

Neutropenic Sepsis Cancer Guideline
Draft Scope Stakeholder Workshop: Group Notes

Group 1:

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General comments

The group felt that a working definition of neutropenic sepsis should be included in the opening section of the scope. The group thought the term neutropenia was more appropriate than neutropenic fever. They also considered whether 'neutropenic infection' was a better term. Sometimes a patient can get sepsis without displaying signs of a fever. The group suggested looking at the relationship between neutropenia and temperature. A fever is defined as $>37.1^{\circ}\text{C}$ and $<34^{\circ}\text{C}$.

The group noted that there was a published consensus definition of sepsis.

One member of the group reported that The Surviving Sepsis Campaign guidelines are now well established and are being implemented across the country. The group discussed how this guideline can fit with the NICE guideline framework. The group thought that these patients should ultimately be treated by oncologists.

The group noted that we do not know what happens across the country for this population of patients and a needs assessment to support the guideline would be welcomed.

The patient should be referred immediately to secondary or tertiary care. The group commented that primary care does not usually see these patients but they should still be given information on signs and symptoms.

Hopefully the patient will present in secondary care at either:

1. Acute medical units (AMU)/emergency department (ED)
2. General medical ward
3. Cancer centre

The group suggested that these patients should go straight to the ED, all be treated in the first hour with antibiotics and then be separated onto appropriate pathways.

However, the group noted that chemotherapy is often given in the community. The AMU see a lot of non-cancer patients who are immunosuppressed and this group should be excluded from the scope.

There are guidelines already in place which deal with treating bacterial infections.

Population

The group agreed with the population section.

Healthcare setting

The group agreed with the content for this section.

Clinical issues that will be covered

- a) The signs and symptoms in people with suspected neutropenic sepsis which necessitate referral to secondary care.

The group agreed that this was an important question, but queried who is supposed to recognise the signs and symptoms. The patients and carers need educating but there is also a need for the GPs to be educated. The group again emphasised that 'neutropenic sepsis' needed defining in the guideline, with a list of signs and symptoms.

- b) The emergency assessment in the secondary care setting of a person with suspected neutropenic sepsis.

The Surviving Sepsis Campaign and other guidelines on how to treat bacterial infections would be useful for this topic.

This is a very complicated issue for junior doctors and possibly nurses too. The issue of resources was also raised as a potential issue for this topic.

- c) Appropriate investigations of suspected infection in a neutropenic patient in secondary care.
 - a. Definition of neutropenia and fever.
 - b. Routine investigations (for example, chest radiography, urine culture, throat swabs, peripheral blood cultures).

The Group were happy with the composition of this topic.

- d) Risk stratification and management of suspected bacterial infection
 - a. Use of clinically applied risk stratification scores or algorithms.
 - b. Use of ambulatory versus inpatient management.

The group discussed issues for patients living in isolation and for those patients who were taking a 'holiday' from their medication. Resource implications were also considered for ambulatory versus inpatient management.

- c. Use of oral, intravenous monotherapy or intravenous dual antibiotic therapy

Clarity would be needed as to when, where and what for administration of antibiotic therapy

- d. Switching from intravenous to oral antibiotic therapy.
- e. Management of unresponsive fever (excluding fungal infection)

The group queried whether we should exclude fungal infections but agreed this would only account for a small number of patients and so should probably be excluded from the scope.

- f. Duration of empiric antibiotic therapy.
- g. Duration of inpatient care.

No changes were suggested.

- e) Primary and secondary prophylaxis in people at risk of neutropenic sepsis during anti-cancer treatment.

The group thought the generally agreed definitions of prophylaxis are important and therefore needed to be included in the guideline.

- a. Use of primary prophylaxis with growth factors (e.g. granulocyte colony stimulating factor) and/or antibiotics (e.g. fluoroquinolones).

The group thought that risk assessment should be included here as well. The following should also be considered: dietary requirements, dental care, follow-up, and supportive care during chemotherapy. The group noted that there is wide variation in follow up arrangements for this group of patients and risk categories should be assigned.

- b. Use of secondary prophylaxis with growth factors and/or antibiotics.

No changes were suggested.

- f) Management of central venous catheters in chemotherapy patients with neutropenia or neutropenic sepsis.

