

Non-Hodgkin's lymphoma: diagnosis and management

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	4
Who is it for?	4
Recommendations	5
1.1 Diagnosis	5
1.2 Staging using FDG-PET-CT (fluorodeoxyglucose-positron emission tomography-CT)	6
1.3 Management of follicular lymphoma	7
1.4 Management of MALT lymphoma	10
1.5 Management of mantle cell lymphoma	12
1.6 Management of diffuse large B-cell lymphoma	13
1.7 Management of Burkitt lymphoma	15
1.8 Management of peripheral T-cell lymphoma	15
1.9 Information and support	16
1.10 Follow-up for people with diffuse large B-cell lymphoma	17
1.11 Survivorship	18
Putting this guideline into practice	20
Context	22
More information	23
Recommendations for research	24
1 Baseline FDG-PET-CT imaging for people with diffuse large B-cell lymphoma stage II or above	24
2 Factors predicting outcomes for people with high-grade transformation of follicular lymphoma	24
3 Radiotherapy in first-line treatment of diffuse large B-cell lymphoma	25

Overview

This guideline covers diagnosing and managing non-Hodgkin's lymphoma in people aged 16 years and over. It aims to improve care for people with non-Hodgkin's lymphoma by promoting the best tests for diagnosis and staging and the most effective treatments for 6 of the subtypes. Tests and treatments covered include excision biopsy, radiotherapy, immunochemotherapy and stem cell transplantation.

Who is it for?

- Healthcare professionals
- People with non-Hodgkin's lymphoma and their families and carers

Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in [your care](#).

[Making decisions using NICE guidelines](#) explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.1 Diagnosis

Type of biopsy

- 1.1.1 Consider an excision biopsy as the first diagnostic procedure for people with suspected non-Hodgkin's lymphoma at first presentation.
- 1.1.2 In people with suspected non-Hodgkin's lymphoma for whom the risk of a surgical procedure outweighs the potential benefits of an excision biopsy, consider a needle core biopsy procedure. Take the maximum number of cores of the largest possible calibre.
- 1.1.3 For people with suspected non-Hodgkin's lymphoma in whom a diagnosis is not possible after a needle core biopsy procedure, offer an excision biopsy (if surgically feasible) in preference to a second needle core biopsy procedure.
- 1.1.4 Pathology departments should ensure that tissue is conserved when handling needle core biopsies, so that further analysis can be carried out if needed.

Diagnosing B-cell lymphomas: gene testing strategies

- 1.1.5 Consider using FISH (fluorescence in situ hybridisation) to identify a *MYC* rearrangement in all people newly presenting with histologically high-grade B-cell lymphoma.
- 1.1.6 If a *MYC* rearrangement is found, use FISH to identify the immunoglobulin partner and the presence of *BCL2* and *BCL6* rearrangements.

Stratifying high-grade B-cell lymphomas using laboratory techniques

- 1.1.7 Do not use immunohistochemistry to assess the prognostic value associated with cell of origin in people with diffuse large B-cell lymphoma.
- 1.1.8 Interpret FISH results (*MYC*, *BCL2* and *BCL6* rearrangements) in the context of other prognostic factors (particularly the person's age and International Prognostic Index [IPI]).
- 1.1.9 Explain FISH results and their potential prognostic value to people with B-cell lymphoma.

1.2 Staging using FDG-PET-CT (fluorodeoxyglucose-positron emission tomography-CT)

Confirming staging

- 1.2.1 Offer FDG-PET-CT imaging to confirm staging for people diagnosed with:
- stage I diffuse large B-cell lymphoma by clinical and CT criteria
 - stage I or localised stage II follicular lymphoma if disease is thought to be encompassable within a radiotherapy field
 - stage I or II Burkitt lymphoma with other low-risk features.
- 1.2.2 For people diagnosed with other subtypes or stages of non-Hodgkin's lymphoma not listed in recommendation 1.2.1, consider FDG-PET-CT imaging to confirm staging if the results will alter management.

Assessing response to treatment for diffuse large B-cell lymphoma

- 1.2.3 Do not routinely offer FDG-PET-CT imaging for interim assessment during treatment for diffuse large B-cell lymphoma.

