What happens if lymphoma relapses?

This information gives an overview of what happens if lymphoma comes back (relapses) or doesn’t respond to treatment (refractory lymphoma).

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What is relapse?

Lymphoma can sometimes come back after successful treatment. This is called ‘relapse’.

Relapse means that the lymphoma has come back after going into complete remission (no evidence of lymphoma). In the case of low-grade non-Hodgkin lymphoma (NHL), it might mean the lymphoma has flared up after being stable (staying the same) for some time.

Although a relapse can be very distressing, many people are treated successfully again.

I’m worried about relapse

It is natural to feel worried about your lymphoma relapsing. While in remission, you might find that you are more sensitive to aches, pains and other bodily sensations than you used to be. Many people feel particularly anxious in the lead up to follow-up appointments. As part of your follow-up, your doctor checks for signs of relapse.

If you are in follow-up after successful treatment for your lymphoma you should:

- attend your follow-up appointments
- ask what symptoms to look out for
- report any concerning symptoms to your doctor.

You may find it helpful to talk to your medical team about your worries. They can reassure you and help you find further information and support.

What is ‘refractory’ lymphoma?

A small number of people with lymphoma do not respond to their first course of treatment. Lymphoma that does not go into remission with treatment is known as ‘refractory’ lymphoma. Other treatments may be more successful. Refractory lymphoma is often treated in the same way as relapsed lymphoma.
Sometimes a scan part-way through treatment shows that the treatment is not working as well as was hoped. Should this be the case, you might switch to a more intensive treatment as part of your first treatment.

Rebekah was diagnosed with Hodgkin lymphoma at 18. An interim scan during treatment showed she still had lymphoma and she had to switch to a stronger chemotherapy followed by radiotherapy.

At first I felt disheartened about the lymphoma not responding well to my previous treatment. However, I think looking ahead makes the situation feel more positive.

— Rebekah
**Why does lymphoma relapse?**

There may be no evidence of lymphoma on your tests and scans after treatment. However, it is still possible that a small number of abnormal cells remain. These cells can cause a relapse.

Lymphoma treatments are usually most effective at killing fast-growing cells. Some of the slow-growing cells in low-grade lymphoma may ‘escape’ treatment. Relapse happens when these cells build up. This is why relapse is generally more likely in low-grade lymphomas.

**What happens when lymphoma relapses?**

Your lymphoma might come back where it was before or it could affect another part of your body. You might have the same symptoms as before or different symptoms. Your doctor should tell you what to look out for. Contact your medical team if you have any symptoms you are worried about between appointments. Your medical team can reassure you or they might bring your appointment forward.

If your doctor thinks you might have relapsed, you are likely to have tests, including blood tests and scans. If your lymphoma has relapsed or got worse after being stable, your doctor needs to find out how the lymphoma affects you, just as they did when you were first diagnosed.

If you have low-grade lymphoma, you might have another biopsy to check if your lymphoma has transformed (changed) into a faster-growing type. In most cases, the lymphoma won’t have transformed but it is important to find out if it has. Transformed lymphoma needs different treatment.
How is relapse treated?

Your treatment options depend on several factors, including:

- the type of lymphoma you have
- your symptoms and your test results
- your general health and any other conditions you have
- what treatment you had previously and how well your lymphoma responded to it
- how you coped with any treatment you had previously
- how long it has been since you were treated.

Treatment depends on your individual circumstances and the usual practice at your hospital. There is no standard treatment for most cases of relapsed lymphoma.

We give some detail below about relapse in Hodgkin lymphoma and high-grade NHL and low-grade NHL and outline the most likely treatment options. Our pages on different types of lymphoma give more specific information on relapse for each type.

Relapsed Hodgkin lymphoma and high-grade non-Hodgkin lymphoma

Most types of high-grade NHL and Hodgkin lymphoma are usually treated with the aim of curing the lymphoma.

Most people who go into remission (no evidence of lymphoma) stay in remission. However, some types of high-grade NHL are likely to relapse, including:

- mantle cell lymphoma
- many types of T-cell lymphoma.
A small proportion of people with other types of high-grade NHL or Hodgkin lymphoma relapse.