The group thought that this topic should exclude aspects of good general medical care practice, specifically related to the patient with bacterial infection. The group discussed whether this should be management of 'chronic' or 'acute' central venous catheters.

- a. Role of empiric glycopeptide antibiotics in patients with central lines.
- b. Indications for removal of central lines.

No changes were suggested.

- g) Information and support for patients/carers on the identification of neutropenic sepsis.

The group suggested replacing identification with alarm signals/triggers.

- h) Information and support for patients/carers on choices in alternative management strategies.

The group thought that sometimes a patient/carer is given an excess of information. It was also suggested that this topic was already covered elsewhere and should be removed from the scope.

- i) Training of healthcare professionals on the identification and management of neutropenic sepsis.

No changes were suggested.

The following additional topics were suggested by the group as a high-priority issue that needs investigating in the guideline:

- j) Complications of antibiotics for *c. difficile*.
- k) The effect of neutropenic sepsis on subsequent chemotherapy.

Clinical issues that will not be covered

- a) Prophylaxis, investigation and management of non-bacterial infection.
- b) Investigation and management of graft versus host disease.
- c) Treatment of specific bacterial infections (e.g. bacterial pneumonia).
- d) Intensive care management of severe sepsis.

The group thought this list was exhaustive.

Main outcomes

- e) Mortality rate
- f) Morbidity (e.g. renal impairment)
- g) Hospitalisation rates and the length of hospital stay
- h) Recurrence rate

Instead of 'recurrence' use 'response' rate

- i) Time to treatment of neutropenic sepsis

Time of antibiotics administered rather than time to treatment of neutropenic sepsis.

- j) Health-related quality of life assessments (or surrogates, such as 'acceptability' or 'preference')

GDG membership

- Medical oncologist
- Clinical oncologist
- Paediatric haematologist/oncologist
- Adult haematologist
- GP
- Community Nurse
- Adult inpatient nurse
- Paediatric inpatient nurse
- Chemotherapy nurse
- Microbiologist
- PCT /cancer network commissioning representative
- General physician in a medical admission unit

The group suggested this reads ‘... in a acute medical unit’

- Pharmacist

The following additional GDG members were suggested by the group:

- An Emergency Physician from an ED (based within a DGH and not within a Cancer Centre)
- Clinical Nurse Specialist or Key Worker
- One of the patient/carer members should be a parent of/or a teenager with cancer
- One of the patient/carer members should be someone from the Surviving Sepsis Campaign

Potential expert advisers to attend relevant GDG meetings:

- Bone marrow transplant
- Pharmacist
- Radiologist
- Front line – NHS direct/paramedic

The following additional expert advisers were suggested by the group:

- AMU and ED representatives (preferably from a non-oncologist centres)

Group 2:

Dr Bob Phillips
Dr Paul Beckett
Mr Ravi Chana
Dr Effie Grand
Cathy Hughes
Elaine Lennan
Eric Low

Dr H McDowell
Dr Julia Chisholm

Victoria Titshall
Claire Turner
Judith Thornton
Dr Karen Francis

Population

The group discussed that non-cancer patients were outside the remit from the DoH, and that this should be addressed in the background text of the final guideline.

Clinical issues that will be covered

- j) The signs and symptoms in people with suspected neutropenic sepsis which necessitate referral to secondary care.

The group agreed that this was a high priority topic as there is large variation in practice. The group discussed that although patients are told who to contact if they have a fever, many are contacting their GP or NHS direct instead, and are therefore not getting to secondary care as timely as they should (this was especially so for adult patients). Currently patients are told to go straight to secondary care if they suspect neutropenic sepsis.

- k) The emergency assessment in the secondary care setting of a person with suspected neutropenic sepsis.

The group agreed that this was a high priority topic as there is currently poor communication between departments.

- l) Appropriate investigations of suspected infection in a neutropenic patient in secondary care.
a. Definition of neutropenia and fever.

The group agreed that this was a high priority topic.

- b. Routine investigations (for example, chest radiography, urine culture, throat swabs, peripheral blood cultures).

The group suggested this list was not exhaustive and could include new technologies such as PCR.

- m) Risk stratification and management of suspected bacterial infection
a. Use of clinically applied risk stratification scores or algorithms.

