

COVID-19 rapid guideline: haematopoietic stem cell transplantation

NICE guideline

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www.nice.org.uk/guidance/ng164

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.

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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. It will also enable services to match the capacity for transplantation to patient needs if services become limited because of the COVID-19 pandemic.

This guidance was first published on 1 April 2020.

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.

NICE has developed these recommendations in direct response to the rapidly evolving situation and so could not follow the standard process for guidance development. The guideline has been developed using [the interim process and methods for developing rapid guidelines on COVID-19](#). The recommendations are based on evidence and expert opinion and have been verified as far as possible. We will review and update the recommendations as the knowledge base and expert experience develops.



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 no more than 1 family member or carer, or alone if they can, to reduce the risk of contracting or spreading the infection.
- 1.4 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.
- 1.5 When patients with known or suspected COVID-19 have been identified, follow appropriate [UK government guidance on infection prevention and control](https://www.gov.uk/government/guidance/infection-prevention-and-control). This includes recommendations on patient transfers, transport and options for outpatient settings.
- 1.6 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 for health professionals](#).
- 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 [UK government guidance on shielding and protecting people defined on medical grounds as extremely vulnerable from COVID-19](#).
- 3.2 Test patients for respiratory viruses and COVID-19 at least once 72 hours before starting conditioning. See the [BSBMTCT recommendations for the management of adult patients and allogeneic donors during the COVID-19 outbreak \(March 2020\)](#).

Autologous transplant recipients

- 3.3 Defer all but exceptional cases of autologous HSCT for myeloma, low-grade lymphoproliferative diseases and non-malignant indications, with case-by-case decisions made by a multidisciplinary team, until the risks associated with the COVID-19 pandemic have passed. See the [section on prioritising treatment](#).

Allogeneic transplant recipients

- 3.4 Defer most cases of allogeneic HSCT for any non-urgent indications and chronic haematological malignancies, with case-by-case decisions made by a multidisciplinary team, until the risks associated with the COVID-19 pandemic have passed. See the [section on prioritising treatment](#).
- 3.5 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

- 3.6 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](#).

- 3.7 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.
- 3.8 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.

4 Transplant donors

Donors not known to have COVID-19

- 4.1 Advise sibling donors that for at least 4 weeks before donating, they should follow the [UK government advice on staying at home and away from others \(social distancing\)](#).
- 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 for COVID-19 at the assessment and again at harvest of stem cells or donor lymphocytes.
- 4.5 If, in exceptional circumstances, fresh cell donations are needed, test for COVID-19 at the assessment and again 1 to 2 days before starting conditioning. See [recommendation 8.9](#).
- 4.6 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

- 4.7 For donors who test positive for COVID-19, defer donations by 3 months from when their symptoms resolve.
- 4.8 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.

- 4.9 Explain to donors with known or suspected COVID-19 that they should not provide other blood products (including lymphocytes) for at least 3 months from when their symptoms resolve.

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 [UK government guidance on shielding and protecting people defined on medical grounds as extremely vulnerable from COVID-19](#) until the risks associated with the COVID-19 pandemic have passed:
- if they had an autologous HSCT within the last year
 - if they had an allogeneic HSCT within the last 2 years, or they are having continuous immunosuppressive therapy, they have chronic graft versus host disease (GvHD) or there is evidence of ongoing immunodeficiency (or for other extremely vulnerable groups based on clinical assessment).
- 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 symptoms 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 advice on households with possible coronavirus \(COVID-19\) infection](#).
- 6.3 Support staff to keep in touch as much as possible, to support their mental wellbeing.
- 6.4 Provide all staff with visible leadership and supportive messaging, to maintain morale.
- 6.5 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 allogeneic HSCT where delaying the procedure presents a high risk of disease progression, morbidity or mortality.
2	High-grade lymphomas and other urgent cases needing autologous HSCT for curative intent (for example, diffuse large B-cell lymphoma and Hodgkin lymphomas).
3	Chronic conditions including most non-malignant indications and low-risk malignant indications for allogeneic HSCT (most should be deferred until the risks associated with the COVID-19 pandemic have passed).
4	Allogeneic HSCT recipients with a relatively low predicted survival (for example, 20% to 30% at 5 years based on pre-HSCT characteristics; all but exceptional cases should be deferred until the risks associated with the COVID-19 pandemic have passed).
5	Autologous HSCT for myeloma, low-grade lymphoproliferative diseases and non-malignant indications (all but exceptional cases should be deferred until the risks associated with the COVID-19 pandemic have passed).

Adapted from the [BSBMTCT recommendations for the management of adult patients and allogeneic donors during the COVID-19 outbreak \(March 2020\)](#).

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 Consider deferring HSCT in patients with predicted poor outcomes, or if the risk from further treatment and immunosuppression would put them at more risk from COVID-19 in the community.
- 7.4 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.
- 7.5 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 Work within clinical networks to support stem cell processing and harvesting, specialised diagnostics and cryopreservation.
- 8.4 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.
- 8.5 If a centre is temporarily closed, work within clinical networks to prioritise clinically urgent HSCT and transfer patients as needed.
- 8.6 For patients having allogeneic HSCT, identify a back-up donor or cord blood unit in case there are problems with harvesting or transport.
- 8.7 Be aware of the availability of any planned conditioning treatments and arrange alternatives based on availability and clinical indication.
- 8.8 If a donor tests positive for COVID-19, cells to be used should be moved to a marker-positive tank unless they will be used within 1 month.
- 8.9 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.
- 8.10 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 \(March 2020\)](#).

- 8.11 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.
- 8.12 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 \(March 2020\)](#).

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