Relapse is more likely to happen within the first 2 years after treatment. As time goes on, relapse generally becomes less likely.

Some people don’t respond well to their first treatment (refractory lymphoma). Generally, the same treatment options are used for relapsed and refractory lymphoma.

**How might I be treated?**

Most people who relapse can have more treatment. Treatment can still be very successful.

- You are likely to be offered a more intensive treatment than your first treatment.
- Often a different type of [chemotherapy](https://www.cancer.org/cancer/lymphoma-cancer-overview/what-is-lymphoma/chemotherapy.html) is offered.
- If you are fit enough and respond to chemotherapy, a [stem cell transplant](https://www.cancer.org/cancer/lymphoma-cancer-overview/what-is-cancer/stem-cell-transplant.html) may be possible.
- [Newer drugs](https://www.cancer.org/cancer/lymphoma-cancer-overview/what-is-cancer/newer-drugs.html) are available for some people with relapsed and refractory lymphoma.

**Chemotherapy for relapsed or refractory Hodgkin or high-grade non-Hodgkin lymphoma**

If you are fit enough, you are likely to have a stronger [chemotherapy](https://www.cancer.org/cancer/lymphoma-cancer-overview/what-is-lymphoma/chemotherapy.html) regimen (combination of drugs) than your first treatment. This is sometimes called ‘salvage’ chemotherapy.

A variety of [chemotherapy regimens](https://www.cancer.org/cancer/lymphoma-cancer-overview/treatment/chemotherapy.html) can be used, often including gemcitabine or platinum drugs (eg cisplatin), for example:

- GEM-P (gemcitabine, cisplatin and methylprednisolone)
- ICE (ifosfamide, carboplatin and etoposide)
- DHAP (dexamethasone, high-dose cytarabine [Ara-C] and cisplatin [Platinol®]).
You may have to stay in hospital for your chemotherapy.

If you have a B-cell non-Hodgkin lymphoma, like diffuse large B-cell lymphoma (DLBCL) or mantle cell lymphoma, you are likely to have an antibody treatment, eg rituximab, with your chemotherapy.

If you respond to the chemotherapy, you might be offered high-dose chemotherapy and a stem cell transplant to give you the best chance of staying in remission.

People with nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) are likely to have a gentler chemotherapy regimen. NLPHL grows more slowly than classical Hodgkin lymphoma and usually responds very well to treatment.

**What is a stem cell transplant?**

Higher doses of treatment often work well. However, they also cause damage to your bone marrow to the extent that it might not be able to recover on its own.

Stem cells are special cells from the bone marrow that make normal blood cells. If your bone marrow is damaged, you might not have enough stem cells to make the blood cells you need.

A stem cell transplant allows you to have high-dose treatment by giving you healthy stem cells after the treatment. Stem cells are usually collected before high-dose chemotherapy (and sometimes radiotherapy) is given. Most people have an autologous stem cell transplant, which is where your own stem cells are collected and given back to you after the high-dose treatment.

Some people have stem cells from a donor – an ‘allogeneic’ stem cell transplant.

You are given stem cells the same way you are given a blood transfusion. They settle in your bone marrow where they start to grow and make new blood cells for your body.

Stem cell transplants take several weeks to complete. They carry risks as well as benefits, especially if you are having donor stem cells (an allogeneic stem cell transplant). They are not suitable for everyone – you need to be fit
enough for this type of treatment. If your doctors are thinking about this form of treatment for you, they will talk to you in detail about it.

What newer drugs are available?

Some newer, targeted drugs are already approved for use in relapsed high-grade NHL or Hodgkin lymphoma, including for:

- classical Hodgkin lymphoma: brentuximab vedotin and nivolumab
- systemic anaplastic large cell lymphoma (a type of T-cell lymphoma): brentuximab vedotin
- mantle cell lymphoma: ibrutinib, bortezomib, lenalidomide and temsirolimus.

