NICE National Institute for Health and Care Excellence

NICE guideline

COVID-19 rapid guideline: haematopoietic stem cell transplantation

NICE guideline
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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

Overview

The purpose of this guideline is to maximise the safety of patients who need haemopoietic stem cell transplantation and make the best use of NHS resources, while protecting staff from infection.

On **29 July 2020**, we amended recommendations on advice and testing for COVID-19 for patients and donors, and removed recommendations on deferring treatment for some patients to reflect changes in the risk of infection and the capacity in services. See update information for details.

Follow the usual professional guidelines, standards and laws (including those on equalities, safeguarding, communication and mental capacity), as described in making decisions using NICE guidelines.

This guideline is for:

- health and care practitioners
- health and care staff involved in planning and delivering services
- commissioners
- donor registries.

It covers haemopoietic stem cell transplantation in adults, children and young people.

The recommendations bring together:

- existing national and international guidance and policies
- advice from specialists working in the NHS from across the UK. These include people with expertise and experience of treating patients for the specific health conditions covered by the guidance during the current COVID-19 pandemic.

We developed this guideline using the interim process and methods for developing rapid guidelines on COVID-19 in response to the rapidly evolving situation. We will review and update the recommendations as the knowledge base develops using the interim process and methods for guidelines developed in response to health and social care emergencies.

1 Communicating with patients and minimising risk

1.1 Communicate with patients, their families and carers and support their mental wellbeing, signposting to charities and support groups (including NHS volunteers) where available, to help alleviate any anxiety and fear they may have about COVID-19.

1.2 Minimise face-to-face contact by:

- offering telephone or video consultations whenever possible
- cutting non-essential face-to-face follow up
- using alternative ways of delivering medicines, such as postal services, NHS volunteers, or drive-through pick-up points
- coordinating access to blood tests for post-transplant investigations.

1.3 Ask patients to attend appointments with limited family or carers in line with the hospital policy, or alone if they can, to reduce the risk of contracting or spreading the infection. Families and carers who do not physically attend should still be involved in appointments (using telephone or video whenever possible) to ensure the patient is fully supported. **[amended 29 July 2020]**

1.4 Before patients attend the transplant centre, tell them about the measures in place to keep them safe, as well as any steps they need to take. **[29 July 2020]**

1.5 Minimise time in the waiting area by:

- careful scheduling
- encouraging patients not to arrive early
- texting patients when you are ready to see them, so that they can wait in their car, for example.

1.6 When patients with known or suspected COVID-19 have been identified, follow

appropriate UK government guidance on infection prevention and control. This includes recommendations on patient transfers, transport and options for outpatient settings.

1.7 All healthcare workers involved in receiving, assessing and caring for patients who have known or suspected COVID-19 should follow UK government guidance on infection prevention and control. This contains information on using personal protective equipment (PPE), including visual and quick guides for putting on and taking off PPE.

2 Patients with new symptoms of COVID-19

2.1 Advise all patients to contact their dedicated transplant programme helpline (rather than NHS 111) if they feel unwell to ensure their symptoms are appropriately assessed.

2.2 Be aware that patients having haematopoietic stem cell transplantation are immunocompromised and may have atypical presentations of COVID-19. Also, symptoms of COVID-19, neutropenic sepsis and viral pneumonitis may be difficult to differentiate at initial presentation.

2.3 If patients have fever (with or without respiratory symptoms), suspect neutropenic sepsis because this can be rapid and life-threatening, and follow the NICE guideline on neutropenic sepsis, which recommends:

- referring patients with suspected neutropenic sepsis immediately for assessment in secondary or tertiary care
- treating suspected neutropenic sepsis as an acute medical emergency and offering empiric antibiotic therapy immediately.

2.4 If COVID-19 is later diagnosed in a patient not isolated from admission or presentation, follow UK government guidance on management of exposed healthcare workers and patients in hospital settings. **[amended 1 June 2020]**

2.5 If a patient not previously known or suspected to have COVID-19 shows new symptoms suggestive of COVID-19, the general advice is to follow UK government guidance on investigation and initial clinical management of possible cases. This includes information on testing and isolating patients.