End-of-treatment assessment

- 1.2.4 Offer FDG-PET-CT imaging to assess response at completion of planned treatment for people with:
- diffuse large B-cell lymphoma
 - Burkitt lymphoma.
- 1.2.5 For people with other subtypes of non-Hodgkin's lymphoma not listed in recommendation 1.2.4, do not routinely offer FDG-PET-CT imaging to assess response at completion of planned treatment unless the results will alter management.
- 1.2.6 Consider FDG-PET-CT imaging to assess response to treatment before autologous stem cell transplantation for people with high-grade non-Hodgkin's lymphoma.

1.3 Management of follicular lymphoma

First-line treatment for stage IIA follicular lymphoma

- 1.3.1 Offer local radiotherapy as first-line treatment to people with localised stage IIA follicular lymphoma.
- 1.3.2 Consider 'watch and wait' (observation without therapy) as first-line treatment for people with stage IIA follicular lymphoma who are asymptomatic and for whom treatment with a single radiotherapy volume is not suitable.
- 1.3.3 Offer the same treatments that might be offered to people with advanced-stage (stages III and IV) symptomatic follicular lymphoma to people with stage IIA follicular lymphoma who are symptomatic and for whom radiotherapy is not suitable.

Treating advanced-stage asymptomatic follicular lymphoma

- 1.3.4 Offer rituximab induction therapy^[1] to people with advanced-stage (stages III and IV) follicular lymphoma who are asymptomatic.

Treating advanced-stage symptomatic follicular lymphoma

1.3.5 Rituximab, in combination with:

- cyclophosphamide, vincristine and prednisolone (CVP)
- cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP)
- mitoxantrone, chlorambucil and prednisolone (MCP)
- cyclophosphamide, doxorubicin, etoposide, prednisolone and interferon- α (CHVPi) or
- chlorambucil

is recommended as an option for the treatment of symptomatic stage III and IV follicular lymphoma in previously untreated people. [This recommendation is from [rituximab for the first-line treatment of stage III–IV follicular lymphoma](#) (NICE technology appraisal guidance 243).]

1.3.6 Rituximab maintenance therapy is recommended as an option for the treatment of people with follicular non-Hodgkin's lymphoma that has responded to first-line induction therapy with rituximab in combination with chemotherapy. [This recommendation is from [rituximab for the first-line maintenance treatment of follicular non-Hodgkin's lymphoma](#) (NICE technology appraisal guidance 226).]

The guideline committee did not assess evidence or develop recommendations on bendamustine for treating people with follicular lymphoma, because a NICE technology appraisal on 'the clinical and cost effectiveness of bendamustine in combination with rituximab within its licensed indication for the first-line treatment of advanced indolent non-Hodgkin's lymphoma' was in development. This technology appraisal is currently suspended.

Treating advanced-stage relapsed or refractory follicular lymphoma

The recommendations in this section are from [rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma](#) (NICE technology appraisal guidance 137).

1.3.7 Rituximab, within its marketing authorisation, in combination with

chemotherapy, is recommended as an option for the induction of remission in people with relapsed stage III or IV follicular non-Hodgkin's lymphoma.

- 1.3.8 Rituximab monotherapy as maintenance therapy, within its marketing authorisation, is recommended as an option for the treatment of people with relapsed stage III or IV follicular non-Hodgkin's lymphoma in remission induced with chemotherapy with or without rituximab.
- 1.3.9 Rituximab monotherapy, within its marketing authorisation, is recommended as an option for the treatment of people with relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma, when all alternative treatment options have been exhausted (that is, if there is resistance to or intolerance of chemotherapy).

Consolidation with stem cell transplantation

- 1.3.10 Offer consolidation with autologous stem cell transplantation for people with follicular lymphoma in second or subsequent remission (complete or partial) who have not already had a transplant and who are fit enough for transplantation.
- 1.3.11 Consider consolidation with allogeneic stem cell transplantation for people with follicular lymphoma in second or subsequent remission (complete or partial):
- who are fit enough for transplantation and
 - for whom a suitable donor can be found and
 - when autologous stem cell transplantation has not resulted in remission or is inappropriate (for example, because stem cell harvesting is not possible).

Treating transformed follicular lymphoma

- 1.3.12 Consider consolidation with autologous stem cell transplantation for people with transformation of previously diagnosed follicular lymphoma that has responded to treatment and who are fit enough for transplantation.
- 1.3.13 Consider consolidation with autologous or allogeneic stem cell transplantation for people with transformation of follicular lymphoma who need more than 1 line of treatment for a response and who are fit enough for transplantation.

