NICE National Institute for Health and Care Excellence

Appendix A: Summary of evidence from surveillance

2018 surveillance of Pneumonia in adults: diagnosis and management (2018) NICE guideline CG191

Summary of evidence from surveillance

Studies identified in searches are summarised from the information presented in their abstracts.

Feedback from topic experts who advised us on the approach to this surveillance review, was considered alongside the evidence to reach a final decision on the need to update each section of the guideline.

1.1 Presentation with lower respiratory tract infection

Recommendations in this section of the guideline

1.1.1 For people presenting with symptoms of lower respiratory tract infection in primary care, consider a point of care C-reactive protein test if after clinical assessment a diagnosis of pneumonia has not been made and it is not clear whether antibiotics should be prescribed. Use the results of the C-reactive protein test to guide antibiotic prescribing in people without a clinical diagnosis of pneumonia as follows:

- Do not routinely offer antibiotic therapy if the C-reactive protein concentration is less than 20 mg/litre.
- Consider a delayed antibiotic prescription (a prescription for use at a later date if symptoms worsen) if the C-reactive protein concentration is between 20 mg/litre and 100 mg/litre.
- Offer antibiotic therapy if the C-reactive protein concentration is greater than 100 mg/litre.

Surveillance decision

This recommendation should not be updated.

Presentation with lower respiratory tract infection

2018 surveillance summary

No new evidence was identified in the literature search relevant to this recommendation.

Intelligence gathering

Some topic experts noted that there could be uptake issues with the recommendation on C-reactive protein (CRP) testing, suggesting that it is not used in practice due to feasibility and financial constraints in primary care.

Impact statement

Implementation concerns were raised around the recommendation 1.1.1 on CRP testing in primary care, with an expert noting that the test may not be feasible or affordable. It is important to note that the recommendation suggests considering a point of care C-reactive protein test only if after clinical assessment a diagnosis of pneumonia has not been made and it is not clear whether antibiotics should be prescribed. As such, it should only be used in circumstances where it is unclear how to proceed. We did not identify any evidence to suggest that this recommendation is not feasible in practice. However, during guideline development the committee did note that CRP point of care tests were not widely used in the UK and that there would be significant costs associated with training, implementation and subsequent quality assurance of equipment. They also acknowledged that it is unclear whether the benefits would translate as well across all practices and individual prescribers.

However, in the absence of evidence in this area, it is unlikely that the recommendation will be impacted.

New evidence is unlikely to change guideline recommendations.

1.2 Community-acquired pneumonia

Severity assessment in primary care

Recommendations in this section of the guideline

1.2.1 When a clinical diagnosis of community-acquired pneumonia is made in primary care, determine whether patients are at low, intermediate or high risk of death using the CRB65 score (see box 1).

1.2.2 Use clinical judgement in conjunction with the CRB65 score to inform decisions about whether patients need hospital assessment as follows:

- consider home-based care for patients with a CRB65 score of 0

- consider hospital assessment for all other patients, particularly those with a CRB65 score of 2 or more.

Box 1 CRB65 score for mortality risk assessment in primary care*

CRB65 score is calculated by giving 1 point for each of the following prognostic features:

- confusion (abbreviated Mental Test score 8 or less, or new disorientation in person, place or time)[b]
- raised respiratory rate (30 breaths per minute or more)
- low blood pressure (diastolic 60 mmHg or less, or systolic less than 90 mmHg)
- age 65 years or more.

Patients are stratified for risk of death as follows:

- 0: low risk (less than 1% mortality risk)
- 1 or 2: intermediate risk (1-10% mortality risk)
- 3 or 4: high risk (more than 10% mortality risk).

* Lim WS, van der Eerden MM, Laing R, et al. (2003) Defining community-acquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax 58: 377–82

** For guidance on delirium, see the NICE guideline on delirium.

Surveillance decision

This section of the guideline should not be updated.

Severity assessment in primary care

2018 surveillance summary

No new evidence was identified in the literature search relevant to these recommendations.