3 Transplant recipients pre-transplant

Patients not known to have COVID-19

3.1 Advise patients that for at least 2 weeks before having haematopoietic stem cell transplantation (HSCT), they should follow the professional advice from their clinical team on how best to minimise their risk of respiratory infections (including COVID-19). Guidance for clinicians and patients to support risk assessments is available on the BSBMTCT website. **[amended 29 July 2020]**

3.2 Test patients for respiratory viruses, including COVID-19:

- up to 7 days before admission and
- on admission before starting conditioning if local testing turnaround times allow. If not, ensure that a test result is available from within the 72 hours before conditioning. **[amended 29 July 2020]**

3.3 Defer allogeneic HSCT for 3 weeks if possible if the patient has been in close contact with somebody with COVID-19 within the last week.

Patients known or suspected to have COVID-19

3.4 Test any patients with symptoms of COVID-19 for respiratory viruses including COVID-19 and follow UK government guidance on investigation and initial clinical management of possible cases.

3.5 Defer HSCT by at least 3 months in patients who test positive for COVID-19, except patients who have a high risk of disease progression, morbidity or mortality.

3.6 For patients who test positive for COVID-19 and have a high risk of disease progression, morbidity or mortality, defer HSCT until they no longer show symptoms and have 3 repeated negative PCR tests, at least 1 week apart.

3.7 Patients who test positive for, or are suspected of having, COVID-19 should undergo repeat echocardiography, pulmonary function tests and chest X-ray

before starting treatment. **[29 July 2020]**

4 Transplant donors

Donors not known to have COVID-19

4.1 Advise related donors that for at least 4 weeks before donating, they should follow relevant parts of government advice on social distancing (this differs across the UK). **[amended 29 July 2020]**

4.2 Tell donors about the clinical signs and symptoms of COVID-19, transmission risks and related donation restrictions, because this will inform any decision to self-defer from donating.

4.3 For donors who are self-isolating, have previously self-isolated or have been in close contact with someone with COVID-19, defer donations by at least 4 weeks from the first day of isolation.

4.4 For cryopreservation donations, test stem cell donors for COVID-19 at the medical assessment and again at harvest of stem cells or donor lymphocytes.

4.5 If donors get a positive test result for COVID-19 on the day of donation, after cryopreservation of cells, the recipient and clinical team should make a shared decision over the use of these cells, taking into account the risks and the availability of alternative donor cells. Record the decisions in the patient record and confirm them to the patient in writing. **[29 July 2020]**

4.6 If, in exceptional circumstances, fresh cell donations are needed, test for COVID-19:

- at the medical assessment and
- again before conditioning, ensuring that a test result is available within the 72 hours before the start of conditioning. See recommendation 8.11. **[amended 29 July 2020]**

4.7 Tell donors to contact the coordinating registry and the collection centre at which they donated if they develop any illness within 2 weeks after donating.

Donors known or suspected to have COVID-19

4.8 For donors who test positive for COVID-19, defer donations by 3 months from when their symptoms resolve. In line with JPAC, if less than 3 months have passed since testing positive and donation is urgent, refer to a designated clinical support officer for risk assessment. **[amended 29 July 2020]**

4.9 If haematopoietic stem cell transplantation (HSCT) is urgent and there are no suitable available donors, assess risk and liaise with the registry. Alternative sources of haematopoietic stem cells, such as HLA mismatched (haplo-identical) family members and cord blood, may be available. Discuss the options with the recipient and make sure they are kept informed of the donor situation.

4.10 Explain to donors with known or suspected COVID-19 that they should not provide other blood products (including lymphocytes) for at least 28 days from when their symptoms resolve. **[amended 29 July 2020]**

5 Transplant recipients post-transplant

5.1 Ensure that patients are managed in strict protective isolation. Assess the need for any procedures outside of isolation against the risk of exposing the patient to COVID-19.

5.2 Tell patients who have had haematopoietic stem cell transplantation (HSCT) to follow the professional advice from their clinical team on how best to minimise their risk of respiratory infections (including COVID-19). Guidance for clinicians and patients to support risk assessments is available on the BSBMTCT website. **[amended 29 July 2020]**

5.3 Isolate patients who have tested positive for COVID-19 in negative pressure cubicles, or neutral pressure cubicles if this is not possible.