- 1.3.14 Do not offer consolidation with high-dose therapy and autologous or allogeneic stem cell transplantation to people presenting with concurrent diagnoses of follicular lymphoma and diffuse large B-cell lymphoma that have responded to first-line treatment.

1.4 Management of MALT lymphoma

First-line treatment

Gastric MALT lymphoma: localised disease

- 1.4.1 Offer 1 or more lines of *Helicobacter pylori* eradication therapy, without any concurrent therapy, to people with *H. pylori*-positive gastric MALT lymphoma (see the NICE guideline on [gastro-oesophageal reflux disease and dyspepsia in adults](#)).
- 1.4.2 Consider *H. pylori* eradication therapy for people with *H. pylori*-negative gastric MALT lymphoma (see the NICE guideline on [gastro-oesophageal reflux disease and dyspepsia in adults](#)).
- 1.4.3 Consider 'watch and wait' (observation without therapy) for people with gastric MALT lymphoma that responds clinically and endoscopically to *H. pylori* eradication therapy but who have residual disease shown by surveillance biopsies of the stomach, unless high-risk features are present.
- 1.4.4 For people with residual MALT lymphoma after *H. pylori* eradication therapy who are at high risk of progression [*H. pylori*-negative at initial presentation or t(11:18) translocation], consider a choice of the following, in discussion with the person:
- chemotherapy (for example, chlorambucil or CVP) in combination with rituximab^[2] or
 - gastric radiotherapy.
- 1.4.5 For people with progressive gastric MALT lymphoma, offer a choice of:
- chemotherapy (for example, chlorambucil or CVP) in combination with rituximab^[2] or
 - gastric radiotherapy.

Gastric MALT lymphoma: disseminated disease

- 1.4.6 Offer *H. pylori* eradication therapy to people with disseminated *H. pylori*-positive gastric MALT lymphoma (see the NICE guideline on [gastro-oesophageal reflux disease and dyspepsia in adults](#)).
- 1.4.7 Offer chemotherapy (for example, chlorambucil or CVP) in combination with rituximab^[2] to people with disseminated gastric MALT lymphoma who need treatment; for example, people who are symptomatic or with threatened vital organ function.
- 1.4.8 Consider 'watch and wait' (observation without therapy) for people with disseminated gastric MALT lymphoma who are asymptomatic and do not have threatened vital organ function.

Non-gastric MALT lymphoma

- 1.4.9 For people with non-gastric MALT lymphoma, take into account the following before recommending any treatment:
- site of involvement and potential for organ dysfunction
 - whether it is localised or disseminated
 - the morbidity associated with any treatment proposed
 - the person's overall fitness.
- 1.4.10 Offer chemotherapy (for example, chlorambucil or CVP) in combination with rituximab^[2] to people with non-gastric MALT lymphoma for whom radiotherapy is not suitable or who have disseminated disease and need treatment.
- 1.4.11 Consider radiotherapy for people with localised disease sites of non-gastric MALT lymphoma, irrespective of stage.
- 1.4.12 Consider 'watch and wait' (observation without therapy) for people with clinically non-progressive localised non-gastric MALT lymphoma that is unlikely to result in vital organ dysfunction, who are asymptomatic and for whom radiotherapy is not suitable.

1.5 Management of mantle cell lymphoma

First-line treatment

- 1.5.1 Offer chemotherapy in combination with rituximab^[2] as first-line treatment for people with advanced-stage mantle cell lymphoma who are symptomatic. Take the person's fitness into account when deciding on the intensity of chemotherapy.
- 1.5.2 Consider cytarabine^[3]-containing immunochemotherapy for people with advanced-stage mantle cell lymphoma who are fit enough to tolerate an intensive approach.
- 1.5.3 Consider radiotherapy for people with localised stage I or II mantle cell lymphoma.
- 1.5.4 Consider 'watch and wait' (observation without therapy) until disease progression for people with clinically non-progressive mantle cell lymphoma who are asymptomatic and for whom radiotherapy is not suitable.
- 1.5.5 Bortezomib is recommended, within its marketing authorisation, as an option for previously untreated mantle cell lymphoma in adults for whom haematopoietic stem cell transplantation is unsuitable. [This recommendation is from [bortezomib for previously untreated mantle cell lymphoma](#) (NICE technology appraisal guidance 370).]