Intelligence gathering

An expert also called for further guidance on predictive tools, to help with advanced planning. Regarding the use of the CRB65 score in primary care, there was a concern that the inclusion of a mini mental score in primary care may not be practical and that, overall, recommendation 1.2.1 is based on poor evidence. A suggestion was put forward to consider using more basic clinical tools, such as those recommended in guidelines on sepsis, acute respiratory conditions and chronic obstructive pulmonary disease (COPD).

Impact statement

A topic expert raised a concern around the practicality of using the CRB-65 score to determine the severity of community-acquired pneumonia (CAP) in primary care. As a solution, there was a request for more basic clinical tools to be recommended, based on similar guidelines on sepsis and COPD. NICE guideline NG51 on Sepsis: recognition, diagnosis and early management does not recommend a specific tool for assessing the severity of the illness, making a comparison difficult. Furthermore we did not identify any evidence to suggest any implementation issues with using the CRB65 score in primary care, nor did we find any evidence on more basic clinical tools. Furthermore, the original guideline development committee agreed that CRB65 was the only severity assessment tool with suitable available evidence. We also noted that recommendation 1.2.1 allows confusion to be assessed simply in terms of 'new disorientation in person, place or time' and does not necessarily require clinicians to use the abbreviated Mental Test score. Therefore it is unlikely that the recommendations will be impacted at this time, however we will make a note of these concerns for future surveillance reviews.

New evidence is unlikely to change guideline recommendations.

Severity assessment in hospital

1.2.3 When a diagnosis of community-acquired pneumonia is made at presentation to hospital, determine whether patients are at low, intermediate or high risk of death using the CURB65 score (see box 2).

1.2.4 Use clinical judgement in conjunction with the CURB65 score to guide the management of community-acquired pneumonia, as follows:

- consider home-based care for patients with a CURB65 score of 0 or 1

- consider hospital-based care for patients with a CURB65 score of 2 or more
- consider intensive care assessment for patients with a CURB65 score of 3 or more.

1.2.5 Stratify patients presenting with community-acquired pneumonia into those with low-, moderate- or high-severity disease. The grade of severity will usually correspond to the risk of death.

Box 2 CURB65 score for mortality risk assessment in hospital*

CRB65 score is calculated by giving 1 point for each of the following prognostic features:

- confusion (abbreviated Mental Test score 8 or less, or new disorientation in person, place or time)[b]
- raised blood urea nitrogen (over 7 mmol/litre)
- raised respiratory rate (30 breaths per minute or more)
- low blood pressure (diastolic 60 mmHg or less, or systolic less than 90 mmHg)
- age 65 years or more.

Patients are stratified for risk of death as follows:

- 0 or 1: low risk (less than 3% mortality risk)
- 2: intermediate risk (3-15% mortality risk)
- 3 to 5: high risk (more than 15% mortality risk).

* Lim WS, van der Eerden MM, Laing R, et al. (2003) Defining community-acquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax 58: 377–82

** For guidance on delirium, see the NICE guideline on delirium.

Surveillance decision

This section of the guideline should not be updated.

Severity assessments in hospital

2018 surveillance summary

One retrospective cohort study (1) (n = 1902) compared the prognostic performance of 3 severity scoring tools and procalcitonin in patients presenting to the emergency department with CAP. The tools compared to each other were CURB-65, CRB-65 and the pneumonia severity index (PSI). The results from the procalcitonin comparison are not reported here as they are not relevant to the review question behind this part of the guideline. Results indicated that the most accurate tool for predicting mortality was the PSI, with an area under the receiver operating characteristic curve (AUC) of 0.82. The CURB-65 and CRB-65 scores were found to have lower prognostic performance, with an AUC of 0.71 and 0.67 respectively. The difference in performance between the tools was found to be significant. The 95% confidence intervals (CI) were not reported in the abstract.

A cross-sectional study (2) (n = 109) was identified which compared the prognostic performance of the PSI and CURB-65 tools in predicting 30-day mortality in patients with healthcare-associated pneumonia (HCAP). The results indicate that the AUC was 0.74 (95% CI: 0.65-0.83) and 0.7 (95% CI: 0.6-0.8) for PSI and CURB-65 respectively, however this difference was not significant.

