Genetics in acute myeloid leukaemia (AML)

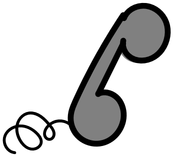
A Guide for Patients

Leukaemia Care
YOUR Blood Cancer Charity

About Leukaemia Care

Leukaemia Care is the UK's leading leukaemia charity. For over 50 years, we have been dedicated to ensuring that everyone affected receives the best possible diagnosis, information, advice, treatment and support.

Our services



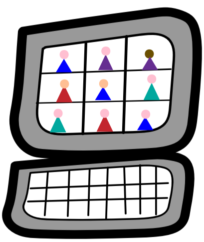
Helpline

Our helpline is available 9:00am - 5:00pm Monday - Friday. If you need someone to talk to, call **08088 010 444**.

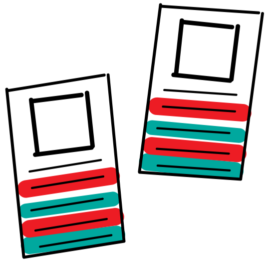
Alternatively, you can send a message via WhatsApp on **07500 068065** on weekdays 9:00am – 5:00pm.

Support Groups

Our nationwide support groups are a chance to meet and talk to other people who have been affected by an AML diagnosis. For more information about a support group local to your area, scan this QR code:



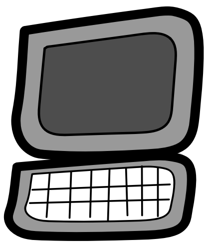
Buddy Support



We offer one-to-one phone support with volunteers who have had AML themselves or been affected by it in some way. You can speak to someone who knows what you are going through. For more information on how to get a buddy call **08088 010 444** or email support@leukaemiacare.org.uk

Online Forum

Our HealthUnlocked online forum is a place for people to ask questions anonymously or to join in the discussion with other people affected by an AML diagnosis. If you'd like to join, scan this QR code:



Webinars

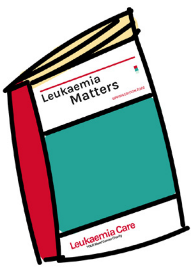
Our webinars provide an opportunity to ask questions and listen to patient speakers and medical professionals who can provide valuable information and support. For information on upcoming webinars, scan this QR code:

Advocacy and Welfare

Our advocacy and welfare officers are here to help you find the support you need for many issues surrounding an AML diagnosis. These include insurance, benefits and clinical trials. If you would like support from our advocacy or welfare officer, email advocacy@leukaemiacare.org.uk or call **08088 010 444**.

Patient magazine

Our magazine includes inspirational patient and carer stories as well as informative articles by medical professionals. To subscribe to our magazine, just scan this QR code:



Counselling Service

Our counselling service helps AML patients and their loved ones access up to six sessions of counselling. To apply, scan this QR code:

Cost of Living Fund

This fund provides grants of up to £100 for essential living costs to patients and families affected by AML. All applications must be made via the form which can be found by scanning this QR code:

Write a free will

Using our complimentary service, you can write a simple will so you know what happens to your estate when you die. Scan this QR code to start writing your free will today:

In this booklet

In compiling this booklet we are grateful to the following expert contributors: Clair Engelbrecht, Kelly Kohut and Beverley Speight. This booklet was also reviewed by patient reviewers, Martin Burr, Judy Hall and Kirsty Jamieson. We thank them all for their valuable contribution.

Financial support was provided as an Independent Medical Education Grant from Pfizer Limited. In accordance with our policies, Pfizer had no editorial input into the content.

There is a lot of information about cancer on the internet. Some of it may not be reliable or up-to-date, and much of it will not be applicable to you. Your haematology team is best placed to give you information that is specific to you because they know your individual circumstances. If you want to search for information yourself, look for reputable organisations like the NHS or national charities. Look for a quality mark, such as the Patient Information Forum (PIF) tick.

Introduction

Acute myeloid leukaemia (AML) is a fast-growing type of blood cancer that starts in blood-forming cells in your bone marrow called myeloid stem cells.