Heather was diagnosed with mantle cell lymphoma in 2007 at the age of 59. She received chemotherapy with R-CHOP and R-DHAP and recovered well over the following 6 months. Her lymphoma returned twice in the next 5 years. She had FCR chemotherapy followed by radioimmunotherapy on her first relapse and lenalidomide on her second relapse. She has now been in remission for more than 4 years.
Most newer drugs are only available for certain people with relapsed or refractory lymphoma. Not all of these are funded on the National Health Service (NHS) throughout the UK, but funding indications change frequently. Newer drugs are being approved for use in lymphoma all the time. Many others are being tested in clinical trials. Ask your doctor if there is a trial you can take part in. You can also search our database at Lymphoma TrialsLink to find a trial that might be suitable for you.

**What happens if I relapse again?**

Some people experience relapse more than once. Lymphoma that’s relapsed again can still be treated. If you cannot have an autologous stem cell transplant or you have already had this treatment, you may be able to have a newer drug, possibly through a clinical trial.

Other treatment options include:

- a different chemotherapy regimen
- an allogeneic stem cell transplant
- radiotherapy, if the lymphoma is in a single location.

More treatment options are becoming available for relapsed lymphoma all the time.

Ron was first diagnosed with DLBCL in 2005 at the age of 57. He has a busy life with community activities and breeding, showing and judging championship King Charles Spaniels. Throughout all this, his lymphoma has been persistent. Ron initially had R-CHOP chemotherapy, but his lymphoma relapsed 2 years later. He has since had a variety of treatments including

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“— Heather

much from this research. Just this last year, my clinician suggested it might be valuable to have a course of maintenance rituximab and currently I am half way through this.”

— Heather
further chemotherapy, an autologous stem cell transplant, maintenance rituximab, and radiotherapy.

It has felt fairly non-stop, but on each occasion a suitable treatment was found.

— Ron

Relapsed and refractory low-grade non-Hodgkin lymphoma

Low-grade non-Hodgkin lymphomas (NHL) grow slowly. Doctors aim to control most low-grade NHLs rather than cure them. Although these lymphomas are usually considered incurable, it doesn't mean they are untreatable.
There are many good treatment options for low-grade NHL. Low-grade NHLs can often be controlled for many years. You should feel quite well when your lymphoma is under control.

While you are feeling well, you may not need treatment. Instead, you are seen regularly in the clinic and monitored carefully. This is known as ‘active monitoring’ or ‘watch and wait’. Some people may never need treatment for their lymphoma. Most people with low-grade NHL only need treatment from time to time when their lymphoma gets worse.

Treatment for low-grade NHL aims to achieve a remission.

- Complete remission – there is no evidence of lymphoma in tests and scans.
- Partial remission – the lymphoma has reduced with treatment but small amounts can still be seen on scans or in bone marrow tests.

As the range of treatment options grows and and their effectiveness improves, remissions are becoming longer. However good the remission is, low-grade NHL usually comes back or progresses (gets worse) after a quiet period of months or years. This is a relapse.

Although relapse is common, it can be very distressing. It is important to remember that relapsed low-grade NHL can be treated. Most people with low-grade NHL relapse several times and have several different treatments in the course of their illness.

**How might I be treated?**

Treatment options might include:

- ‘watch and wait’ if the lymphoma is not causing symptoms; sometimes the lymphoma shrinks again without any treatment
- radiotherapy if the lymphoma is localised to 1 or a few locations
- chemo-immunotherapy (chemotherapy with antibody therapy) – either the same regimen you’ve had before or a different regimen
- antibody therapy on its own
- radio-immunotherapy – a radioactive particle joined to an antibody; the antibody takes the radioactive particle directly to the lymphoma cells
A newer drug that is already approved in the UK and funded by the NHS for some types of relapsed and refractory low-grade NHL.

Other new treatments may be available through clinical trials.

Once their lymphoma is in remission, some people are offered maintenance antibody treatments, eg rituximab or a newer antibody like obinutuzumab. You have these treatments once every 2–3 months for up to 2 years to keep your lymphoma in remission.