Intelligence gathering

A topic expert raised a concern that established scoring systems may not perform well in very old patients as they have significantly different presentations of CAP compared with younger adults. In these patients, the condition can be very complex to recognise and treat as it may be co-morbid with other conditions such as COPD and chronic heart failure.

Impact statement

New evidence was identified to suggest that the PSI may be more accurate than CURB-65 and CRB-65 in predicting 30-day mortality in patients with CAP. Other evidence supported the use of CURB-65, however no comparison was made with another tools. The guideline currently recommends using the CURB-65 score to assess mortality risk in hospital (see recommendation 1.2.3). During guideline development, the AUC ranges for PSI and CURB-65 were 0.71-0.89 and 0.67-0.87 respectively. However, the committee considered the simplicity of the CURB-65 score to be an advantage over PSI. As the new evidence is in line with that considered during guideline development, it is unlikely that there will be an impact on the recommendations at this time.

Findings from another study supported the use of both PSI and CURB-65 for predicting 30-day mortality in patients with HCAP. The guideline does not currently class HCAP as a separate category of pneumonia. As stated in the guideline, studies in Europe have found microbial causes in this group to be similar to hospital-acquired pneumonia (HAP) and CAP and this terminology has not been generally adopted in the UK. The new evidence is consistent with the recommendations which advise using the CURB-65 score.

A concern was raised around the suitability of scoring systems for very old patients. We did not identify any evidence to

suggest the performance of CURB-65 varies for different subpopulations. However, during guideline development the committee considered that age, comorbidities and malignancies could skew the predictive ability of the tools to assess mortality and intensive treatment unit (ITU) admission. In light of this, they emphasised that the role of severity assessment tools is to help guide management, not to replace or overrule clinical judgement. It is therefore unlikely that the recommendations will be impacted.

New evidence is unlikely to change guideline recommendations.

Microbiological tests

1.2.6 Do not routinely offer microbiological tests to patients with low-severity community-acquired pneumonia.

1.2.7 For patients with moderate- or high-severity community-acquired pneumonia:

- take blood and sputum cultures and
- consider pneumococcal and legionella urinary antigen tests.

Surveillance decision

No new information was identified at any surveillance review.

Timely diagnosis and treatment

1.2.8 Put in place processes to allow diagnosis (including X-rays) and treatment of community-acquired pneumonia within 4 hours of presentation to hospital.

1.2.9 Offer antibiotic therapy as soon as possible after diagnosis, and certainly within 4 hours to all patients with community-acquired pneumonia who are admitted to hospital.

Surveillance decision

No new information was identified at any surveillance review.

Antibiotic therapy

Low severity community-acquired pneumonia

1.2.10 Offer a 5-day course of a single antibiotic to patients with low-severity community-acquired pneumonia.

1.2.11 Consider amoxicillin in preference to a macrolide or a tetracycline for patients with low-severity community-acquired pneumonia. Consider a macrolide or a tetracycline for patients who are allergic to penicillin.

1.2.12 Consider extending the course of the antibiotic for longer than 5 days as a possible management strategy for patients with low-severity community-acquired pneumonia whose symptoms do not improve as expected after 3 days.

1.2.13 Explain to patients with low-severity community-acquired pneumonia treated in the community, and when appropriate their families or carers, that they should seek further medical advice if their symptoms do not begin to improve within 3 days of starting the antibiotic, or earlier if their symptoms are worsening.

1.2.14 Do not routinely offer patients with low-severity community-acquired pneumonia:

- a fluoroquinolone
- dual antibiotic therapy.

Surveillance decision

This section of the guideline did not undergo surveillance. NICE are currently developing guidance in this area as part of the 'Management of Common Infections' guidelines on community-acquired pneumonia and hospital-acquired pneumonia. We will review this area again when these guidelines are published.

Moderate- and high-severity community-acquired pneumonia

1.2.15 Consider a 7- to 10-day course of antibiotic therapy for patients with moderate- or high-severity community-acquired pneumonia.

