps, complaints, staff, or patient surveys:**<br>No. |

**7. The Impact**

Following consultation with key groups, has a negative impact been identified for any protected characteristic? Please note that a rationale is required for each one.

Where a negative impact is identified without rationale, the key groups will need to be consulted again.

| Protected Characteristic | (Yes or No) | Rationale |
|---|---|---|
| **Age** | No | |
| **Sex** (male or female) | No | |
| **Gender reassignment** (Transgender, non-binary, gender fluid etc.) | No | |
| **Race** | No | |
| **Disability** (e.g. physical or cognitive impairment, mental health, long term conditions etc.) | No | |
| **Religion or belief** | No | |

| Protected Characteristic | (Yes or No) | Rationale |
|---|---|---|
| **Marriage and civil partnership** | No | |
| **Pregnancy and maternity** | No | |
| **Sexual orientation** (e.g. gay, straight, bisexual, lesbian etc.) | No | |

**A robust rationale must be in place for all protected characteristics. If a negative impact has been identified, please complete section 2. If no negative impact has been identified and if this is not a major service change, you can end the assessment here.**

I am confident that section 2 of this EIA does not need completing as there are no highlighted risks of negative impact occurring because of this policy.

Name of person confirming result of initial impact assessment: Neil Powell, Consultant Antimicrobial Pharmacist

**If a negative impact has been identified above OR this is a major service change, you will need to complete section 2 of the EIA form available here:**
Section 2. Full Equality Analysis