If you relapse several times in a short space of time or have widespread lymphoma, your doctor might recommend a more intensive approach, such as a stem cell transplant.

If you have had a long remission before your relapse, or if your lymphoma is not widespread, you are more likely to have less intensive treatments when you relapse. You may have a period of ‘watch and wait’ before starting active treatment.

Your doctor might suggest a treatment option or discuss a range of options with you. When your doctor recommends a treatment, ask why they feel it is the best treatment for you.

What newer drugs are available for low-grade lymphoma?

Newer drugs are beginning to be used more for low-grade NHL. There are drugs already approved for use in some types of low-grade NHL:

- small lymphocytic lymphoma (SLL)/chronic lymphocytic leukaemia (CLL): ibrutinib, idelalisib, obinutuzumab, ofatumumab and venetoclax
- Waldenström’s macroglobulinaemia: ibrutinib
- follicular lymphoma: idelalisib and obinutuzumab.

Most newer drugs are only available for certain people with relapsed or refractory lymphoma and they are not all funded on the NHS throughout the UK. Newer drugs are being approved for use in lymphoma all the time. Many others are being tested in clinical trials. There are lots of clinical trials exploring chemotherapy-free treatment options for low-grade NHL. Ask your doctor if there is a trial you can take part in. You can also search our
database at **Lymphoma TrialsLink** to find a trial that might be suitable for you.

**What happens if I relapse again?**

Many people with low-grade NHL relapse more than once over the course of their illness. You are likely to receive a number of different treatments.

Linda was first diagnosed with follicular lymphoma in 2000 at the age of 46. She was first treated with chemotherapy as part of a clinical trial and went into remission. She relapsed 10 years later, in 2011, and was offered a choice of treatments. She had oral chemotherapy with chlorambucil, which kept her lymphoma under control. She had radiotherapy in 2014.

I was offered a choice of 4 treatments in 2011 and decided to keep rituximab as an option for the future. I have carried on with my life, although at a slower pace, and treasure it. I do some dog training, swimming and walk as much as I can. Exercise is a vital part of feeling well.

— Linda
You may be offered a **stem cell transplant** if you have several relapses or are considered to be at high risk of relapsing soon after treatment.

Trevor was diagnosed with follicular lymphoma in 2012 at the age of 42. Trevor has received several types of treatment including several courses of chemotherapy and chemo-immunotherapy, an **autologous stem cell transplant** using his own stem cells and in January 2016, an **allogeneic (donor) stem cell transplant**.

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We still have to wait and see what happens in the future and whether the lymphoma comes back, but for now it feels like we’ve all walked across burning coals and are on the other side.

— Sue, Trevor's wife
Transformation from low-grade to high-grade lymphoma

Sometimes low-grade NHL can transform (change) into a faster-growing lymphoma as it relapses. Low-grade NHLs are normally made up of mainly small, slow-growing cells. If the proportion of larger, faster-growing lymphoma cells increases, the lymphoma begins to behave more like a high-grade lymphoma.

Transformation can happen with any low-grade NHL, but it’s most likely with:

- follicular lymphoma
- marginal zone lymphomas (including MALT lymphomas)
- lymphoplasmacytic lymphomas (including Waldenström’s macroglobulinaemia)
- small lymphocytic lymphoma/chronic lymphocytic leukaemia (this transformation is called Richter syndrome).

Transformation is most common in follicular lymphoma, which usually transforms into diffuse large B-cell lymphoma (DLBCL). Around 2 in 100 follicular lymphomas transform each year.

Transformation can also happen in nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL), which is a slower growing form of Hodgkin lymphoma. This type of lymphoma can relapse or transform many years after it has been treated.

The symptoms that might suggest your lymphoma has transformed after a period of being slow growing or stable might include:

- a rapid increase in the size of one of your lymph nodes (glands)
- swelling of your liver or spleen
- weight loss, sweats or fever (B symptoms).