1.2.16 Consider dual antibiotic therapy with amoxicillin and a macrolide for patients with moderate-severity community-acquired pneumonia.

1.2.17 Consider dual antibiotic therapy with a beta-lactamase stable beta-lactam* and a macrolide for patients with high-severity community-acquired pneumonia.

*Available beta-lactamase stable beta-lactams include: co-amoxiclav, cefotaxime, ceftaroline fosamil, ceftriaxone, cefuroxime and piperacillin with tazobactam.

Surveillance decision

This section of the guideline did not undergo surveillance. NICE are currently developing guidance in this area as part of the 'Management of Common Infections' guidelines on community-acquired pneumonia and hospital-acquired pneumonia. We will review this area again when these guidelines are published.

Glucocorticosteroid treatment

1.2.18 Do not routinely offer a glucocorticosteroid to patients with community-acquired pneumonia unless they have other conditions for which glucocorticosteroid treatment is indicated.

Surveillance decision

This recommendation should not be updated.

Editorial amendment

The term "glucocorticosteroids" should be amended to "glucocorticoids", which is now the preferred term used by the British National Formulary.

Glucocorticoid treatment

2018 surveillance summary

An update of a Cochrane review (3) including 17 studies (n = 2264) examined the safety and efficacy of glucocorticoids, given as adjunct to antibiotic treatment, for adults and children with pneumonia (CAP, HAP, CAP and ventilator associated pneumonia). The intervention included oral prednisone in 3 trials and intravenous dexamethasone, hydrocortisone, or methylprednisolone in 13 trials. One trial used prednisone without limiting the administration route. For the purposes of this surveillance review, only the results of the adults with CAP or HAP were considered. See below for a breakdown of included studies:

- 8 randomised controlled trials (RCTs) considered non-severe CAP (n = 1636)

- 4 RCTs considered severe CAP (n = 192).
- 1 RCT considered adults and children with pneumonia (type not specified) (n = 126 adults and children)
- The authors did not identify any studies that considered patients with HAP.

The findings indicated that glucocorticoids significantly reduced mortality and morbidity in adults with severe CAP. Glucocorticoid therapy also reduced morbidity, but not mortality, for adults with non-severe CAP. There was also a reduction in time to clinical cure, length of hospital and intensive care unit (ICU) stay, development of respiratory failure or shock not present at pneumonia onset, and rates of pneumonia complications (however, significance was not reported in the abstract and the authors do not distinguish between severity of cases for these findings). Regarding adverse events, hyperglycaemia was significantly more common in adults treated with glucocorticoids however authors concluded that the benefits of the treatment seemed to outweigh the harms.

Two systematic reviews (published prior to the Cochrane review) have examined the safety and efficacy of adjunctive glucocorticoids for patients with CAP (severity not reported in the abstracts), one with 10 RCTs (4) and one with 12 RCTs (n = 1974) (5). Both reviews showed no significant difference in all-cause mortality, however significant reductions were reported in length of ICU stay (4), length of hospital stay (4,5), length of time to clinical stability (4,5). One of the reviews identified an increased risk of hyperglycaemia in the glucocorticoid-treated patients (5).

An RCT (6) (n = 120) examined the effect of adjunctive glucocorticoid in patients with severe CAP however this study was considered in the Cochrane review described above and therefore the results are not summarised here.

Intelligence gathering

Topic experts highlighted the new evidence on use of glucocorticoids for CAP, suggesting that this area may need reviewing again. However, they also mentioned 2 ongoing trials which will contribute to the evidence base in this area.

Impact statement

The majority of the new evidence supports the use of adjunctive glucocorticoids in patients with severe CAP in the ICU. The findings are driven by a recent updated Cochrane review highlighted by many topic experts, which shows a significant decrease in mortality for patients with severe CAP when treated with adjunctive glucocorticoids. Whilst the review indicates that hyperglycaemia is more common in those treated with glucocorticoids, the authors concluded that overall the benefits outweigh the harms.

Earlier reviews illustrate similar benefits of glucocorticoid treatment, such as reduced length of hospital stay and reduced length of time to clinical stability, however they did not find any significant impact on mortality.