This topic was not discussed by group 2.

b. Use of ambulatory versus inpatient management.

The group would like to see the PICO outcome include patient choice.

c. Use of oral, intravenous monotherapy or intravenous dual antibiotic therapy

d. Switching from intravenous to oral antibiotic therapy.

e. Management of unresponsive fever (excluding fungal infection)

The group thought this topic would include Granulocyte colony Stimulating Factors.

f. Duration of empiric antibiotic therapy.

g. Duration of inpatient care.

The group thought this would be different for all patients but agreed that there is a huge health economic impact associated with this if duration guidelines could be more defined.

n) Primary and secondary prophylaxis in people at risk of neutropenic sepsis during anti-cancer treatment.

a. Use of primary prophylaxis with growth factors (e.g. granulocyte colony stimulating factor) and/or antibiotics (e.g. fluoroquinolones).

b. Use of secondary prophylaxis with growth factors and/or antibiotics.

The group commented that there is large variation in practice and affects lots of patients.

o) Management of central venous catheters in chemotherapy patients with neutropenia or neutropenic sepsis.

The group suggested that the wording was changed to include 'in those who already have central lines'.

a. Role of empiric glycopeptide antibiotics in patients with central lines.

b. Indications for removal of central lines.

The group thought this topic was a high priority for paediatric patients.

p) Information and support for patients/carers on the identification of neutropenic sepsis.

The group discussed whether this topic could be combined with topic a. As topic a is about what the signs are and this topic is about how to educate patients on the signs it was agreed they were two separate topics.

q) Information and support for patients/carers on choices in alternative management strategies.

The group suggested deleting this question as it is thought more of an implementation issue, there is not always a choice for patients and where there is it only affects a small number of patients. The group noted that the guideline would not remove the need for clinical judgement. The group thought it was more important to prevent neutropenic sepsis.

- r) Training of healthcare professionals on the identification and management of neutropenic sepsis.

The group suggested that the wording was changed to include 'in primary, secondary and tertiary care'.

The following additional topic was suggested by the group as a high-priority issue that needs investigating in the guideline:

- l) Impact on delay in receiving antibiotic treatment.

The group questioned whether faster recovery was related to the timing of receiving antibiotic treatment and patients carrying packs may be one way to reduce delay. The group discussed patients with meningitis who receive antibiotic treatment before diagnosis, and how patients in countries such as Pakistan and Australia are given antibiotics to carry with them so that they can be taken either before they reach an emergency department or to reduce the delay in treatment at the emergency department.

Clinical issues that will not be covered

- k) Prophylaxis, investigation and management of non-bacterial infection.
l) Investigation and management of graft versus host disease.
m) Treatment of specific bacterial infections (e.g. bacterial pneumonia).
n) Intensive care management of severe sepsis.

The following additional topics were suggested by the group as issues that the guideline could not cover:

- o) Handling of central lines and prophylaxis of central line infections.
p) Management of FBC's.

These topics were considered not specific to neutropenic sepsis and are more appropriate for a chemotherapy wide guideline.

GDG membership

- Medical oncologist
- Clinical oncologist
- Paediatric haematologist/oncologist
- Adult haematologist

- GP
- Community Nurse

The group suggested this was not needed for adult patients but would be for paediatric patients.

- Adult inpatient nurse
- Paediatric inpatient nurse
- Chemotherapy nurse
- Microbiologist
- PCT /cancer network commissioning representative
- General physician in a medical admission unit
- Pharmacist

The following additional GDG members were suggested by the group:

- ED physician

Potential expert advisers to attend relevant GDG meetings:

- Bone marrow transplant
- Pharmacist
- Radiologist
- Front line – NHS direct/paramedic

Group 3:

Dr John Graham
Dr Emma de Winton
Dr John Grainger
Phillipa Jones
Tim Mephram
Rachel Morgan
Catherine Oakley

Mrs Jane Whittome
Beryl Roberts
Nathan Bromham
Barbara Meredith
Francis Ruiz
Bernadette Li

Population

In groups that will be covered section 4.1.1.a, Group 3 suggested removing “with cancer” to include patients without cancer but who are receiving anti-cancer treatment (for example those with Thalassaemia or certain bone marrow disorders).