A transformed lymphoma needs to be treated in the same way as a high-grade lymphoma. You are most likely to be treated with chemotherapy together with an antibody treatment like rituximab. Your doctor might suggest a stem cell transplant if you respond well to further chemotherapy and are fit enough for this treatment.
Your feelings when lymphoma relapses

Even if you expect a relapse, you are still likely to feel disappointed and upset when it happens. Most people with high-grade NHL and Hodgkin lymphoma are treated with the intention of curing the lymphoma, so it can be a shock when the lymphoma comes back.

People react differently to relapse. It is natural to have strong and difficult feelings. For many people, the news brings back a whole range of emotions they felt when they were first diagnosed. These emotions are often no easier to cope with the second time round, even if you are aware that there are good treatments available. Some people feel frightened about having more treatment, particularly if they found treatment hard the first time.

Let your medical team know how you feel. You might find it helpful to have a friend or relative with you when you talk to your medical team. Ask all the questions you have – although definitive answers may not always be possible, your medical team are best-placed to give you information based on your individual circumstances. Learning a bit about your treatment can also help you to feel more prepared and in control.

Talking through your concerns helps you process your thoughts and lower your anxiety. You may wish to speak to a friend or relative. For some people, though, having such conversations with the people closest to them is difficult. If this is the case for you, you may like to get in touch with a member of our Information and Support Team.

If your feelings are very intense and are affecting your day-to-day life, you might also consider counselling. A counsellor is trained to offer support in coping with challenging feelings. If you are interested in counselling, ask your doctor or clinical nurse specialist if they can refer you. Alternatively, you can search for a private, registered counsellor using the British Association for Counselling & Psychotherapy’s (BACP) online search tool.
What happens if there is no further treatment for my lymphoma?

For most people, lymphoma is treatable. This is the case even if the disease comes back several times. The range of treatment options for lymphoma is improving all the time.

In some people, however, lymphoma keeps relapsing. The best treatment options might have been tried already. Together, you and your medical team decide whether to continue active treatment, taking into account how likely it is to work. You also consider the possibility of more severe side effects from stronger treatments and whether you are well enough to tolerate them.

Deciding to end active treatment is deeply emotional and personal. If there is no further treatment for your lymphoma, your medical team should continue to offer you palliative care. Although palliative care does not treat your lymphoma, it can provide relief from your symptoms. At the end of life, palliative care is given to make your final days as comfortable as possible.

Further information and support

If you would like further information or would like to talk about any aspect of your lymphoma, please call our confidential Freephone helpline on 0808 808 5555, email us on information@lymphoma-action.org.uk or Live Chat with our Information and Support team. You can find more information on relapse for each type of lymphoma on our website.

It can help to talk to people who have been through a similar experience. Our Information and Support team might be able to put you in touch with someone who has experienced relapse through our buddy scheme. You may also find our support groups helpful. You can chat to others affected by lymphoma on our online forums.

Healthtalk have a range of videos where people describe their personal experience of relapsed lymphoma.
We provide a shortlist of other organisations that offer support to people affected by cancer. There are many more. Your medical team might be able to put you in touch with local organisations that can help.

**Maggie’s Centres** offer free practical, emotional and social support to people with cancer and their families and friends. They have drop-in centres and an online centre.

**British Association for Counselling and Psychotherapy (BACP)** provides a register of accredited counsellors throughout the UK.

**Macmillan Cancer Support** provides practical, medical, emotional and financial support to people living with cancer.

**CLIC Sargent** and **Teenage Cancer Trust** offer support to children and young people affected by cancer.

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**References**

Here are some of the sources we used to prepare this information. The full list of sources is available on request. Please contact us by email at publications@lymphoma-action.org.uk or phone on 01296 619409 if you would like a copy.


Healthtalk. When lymphoma comes back. Available at: 

Further reading

- Glossary
- Types of lymphoma
- Treatment for lymphoma

Acknowledgements

- We would like to thank the Expert Reviewers and members of our Reader Panel who gave their time to review this information.

Content last reviewed: February 2017
Updated: April 2018
Next planned review: February 2020

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