The guideline currently states “Do not routinely offer a glucocorticosteroid to patients with community-acquired pneumonia unless they have other conditions for which glucocorticosteroid

treatment is indicated" (recommendation 1.2.18). When this recommendation was developed, all but 2 of the studies included in the Cochrane review (described above) were considered by the guideline committee. During this time, they acknowledged the apparent benefits of glucocorticoid treatment seen in the studies conducted in the ITU setting. However, after extensive debate, the committee members concluded that they could not make a specific positive recommendation for the use of glucocorticoid treatment in this setting. This was primarily due to reservations regarding the quality of the evidence and the lack of studies from a UK setting. Given that only 2 new studies have been published since this time, each showing no significant effect on mortality, it is unlikely that the guideline will be impacted as the evidence has not substantially moved on. However, we have added the ongoing trials highlighted by topic experts to our event tracker and we will review the area again when the results are published.

New evidence is unlikely to change guideline recommendations.

Monitoring in hospital

1.2.19 Consider measuring a baseline C-reactive protein concentration in patients with community-acquired pneumonia on admission to hospital, and repeat the test if clinical progress is uncertain after 48 to 72 hours.

Surveillance decision

No new information was identified at any surveillance review.

Safe discharge from hospital

1.2.20 Do not routinely discharge patients with community-acquired pneumonia if in the past 24 hours they have had 2 or more of the following findings:

- temperature higher than 37.5°C
- respiratory rate 24 breaths per minute or more
- heart rate over 100 beats per minute
- systolic blood pressure 90 mmHg or less
- oxygen saturation under 90% on room air

- abnormal mental status
- inability to eat without assistance.

1.2.21 Consider delaying discharge for patients with community-acquired pneumonia if their temperature is higher than 37.5°C.

Surveillance decision

This section of the guideline should not be updated.

Safe discharge from hospital

2018 surveillance summary

No new evidence was identified in the literature search relevant to this recommendation.

Intelligence gathering

A topic expert noted that moderate CAP may now be treated in ambulatory units or in the community by outreach home teams, day care, community ambulatory units. This affects choice of monitoring strategy and antibiotics. They suggested that this could be acknowledged in the guideline by adding further information to the section on safe discharge from hospital.

Impact statement

A topic expert highlighted that since the guideline was first published, there has been a change in the way treatment for moderate CAP may be delivered. It is now possible to treat moderate CAP in ambulatory units or in the community by various specialist services. The guideline currently recommends considering hospital-based care for moderate CAP (see recommendation 1.2.4), however it also states that clinical judgement should be used alongside the CURB-65 score. We did not identify any evidence in this area, however we will ask a question at consultation in order to identify any change in practice that is not reflected in the published evidence.

New evidence is unlikely to change guideline recommendations.

Patient information

1.2.22 Explain to patients with community-acquired pneumonia that after starting treatment their symptoms should steadily improve, although the rate of

improvement will vary with the severity of the pneumonia, and most people can expect that by:

- 1 week: fever should have resolved
- 4 weeks: chest pain and sputum production should have substantially reduced
- 6 weeks: cough and breathlessness should have substantially reduced
- 3 months: most symptoms should have resolved but fatigue may still be present
- 6 months: most people will feel back to normal.

1.2.23 Advise patients with community-acquired pneumonia to consult their healthcare professional if they feel that their condition is deteriorating or not improving as expected.

Surveillance decision

No new information was identified at any surveillance review.

1.3 Hospital-acquired pneumonia

Antibiotic therapy

1.3.1 Offer antibiotic therapy as soon as possible after diagnosis, and certainly within 4 hours, to patients with hospital-acquired pneumonia.

1.3.2 Choose antibiotic therapy in accordance with local hospital policy (which should take into account knowledge of local microbial pathogens) and clinical circumstances for patients with hospital-acquired pneumonia.