The guideline committee did not assess evidence or develop recommendations on bendamustine for treating people with mantle cell lymphoma, because a NICE technology appraisal on 'the clinical and cost effectiveness of bendamustine in combination with rituximab within its licensed indication for the first-line treatment of mantle cell lymphoma' was in development. This technology appraisal is currently suspended.

Consolidation with stem cell transplantation

- 1.5.6 Consider consolidation with autologous stem cell transplantation for people with chemosensitive mantle cell lymphoma (that is, there has been at least a partial response to induction chemotherapy) who are fit enough for transplantation.

Maintenance strategies

- 1.5.7 Consider maintenance rituximab^[4], every 2 months until disease progression, for people with newly diagnosed mantle cell lymphoma who are not fit enough for high-dose chemotherapy and where there has been a response to R-CHOP-based immunochemotherapy.
- 1.5.8 Consider maintenance rituximab^[5], every 2 months for 3 years, for people with newly diagnosed mantle cell lymphoma who are in remission after cytarabine-based induction and high-dose chemotherapy.

1.6 Management of diffuse large B-cell lymphoma

Radiotherapy in first-line treatment

- 1.6.1 Consider consolidation radiotherapy delivering 30 Gy to sites involved with bulk disease at diagnosis for people with advanced-stage diffuse large B-cell lymphoma that has responded to first-line immunochemotherapy. For each person, balance the possible late effects of radiotherapy with the possible increased need for salvage therapy if it is omitted, and discuss the options with them.

Central nervous system prophylaxis

- 1.6.2 Explain to people with diffuse large B-cell lymphoma that they have an increased risk of central nervous system lymphoma if the testis, breast, adrenal gland or kidney is affected.
- 1.6.3 Explain to people with diffuse large B-cell lymphoma that they may have an increased risk of central nervous system lymphoma if they have 2 or more of the following factors:
- elevated lactate dehydrogenase (LDH)
 - age over 60 years
 - poor performance status (ECOG score of 2 or more)
 - more than one extranodal site involved

- stage III or IV disease.

Explain that the level of risk increases with the number of factors involved.

1.6.4 Offer central nervous system-directed prophylactic therapy to people with diffuse large B-cell lymphoma:

- that involves the testis, breast, adrenal gland or kidney or
- who have 4 or 5 of the factors associated with increased risk of central nervous system relapse listed in recommendation 1.6.3.

1.6.5 Consider central nervous system-directed prophylactic therapy for people with diffuse large B-cell lymphoma who have 2 or 3 of the factors associated with increased risk of central nervous system relapse listed in recommendation 1.6.3.

Salvage therapy and consolidation with stem cell transplantation

1.6.6 Offer salvage therapy with multi-agent immunochemotherapy to people with relapsed or refractory diffuse large B-cell lymphoma who are fit enough to tolerate intensive therapy:

- explain that this is primarily to obtain sufficient response to allow consolidation with autologous or allogeneic stem cell transplantation, but is also beneficial even if not followed by transplantation
- consider R-GDP immunochemotherapy, which is as effective as other commonly used salvage regimens and less toxic.

1.6.7 Offer consolidation with autologous stem cell transplantation to people with chemosensitive diffuse large B-cell lymphoma (that is, there has been at least a partial response to chemotherapy) who are fit enough for transplantation.

1.6.8 Consider consolidation with allogeneic stem cell transplantation for people with chemosensitive diffuse large B-cell lymphoma (that is, there has been at least a partial response to chemotherapy):

- that relapses after autologous stem cell transplantation or
- in whom stem cell harvesting is not possible.

1.7 Management of Burkitt lymphoma

First-line treatment

- 1.7.1 Offer intensive immunochemotherapy to people with Burkitt lymphoma who are fit enough to tolerate it. Consider using one of the following:
- R-BFM
 - R-CODOX-M/R-IVAC
 - R-HyperCVAD (HDMTX)
 - R-LMB.
- 1.7.2 For people with low-risk Burkitt lymphoma, consider using the less intensive DA-EPOCH-R regimen supplemented with intravenous and/or intrathecal methotrexate.
- 1.7.3 Offer less intensive immunochemotherapy to people with Burkitt lymphoma who are not fit enough to tolerate intensive chemotherapy. Consider using one of the following, alone or supplemented with intravenous and/or intrathecal methotrexate:
- R-CHOP
 - R-CHEOP
 - DA-EPOCH-R.