6 Supporting staff, including staff who are self-isolating

6.1 If a healthcare professional needs to self-isolate, ensure that they can continue to help by:

- enabling telephone or video consultations and attendance at multidisciplinary team meetings
- identifying patients who are suitable for remote monitoring and follow up and those who are vulnerable and need support
- carrying out tasks that can be done remotely, such as entering data.

6.2 Staff who test positive for or have symptoms of COVID-19 should self-isolate and not return to working directly with haematopoietic stem cell transplantation patients until they:

- show no signs of fever for 1 week **and**
- test negative for COVID-19.

Staff can return to work in other clinical areas after self-isolating in line with UK government guidance (COVID-19) on management of staff and exposed patients or residents in health and social care settings. **[amended 29 July 2020]**

6.3 Staff should participate in screening programmes for asymptomatic COVID-19 to ensure that services can minimise potential transmission. Prioritise HSCT programme staff for hospital COVID-19 screening programmes. **[29 July 2020]**

6.4 Support staff to keep in touch as much as possible, to support their mental wellbeing.

6.5 Provide all staff with visible leadership and supportive messaging, to maintain morale.

6.6 Take account of the information on the NHS Employers website about good partnership working and issues to consider when developing local plans to

combat COVID-19.

7 Prioritising treatment

7.1 Use table 1 to help assess the risks and benefits for patients having haematopoietic stem cell transplantation (HSCT). Take into account:

- the balance of risks posed by their disease compared with the post-HSCT risks of becoming seriously ill from COVID-19
- the risk of needing critical care support and risk of disease relapse
- service capacity issues, such as limited resources (workforce, facilities, intensive care, equipment).

Table 1 Prioritising treatment for patients having haematopoietic stem cell transplantation

Priority level	Categorisation based on treatment intent and risk:benefit ratio of treatment
1	Urgent HSCT procedures where delaying the procedure presents a high risk of disease progression, morbidity or mortality. This group will include consideration of: • high cure fraction or other clinical and long term effectiveness.
2	HSCT procedures where there is risk of disease progression or clinical complications if delayed significantly (as determined by the relevant multidisciplinary team): • intermediate cure fraction or effectiveness.
3	HSCT procedures where the risk of disease progression or clinical complications if significantly delayed is low (as determined by the relevant multidisciplinary team), including: • procedures where the risks associated with undertaking an HSCT procedure within the current environment are deemed to be higher than the benefits of the procedure • procedures that are not of curative intent or limited long-term effectiveness.

Adapted from the BSBMTCT recommendations for the management of adult patients and

allogeneic donors during the COVID-19 outbreak. **[amended 29 July 2020]**

7.2 Consider using transplant outcome predictive tools such as the refined disease risk index (DRI) and the haematopoietic cell transplantation-specific comorbidity index (HCT-CI), when appropriate, to inform decision-making with patients, but be aware of the limitations of these tools.

7.3 Discuss the risks, benefits and possible likely outcomes of the different treatment options with patients, families and carers using decision support tools (where available) so that they can make informed decisions about their treatment whenever possible. Communicate decisions with written documentation.

7.4 Make treatment decisions as part of a multidisciplinary team and ensure each patient is considered on an individual basis. Ensure the reasoning behind each decision is recorded.

8 Modifications to usual care

8.1 Report all cases of COVID-19 in patients having haematopoietic stem cell transplantation (HSCT) to the European Society for Blood and Marrow Transplantation prospective survey.

8.2 Think about how to modify usual care to reduce patient exposure to COVID-19 and make best use of resources (workforce, facilities, intensive care, equipment), such as by minimising in-patient and day-case admissions.

8.3 Risk assess ambulatory transplant pathways to minimise exposure to COVID-19. This review should be reflected in the quality management plans and standard operating procedures in line with NICE's guideline on haematological cancers and JACIE standards. **[29 July 2020]**

8.4 Work within clinical networks to support stem cell processing and harvesting, specialised diagnostics and cryopreservation.

8.5 Make decisions about modifications to usual care at an organisational level according to current quality management systems within the HSCT programme and other JACIE accreditation requirements. If a centre cannot meet quality standards, temporary closure is an option.

