NICE National Institute for Health and Care Excellence

2019 surveillance of neutropenic sepsis: prevention and management in people with cancer (NICE guideline CG151)

Surveillance report

Published: 7 February 2019

www.nice.org.uk

Contents

Surveillance decision

We will not update the guideline on neutropenic sepsis.

Reasons for the decision

No new evidence was identified which suggested the guideline should be updated. We did not identify any new evidence that would change or invalidate the current recommendations.

Overview of 2019 surveillance methods

NICE's surveillance team checked whether recommendations in neutropenic sepsis (NICE guideline CG151) remain up to date. The 2019 surveillance followed the static list review process, consisting of:

- Feedback from topic experts via a questionnaire.
- A search for new or updated Cochrane reviews.
- Examining related NICE guidance and quality standards and NIHR signals.
- A search for ongoing research.
- Examining the NICE event tracker for relevant ongoing and published events.
- Consulting on the proposal with stakeholders.
- Considering comments received during consultation and making any necessary changes to the proposal.

For further details about the process and the possible update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

Evidence considered in surveillance

Cochrane reviews

We searched for new Cochrane reviews related to the whole guideline. We found 13 relevant Cochrane reviews published between November 2011 and September 2018.

Antibiotic prophylaxis

The use of fluoroquinolones for the prophylaxis of neutropenic sepsis is advised in recommendations 1.2.1.1 and 1.2.1.2 in the NICE guideline. One Cochrane review (Gafter-Gvili et al. 2012) is an update to a Cochrane review first published in 2005 which was included as evidence during the development of recommendations in the original

guideline. The results of the updated Cochrane review found significant reductions in mortality with quinolone prophylaxis which supports the current recommendations in the guideline.

Recommendation 1.2.1.3 states that granulocyte colony-stimulating factor (G-CSF) should not be routinely offered for the prevention of neutropenic sepsis in adults receiving chemotherapy. Two Cochrane reviews (Renner et al. 2012 and Estcourt et al. 2015) found prophylactic colony-stimulating factors (CSFs) reduced febrile neutropenia in patients undergoing chemotherapy. However, the Cochrane authors assessed the included trials as very low quality. Although these reviews do not support recommendation 1.2.1.3, further evidence is required to confirm the results and there is no impact on the current recommendations.

In contrast, several new Cochrane reviews support the current recommendation 1.2.1. The review from Estcourt et al. 2016, suggests there is insufficient evidence to determine whether granulocyte transfusions affect all-cause mortality in people who are neutropenic. This finding is supported Mhaskar et al. 2014 who concluded that it is unclear whether a combination of CSF and antibiotics reduce the rate of infection-related mortality in people with chemotherapy induced febrile neutropenia. Two further reviews (Skoetz et al. 2015 and Hutzschenreuter et al. 2016) concluded that there was a lack of data to inform the use of G-CSF in people receiving chemotherapy.

Initial antibiotic therapy

Recommendation 1.4.3.1 advises offering beta lactam monotherapy as initial empiric antibiotic therapy and recommendation 1.4.3.2 advises not to offer aminoglycoside to patients with suspected neutropenic sepsis. In support of these recommendations, 1 review (Paul et al. 2013) found significantly lower rates of mortality, adverse events and super-infections following the use of beta lactam monotherapy compared to combination therapy with aminoglycoside.

Glycopeptide antibiotics

Recommendation 1.4.3.3 advises not offering empiric glycopeptide antibiotics to patients with suspected neutropenic sepsis who have central venous access devices. This recommendation is supported by a review (Beyar-Katz et al. 2017), which found no benefit of additional antibiotic treatment with glycopeptides and a further review (van de Wetering et al. 2013), which found no benefit of antibiotics administered prior to the insertion of a

catheter.

Switch to oral antibiotics

Recommendation 1.5.3.3 advises that after 48 hours and in patients whose risk of developing septic complications has been reassessed as low, antibiotic therapy can be switched from intravenous to oral administration. This is supported by 1 review (Vidal et al. 2013), which found no significant differences in mortality and treatment failure rates between intravenous and oral treatment for febrile neutropenia.

Hospital discharge

Recommendation 1.5.3.4 advises on the use of a scoring system and clinical judgement to determine low risk for discharge from hospital. One review (Loeffen et al. 2016) concluded that there is no evidence to suggest that early discharge from hospital is less safe in children with febrile neutropenia at low risk of bacterial infections. However, the review does not specify any criteria for determining low risk and children should still be carefully assessed before discharge.