1.8 Management of peripheral T-cell lymphoma

First-line treatment

- 1.8.1 Consider CHOP chemotherapy as first-line treatment for people with peripheral T-cell lymphoma.

Consolidation therapy

- 1.8.2 Consider consolidation with autologous stem cell transplantation for people with chemosensitive peripheral T-cell lymphoma (that is, there has been at least

a partial response to first-line chemotherapy) who are fit enough for transplantation.

1.9 Information and support

1.9.1 To help people with non-Hodgkin's lymphoma (and their family members or carers as appropriate) to make decisions about care, follow the recommendations in the NICE guidelines on [patient experience in adult NHS services, improving outcomes in haematological cancers – the manual \(patient-centred care\)](#), [improving supportive and palliative care for adults with cancer](#) and [care of dying adults in the last days of life](#). Pay particular attention to the following areas:

- establishing the best way of communicating with the person
- timing and format of information
- information about treatment, including benefits, short-term risks and late effects
- financial support and benefit advice
- fertility issues
- sexual function
- support groups
- access to wellbeing services and psychological support.

1.9.2 Give people with non-Hodgkin's lymphoma (and their family members or carers as appropriate) detailed information about the nature and purpose of diagnostic and staging tests, including:

- bone marrow biopsies
- central line insertion
- core and excision biopsies
- CT and PET-CT scans
- lumbar punctures.

- 1.9.3 If 'watch and wait' (observation without therapy) is suggested for a person with non-Hodgkin's lymphoma:
- explain to them (and their family members or carers as appropriate) about what this involves and why it is being advised
 - address any increased anxiety that results from this approach.
- 1.9.4 Explain to people with low-grade non-Hodgkin's lymphoma about the possibility of transformation to high-grade lymphoma, taking into account the person's needs and preferences. Involve family members or carers as appropriate.
- 1.9.5 Ensure that people with non-Hodgkin's lymphoma have:
- a named key worker at diagnosis and during treatment and
 - contact details for the specialist team after treatment.
- 1.9.6 Discuss exercise and lifestyle with people with non-Hodgkin's lymphoma from diagnosis onwards.

1.10 Follow-up for people with diffuse large B-cell lymphoma

- 1.10.1 For people in complete remission after first-line treatment with curative intent for diffuse large B-cell lymphoma:
- offer regular clinical assessment
 - consider stopping regular clinical assessment aimed at detecting relapse 3 years after completing treatment for people in ongoing complete remission
 - offer urgent appointments to people who experience a recurrence of lymphoma symptoms or new symptoms that suggest disease relapse
 - do not offer LDH surveillance for detecting relapse
 - do not offer routine surveillance imaging (including chest X-ray, CT and PET-CT) for detecting relapse in people who are asymptomatic.

1.11 Survivorship

- 1.11.1 Provide end-of-treatment summaries for people with non-Hodgkin's lymphoma (and their GPs). Discuss these with the person, highlighting personal and general risk factors, including late effects related to their lymphoma subtype and/or its treatment.
- 1.11.2 Provide information to people with non-Hodgkin's lymphoma when they complete treatment about how to recognise possible relapse and late effects of treatment.
- 1.11.3 At 3 years after a person with non-Hodgkin's lymphoma completes a course of treatment, consider switching surveillance of late effects of treatment to nurse-led or GP-led services.

^[1] At the time of publication (July 2016) rituximab did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Prescribing guidance: prescribing unlicensed medicines](#) for further information. The evidence reviewed for the guideline supports the standard monotherapy dosage of 4 doses of 375 mg/m² at weekly intervals.

^[2] At the time of publication (July 2016) rituximab did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Prescribing guidance: prescribing unlicensed medicines](#) for further information.

^[3] At the time of publication (July 2016) cytarabine did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Prescribing guidance: prescribing unlicensed medicines](#) for further information.

^[4] At the time of publication (July 2016) rituximab did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Prescribing guidance: prescribing unlicensed medicines](#) for further

information. The evidence reviewed for the guideline supports a dosage of 375 mg/m² every 2 months until disease progression.

^[5] At the time of publication (July 2016) rituximab did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Prescribing guidance: prescribing unlicensed medicines](#) for further information. The evidence reviewed for the guideline supports a dosage of 375 mg/m² every 2 months for 3 years.