8.6 If a centre is temporarily closed, work within clinical networks to prioritise clinically urgent HSCT and transfer patients as needed. If patients are transferred:

- tell them who is in charge of their care
- ensure that they have a named key worker that they can contact with any questions, and
- take into account their practical needs, for example transport and accommodation. **[amended 29 July 2020]**

8.7 For patients having allogeneic HSCT, identify a back-up donor or cord blood unit in case there are problems with harvesting or transport.

8.8 Be aware of the availability of any planned conditioning treatments and arrange alternatives based on availability and clinical indication.

8.9 If a donor tests positive for COVID-19, assess the storage of cells for risk of cross contamination to other stored products and manage accordingly. **[amended 29 July 2020]**

8.10 Think about undertaking viability testing on cryopreserved stem cells if there is any concern about the collection, transfer or cryopreservation of cells. This includes discretionary viability testing of cell therapy products cryopreserved in laboratories not associated with the transplant centre or at the request of the transplant director. **[29 July 2020]**

8.11 Ship and cryopreserve all donations before starting conditioning, unless exceptional circumstances mean this is not possible. Cryopreserve separate graded dose aliquots of lymphocytes for potential donor lymphocyte infusions from donor stem cell harvests, when possible. Work with local processing laboratories to warn them of each donation and whether to cryopreserve or not.

8.12 For stem cell mobilisation in adults having autologous HSCT, use granulocyte-colony stimulating factor (G-CSF) alone to minimise the use of chemotherapy priming. See the BSBMTCT recommendations for the management of adult patients and allogeneic donors during the COVID-19 outbreak.

8.13 Use G-CSF mobilised peripheral blood stem cells as the primary choice of haematopoietic stem cells from adult donors, to reduce demand on theatres for bone marrow harvesting.

8.14 For children and young people under 16 years, use the most appropriate source of stem cells based on donor age, access to theatres for bone marrow harvesting, urgency of HSCT and drug licensing considerations. See the UK/ Ireland Paediatric BMT Group guidelines on prevention and management of COVID-19 in paediatric HSCT patients.

8.15 Services, including satellite units, should have separate pathways and accommodation for patients who test positive for COVID-19, to minimise the risk of COVID-19 for other patients. These should be reflected in quality management plans and standard operating procedures and should meet JACIE

standards. **[29 July 2020]**

Update information

29 July 2020: We have made changes in recommendations on:

- advice for patients to limit the number of family members who attend appointments (recommendation 1.3) and explaining measures to limit infection risk (new recommendation 1.4)
- advice for patients on minimising risk of respiratory infections before transplantation (recommendation 3.1)
- testing for respiratory viruses before transplantation (recommendation 3.2).
- additional investigations for patients who test positive for or are suspected of having COVID-19 (new recommendation 3.7)
- tests for donors and actions if the results are positive (new recommendation 4.5 and recommendation 4.6); these recommendations now apply to related donors, not just sibling donors (recommendation 4.1)
- risk assessment for donors who test positive (recommendation 4.8) and a reduction in the delay in providing blood products after a positive test (recommendation 4.10)
- advice for patients post-transplant (recommendation 5.2)
- assessing when staff who test positive or have symptons can return to work (recommendation 6.2)
- routine screening for staff (new recommendation 6.3)
- prioritising treatment (table 1)
- risk assessments for ambulatory transplant pathways (new recommendation 8.3)
- what to do when a centre is temproarily closed (recommendation 8.6)
- assessing risk in storing cells from a donor with COVID-19 (recommendation 8.9) and the viability of cryopreserved stem cells (new recommendation 8.10)
- using granulocyte-colony stimulating factor to minimise the use of chemotherapy priming.

We have also removed recommendations (originally numbered 3.3, 3.4 and 7.3) that advised deferring most autologous and allogeneic haematopoietic stem cell transplants, and deferring transplants if further treatment or immunosuppression would put then at more risk from COVID-19 in the community. This is to reflect changes in the risk of infection and the capacity in services.

Minor changes since publication

1 June 2020: We amended the cross-reference in recommendation 2.4 to link to UK government guidance on managing exposure to COVID-19 in hospital settings. We also aligned recommendation 4.1 with current government advice on social distancing.

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