1.3.3 Consider a 5- to 10-day course of antibiotic therapy for patients with hospital-acquired pneumonia.

Surveillance decision

This section of the guideline did not undergo surveillance. NICE are currently developing guidance in this area as part of the 'Management of Common Infections' guidelines on community-acquired pneumonia and hospital-acquired pneumonia. We will review this area again when these guidelines are published.

Areas not currently covered in the guideline

In surveillance, evidence was identified for areas not covered by the guideline. This new evidence has been considered for possible addition as a new section of the guideline.

New section considered in surveillance

Lung ultrasound to diagnose pneumonia in adults.

Surveillance decision

This section should not be added.

Lung ultrasound

2018 surveillance summary

A meta-analysis (7) of 12 studies (n = 1515) examined the diagnostic test accuracy of lung ultrasound to diagnose pneumonia in adults. The reference standard was chest x-ray or chest computed tomography. The sensitivity and specificity of lung ultrasound were 0.88 and 0.86 respectively. The pooled negative LR was 0.13 (95% CI: 0.08-0.23), the positive LR was 5.37 (95% CI: 2.76-10.43), and the diagnostic odds ratio was 65.46 (95% CI: 29.24-146.56). The area under the ROC was 0.95. Details of heterogeneity were not reported in the abstract.

Intelligence gathering

No relevant evidence was identified.

Impact statement

New evidence was identified to support the use of lung ultrasound for the diagnosis of pneumonia. The guideline does not specifically mention the preferred method for confirming diagnosis of pneumonia, but recommendation 1.2.8 does state "Put in place processes to allow diagnosis (including X-rays) and treatment of community-acquired pneumonia within 4 hours of presentation to hospital".

Chest x-rays are currently the accepted 'gold standard' for the diagnosis of pneumonia, however the original guideline committee accepted that this may not be feasible in a non-hospital setting. Although there are promising results for the diagnostic ability of lung ultrasound, there is a large amount of variability in the findings and limited information on the heterogeneity of the studies reviewed. Further evidence is needed on the benefits of lung ultrasound over chest x-ray before any impact on the guideline can be assessed. However, we will monitor this area and review at the next surveillance point.

New evidence is unlikely to change guideline recommendations.

New section considered in surveillance

Other adjunctive treatment for pneumonia.

Surveillance decision

This section should not be added.

Other adjunctive treatment

2018 surveillance summary

An RCT (8) (n = 141) examined the efficacy of adjunctive coenzyme Q10 in the treatment of elderly patients with CAP (aged over 60 years). The treatment group received oral Q10 (200mg per day) alongside antibiotics for 14 days and were compared to patients who received placebo and antibiotics. Results indicated that the coenzyme group showed significantly faster decline in fever and shorter hospital stays compared to the placebo group. The coenzyme group also experienced significantly less treatment failure. Adverse events were reported to be uncommon and similar to the placebo group, however no further details were included in the abstract.

Intelligence gathering

No relevant evidence was identified.

Impact statement

Findings from one small RCT indicate that adjunctive treatment with the coenzyme Q10 may be beneficial to elderly patients with CAP. It is uncertain whether the study had enough power to detect any meaningful differences between groups, therefore more evidence is required before the impact on the guideline can be assessed.

New evidence is unlikely to change guideline recommendations.

Research recommendations

2.1 Urine antigen testing

In moderate- to high-severity community-acquired pneumonia does using legionella and pneumococcal urinary antigen testing in addition to other routine tests improve outcomes?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

2.2 C-reactive protein guided antibiotic duration

In patients hospitalised with moderate- to high-severity community-acquired pneumonia, does using C-reactive protein monitoring in addition to clinical observation to guide antibiotic duration safely reduce the total duration of antibiotic therapy compared with a fixed empirical antibiotic course?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

2.3 Continuous positive pressure ventilation

What is the clinical effectiveness of continuous positive pressure ventilation compared with usual care in patients with community-acquired pneumonia and type I respiratory failure without a history of chronic obstructive pulmonary disease?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

2.4 Hospital-acquired pneumonia

Can rapid microbiological diagnosis of hospital‑acquired pneumonia reduce the use of extended-spectrum antibiotic therapy, without adversely affecting outcomes?

Summary of findings

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

References

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