Diet

One review (van Dalen et al. 2016) examined the use of low bacterial diets for the prevention of cancer chemotherapy related neutropenia. This was an update to a previous Cochrane review which concluded that there was no evidence to suggest that a low bacterial diet prevented infections. No new studies were identified in the updated review and the Cochrane authors could not make definitive conclusions. There are currently no recommendations in the NICE guideline on diet and this is unlikely to change at present as there is no new conclusive evidence in this area.

Ongoing research

We checked for relevant ongoing research; of the ongoing studies identified, 1 study was assessed as having the potential to change recommendations. As the study is planned to complete in May 2019, we will check the publication status regularly and evaluate the impact of the results on current recommendations as quickly as possible. This study relates to recommendation 1.5.3.3 about switching to oral antibiotics for low risk groups:

- Early switch to oral antibiotics in patients with low risk neutropenic sepsis

Intelligence gathered during surveillance

Views of topic experts

We considered the views of topic experts, including those who helped to develop the guideline. For this surveillance review, topic experts completed a questionnaire about developments in evidence, policy and services related to the NICE guideline.

There were 2 responses (out of 9 questionnaires sent) from topic experts who both stated that the guideline does not require updating. No comments or reasons were provided for their decision to not update.

Antibiotics

One topic expert highlighted concerns about the accuracy of antibiotic guidance, however, no supporting evidence was provided and evidence found during the surveillance review generally supports current recommendations.

Age groups

One topic expert highlighted concerns about the applicability of recommendations to different age groups, specifically older age and children. However, no supporting evidence was provided and no new evidence in older children was found during the surveillance review.

Rapid diagnosis

One topic expert suggested that the surveillance review should focus on rapid diagnosis and direct access oncology pathways. However, we did not find any new evidence in these areas during the surveillance review.

Outpatient treatment

Topic experts highlighted 1 study (Taplitz et al. 2018) for consideration. This is a clinical practice guideline from the US which focuses on outpatient treatment of fever and neutropenia in adults. The clinical practice guideline includes evidence that supports recommendation 1.5.2.1 on the provision of outpatient care for this population and also

suggests that the NICE guideline is generally in line with current international practice in this area.

Views of stakeholders

Stakeholders are consulted on all surveillance reviews except if the whole guideline will be updated and replaced. Because this surveillance proposal was to not update the guideline, we consulted with stakeholders.

Of the overall 4 stakeholders who commented, 3 agreed with the proposal to not update and 1 did not answer.

The comments provided by stakeholders to support their responses suggest that there is no new evidence to update the guideline.

A stakeholder commented that the guideline should consider including recommendations for standards for audit or services for screening and antibiotic treatment for neutropenic sepsis. NICE guidelines don't specifically propose audit/service standards and it is expected that these would be for local consideration and implementation. In addition, the surveillance review did not find any relevant evidence for the effectiveness of including recommendations on standards for audit or service standards.

A stakeholder commented that the guideline should be more aligned with the Sepsis Trust to reduce the risk of over treatment by improving risk scoring. However, the guideline already includes recommendations on assessing patients and the use of a validated risk scoring system to determine low risk for discharge from hospital.

A stakeholder commented that the guideline should include recommendations on the need for patient isolation and appropriate treating environments. However, detailed consideration of the environment fall outside the scope of the guideline and this review did not find any evidence in this area to impact the guideline.

A stakeholder commented that further guidance would be helpful to determine a course of treatment for children undergoing diagnosis for neutropenia. Section 1.4 of the guideline currently includes recommendations on managing suspected neutropenic sepsis before diagnosis is confirmed. These recommendations cover all populations including children.

See appendix A for full details of stakeholders' comments and our responses.

See ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual for more details on our consultation processes.

Equalities

No equalities issues were identified during the surveillance process.

Editorial amendments

During surveillance of the guideline, we did not identify any issues with the NICE version of the guideline that should be amended.

Overall decision

After considering all evidence and other intelligence and the impact on current recommendations, we decided that no update is necessary.

Paul Chrisp
Centre Director

Kay Nolan
Associate Director

Janusz Jankowski
Consultant Clinical Adviser

Judith Thornton
Technical Adviser

Omar Moreea
Technical Analyst

ISBN: 978-1-4731-3290-0