Putting this guideline into practice

NICE has produced [tools and resources](#) to help you put this guideline into practice.

Putting recommendations into practice can take time. How long may vary from guideline to guideline, and depends on how much change in practice or services is needed. Implementing change is most effective when aligned with local priorities.

Changes recommended for clinical practice that can be done quickly – like changes in prescribing practice – should be shared quickly. This is because healthcare professionals should use guidelines to guide their work – as is required by professional regulating bodies such as the General Medical and Nursing and Midwifery Councils.

Changes should be implemented as soon as possible, unless there is a good reason for not doing so (for example, if it would be better value for money if a package of recommendations were all implemented at once).

Different organisations may need different approaches to implementation, depending on their size and function. Sometimes individual practitioners may be able to respond to recommendations to improve their practice more quickly than large organisations.

Here are some pointers to help organisations put NICE guidelines into practice:

- 1. Raise awareness** through routine communication channels, such as email or newsletters, regular meetings, internal staff briefings and other communications with all relevant partner organisations. Identify things staff can include in their own practice straight away.
- 2. Identify a lead** with an interest in the topic to champion the guideline and motivate others to support its use and make service changes, and to find out any significant issues locally.
- 3. Carry out a baseline assessment** against the recommendations to find out whether there are gaps in current service provision.
- 4. Think about what data you need to measure improvement** and plan how you will collect it. You may want to work with other health and social care organisations and specialist groups to compare current practice with the recommendations. This may also help identify local issues that will slow or prevent implementation.

5. **Develop an action plan**, with the steps needed to put the guideline into practice, and make sure it is ready as soon as possible. Big, complex changes may take longer to implement, but some may be quick and easy to do. An action plan will help in both cases.

6. For **very big changes** include milestones and a business case, which will set out additional costs, savings and possible areas for disinvestment. A small project group could develop the action plan. The group might include the guideline champion, a senior organisational sponsor, staff involved in the associated services, finance and information professionals.

7. **Implement the action plan** with oversight from the lead and the project group. Big projects may also need project management support.

8. **Review and monitor** how well the guideline is being implemented through the project group. Share progress with those involved in making improvements, as well as relevant boards and local partners.

NICE provides a comprehensive programme of support and resources to maximise uptake and use of evidence and guidance. See our [into practice](#) pages for more information.

Also see Leng G, Moore V, Abraham S, editors (2014) [Achieving high quality care – practical experience from NICE](#). Chichester: Wiley.

Context

Non-Hodgkin's lymphoma is the sixth most common cancer in the UK. There are many different subtypes of the disease, with markedly different clinical courses and requirements for therapy. Diagnosing non-Hodgkin's lymphoma and identifying the precise subtype is challenging, and optimising the diagnostic process is central to improved management. Significant improvements in our understanding of the biology of non-Hodgkin's lymphoma have contributed to improved diagnosis and also allowed for more targeted therapies.

The treatment of non-Hodgkin's lymphoma has been a beacon for the development of specific treatment strategies (now applied to many other forms of cancer), but paradoxically there is a paucity of large randomised clinical trials to define best practice in treating the various subtypes. As a consequence there are considerable differences between centres and countries in the ways in which some subtypes of the disease are diagnosed and managed.

There have been some improvements in outcome for people with non-Hodgkin's lymphoma in the last decade, but these have been relatively modest and there is still a need for improvement. This is a rapidly developing field, with a number of new therapies proving to be exciting in initial studies. It is too soon, however, to judge their long-term impact, and ongoing assessment of these new agents compared with standard therapy will be needed.

This guideline covers adults and young people (16 years and older) who are referred to secondary care with suspected non-Hodgkin's lymphoma, or who have newly diagnosed or relapsed non-Hodgkin's lymphoma. It addresses a number of areas where there is uncertainty or variation in clinical practice, in relation to diagnosing non-Hodgkin's lymphoma and management of the subtypes at different times in the course of the disease. It is not intended as a comprehensive guide to diagnosing and treating lymphomas. Topics include the best type of biopsy for diagnosis, genetic testing, the role of FDG-PET-CT imaging in staging, patient information needs and survivorship. Management of the more common subtypes is covered: that is, follicular lymphoma, MALT lymphoma, mantle cell lymphoma, diffuse large B-cell lymphoma, Burkitt lymphoma and peripheral T-cell lymphoma.