Clinical issues that will be covered

- s) The signs and symptoms in people with suspected neutropenic sepsis which necessitate referral to secondary care.

The group were interested in educating patients about signs and symptoms of neutropenic sepsis, but recognised the overlap with topics g and i. The group also commented that referral might be to tertiary care in some cases.

The group raised the issue of risk factors for the development of neutropenic sepsis and suggested changing the topic to “The signs and symptoms in people at risk of neutropenic sepsis which necessitate referral to secondary care.”

- t) The emergency assessment in the secondary care setting of a person with suspected neutropenic sepsis.

The group pointed out that secondary care should not be narrowly defined – as patients may present to various places: for example wards or Accident and Emergency departments.

- u) Appropriate investigations of suspected infection in a neutropenic patient in secondary care.
a. Definition of neutropenia and fever.
b. Routine investigations (for example, chest radiography, urine culture, throat swabs, peripheral blood cultures).

The group suggested changing wording to “Routine and specific investigations...”

- v) Risk stratification and management of suspected bacterial infection
a. Use of clinically applied risk stratification scores or algorithms.

The group noted that risk stratification could be an ongoing process during the management of a patient with neutropenic sepsis and overlapped with subtopics b to g. It could be difficult to separate risk stratification from treatment in the following topics.

- b. Use of ambulatory versus inpatient management.

The issue of ambulatory versus in-patient care for patients with neutropenic sepsis was discussed as a possible economic priority.

- c. Use of oral, intravenous monotherapy or intravenous dual antibiotic therapy
- d. Switching from intravenous to oral antibiotic therapy.
- e. Management of unresponsive fever (excluding fungal infection)

The group wanted the guideline to address the assessment of fungal infection but not necessarily its management.

- f. Duration of empiric antibiotic therapy.
- g. Duration of inpatient care.

The group suggested restructuring the topic d subtopics c to g into a topic about the appropriate use of antibiotics. The three main parts of this new topic would be:

- Initial choice of antibiotic treatment (incorporating intravenous versus oral antibiotics and ambulatory versus inpatient care)
- The management of unresponsive patients
- The de-escalation of antibiotic therapy (incorporating the duration of treatment and switching from IV to oral antibiotics).

- w) Primary and secondary prophylaxis in people at risk of neutropenic sepsis during anti-cancer treatment.
 - a. Use of primary prophylaxis with growth factors (e.g. granulocyte colony stimulating factor) and/or antibiotics (e.g. fluoroquinolones).

The group identified the prophylactic use of granulocyte stimulating factor as expensive and of unknown cost-effectiveness.

- b. Use of secondary prophylaxis with growth factors and/or antibiotics.

The group suggested that granulocyte infusions could be included as an intervention for secondary prophylaxis.

- x) Management of central venous catheters in chemotherapy patients with neutropenia or neutropenic sepsis.
 - a. Role of empiric glycopeptide antibiotics in patients with central lines.
 - b. Indications for removal of central lines.

- y) Information and support for patients/carers on the identification of neutropenic sepsis.

The group wanted to add education to this topic. Support could include active follow up of patients at risk – for example by telephone.

- z) Information and support for patients/carers on choices in alternative management strategies.

- aa) Training of healthcare professionals on the identification and management of neutropenic sepsis.

The group wanted to add communication to this topic: both between healthcare professionals and between healthcare professionals and patients/carers.

Clinical issues that will not be covered

- q) Prophylaxis, investigation and management of non-bacterial infection.
r) Investigation and management of graft versus host disease.
s) Treatment of specific bacterial infections (e.g. bacterial pneumonia).
t) Intensive care management of severe sepsis.

GDG membership

- Medical oncologist
- Clinical oncologist
- Paediatric haematologist/oncologist
- Adult haematologist
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- Community Nurse
- Adult inpatient nurse
- Paediatric inpatient nurse
- Chemotherapy nurse
- Microbiologist
- PCT /cancer network commissioning representative
- General physician in a medical admission unit
- Pharmacist

The following additional GDG members were suggested by the group:

- Accident and emergency nurse

Potential expert advisers to attend relevant GDG meetings:

- Bone marrow transplant
- Pharmacist
- Radiologist

- Front line – NHS direct/paramedic