This guideline aims to facilitate standardisation of practice in treating non-Hodgkin's lymphoma. But because of the rapid development of new therapies as a result of improved understanding of the biology of the disease, continual re-evaluation will be essential.

More information

You can also see this guideline in the NICE pathway on [non-Hodgkin's lymphoma](#).

To find out what NICE has said on topics related to this guideline, see our web pages on [blood and bone marrow cancers](#) and [complications of cancer](#).

See also the guideline committee's discussion and the evidence reviews (in the [full guideline](#)), and information about [how the guideline was developed](#), including details of the committee.

Recommendations for research

The guideline committee has made the following recommendations for research.

1 Baseline FDG-PET-CT imaging for people with diffuse large B-cell lymphoma stage II or above

In people with diffuse large B-cell lymphoma stage II or above, does a baseline FDG-PET-CT scan have any advantages over a baseline CT scan in the correct interpretation of the end-of-treatment FDG-PET-CT scan?

Why this is important

A number of consensus-based guidelines and a body of clinical opinion advocate baseline FDG-PET-CT imaging as being important for interpreting end-of-treatment response using FDG-PET-CT, although there is little published evidence for this. Baseline FDG-PET-CT is also considered to have an important contribution 'over and above' that of contrast-enhanced diagnostic CT in assigning the International Prognostic Index (IPI), in terms of identifying disease stage and number of extranodal sites involved (influencing the decision to offer central nervous system prophylaxis). A prospective trial is needed to determine whether baseline FDG-PET-CT is needed to interpret end-of-treatment FDG-PET-CT and its role in assigning IPI. People with newly histologically diagnosed diffuse large B-cell lymphoma would have baseline contrast-enhanced CT, baseline FDG-PET-CT and end-of-treatment FDG-PET-CT imaging. Readers would need to be trained in both imaging techniques and be experienced members of lymphoma multidisciplinary teams. The reference standard would be histological confirmation of any positive or equivocal end-of-treatment FDG-PET-CT findings, or follow-up if there is a negative end-of-treatment scan.

2 Factors predicting outcomes for people with high-grade transformation of follicular lymphoma

In people with high-grade transformation of follicular lymphoma, which biological and clinical factors predict good outcomes with immunochemotherapy alone?

Why this is important

Before rituximab, it was accepted that high-grade transformation of follicular lymphoma to diffuse

large B-cell lymphoma portended a poor prognosis. Recent data suggest that although transformation remains an important clinical event, outcomes have improved. It is unclear which people are likely to do well with conventional treatment (such as R-CHOP) and which people may benefit from intensive treatment with, for example, high-dose therapy and autologous stem cell transplantation. Many factors are likely to influence outcome, including clinical factors (such as age, stage at transformation and extranodal involvement at transformation), radiological findings (such as early improvement of disease identified using an interim FDG-PET-CT scan) and molecular factors (such as certain driver mutations present at transformation, the presence of *MYC* translocation and response of circulating tumour DNA to treatment). A better understanding of which factors are associated with high-risk or low-risk disease would enable therapy to be tailored to the person's needs, reducing unnecessary toxicity for people at low risk and reserving intensive therapy for people at high risk. Outcomes of interest include progression-free survival and overall survival in subgroups defined by clinical factors, radiological findings and molecular analyses.

3 Radiotherapy in first-line treatment of diffuse large B-cell lymphoma

In people presenting with diffuse large B-cell lymphoma and sites of bulky disease, are outcomes improved by radiotherapy to those sites following a full course of chemotherapy?

Why this is important

The role of radiotherapy to sites of original bulky disease in treating diffuse large B-cell lymphoma is uncertain. Some clinical teams will consider radiotherapy in this setting while others will not because of concerns about morbidity and late effects of treatment. In a recent randomised trial of chemotherapy in people over 60 years old with diffuse large B-cell lymphoma, people having radiotherapy were identified and compared with a cohort having no radiotherapy. Significant improvements in event-free, progression-free and overall survival were seen in the group having radiotherapy. These results have encouraged some teams to reconsider radiotherapy for bulky diffuse large B-cell lymphoma. A definitive randomised trial is needed to address this question. Outcomes of interest include overall survival, disease-free survival, progression-free survival, treatment-related mortality, treatment-related morbidity, health-related quality of life, patient satisfaction, patient preference and overall response rate (complete or partial remission).

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Accreditation