People with AML have genetic changes in their leukaemia cells. These genetic changes stop the cells working as they should, leading to abnormal cell growth and cancer. Knowing what genetic changes you have in your leukaemia cells can help your haematology team work out how best to treat you.

This booklet covers the basics of AML genetics to help you and your family understand what your test results mean. Each section has a short summary at the beginning for a quick overview. There is more detail in the section itself.

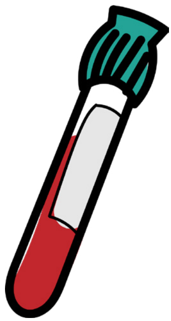
This booklet gives an overview of what you might experience. Your haematology team will give you information that is specific to you.

Throughout this booklet, you will see QR codes that will take you to webpages for further support. Open the camera app on your phone and hover it over the QR code to open the link (suitable for Android, iPhone 7 and above). If you are not able to use QR codes and would like to be sent the webpages as URLs, or you would like the list of references used for this booklet, please email information@leukaemiacare.org.uk.

We have separate booklets about AML in general, and about the different treatments you might have. Scan the QR code to see our full range of booklets about AML.

Summary: Cancer, genetics and AML

- Cancer is the **uncontrolled growth** of **abnormal cells**.
- **Changes to genes or chromosomes** play a fundamental role in the development of cancer.
- People with AML have genetic changes in their leukaemia cells. These **genetic changes stop the cells working as they should**, leading to abnormal cell growth and cancer.
- Your haematology team will test you for the genetic changes in your leukaemia cells. This helps them choose the **best treatment** for you and confirm how they expect your AML to respond.



- Most of the genetic changes in the cancer cells of people with AML occur **by chance**. These genetic changes happen during your lifetime. You do not inherit them from your parents, and you **cannot pass them on to any children**.
- Less commonly, some people with AML have genetic changes that they inherited from their parents. These changes can be passed on to children. AML due to inherited genetic changes is called **familial AML**.
- If you have an inherited genetic change, your chance of getting AML is higher than most other people. However, **having the genetic change does not mean you will definitely get AML**.

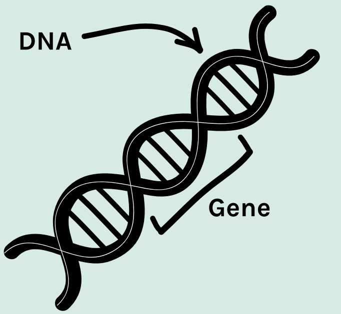
Cancer, genetics and AML

Cancer and genetics

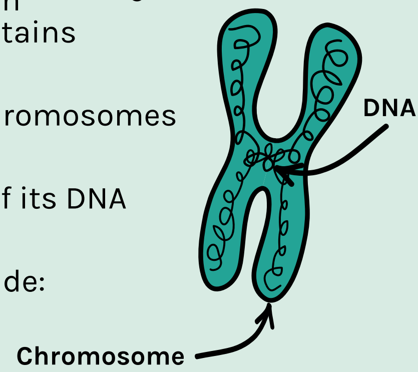
Cancer is the uncontrolled growth of abnormal cells. Certain genes tell our cells how and when to grow. If there are changes that stop these genes working properly, the cells can become abnormal and grow out of control. This leads to a cancer.

Changes to genes or chromosomes play a fundamental role in the development of AML.

About genes and chromosomes



- **Genes** are made up of **DNA**. They are the basic units of heredity. Genes provide instructions for your cells on how to make proteins needed by your body. Changes to your genes can change the proteins your cells make.
- **Chromosomes** are long, coiled strands of DNA that sit in the nucleus of each of your cells. Each chromosome contains lots of different genes.



- Humans usually have 23 pairs of chromosomes – 46 chromosomes in total.
- Changes to a chromosome or part of its DNA can affect the way the genes work.
- Changes in chromosomes can include:
  - Having extra chromosomes
  - Losing chromosomes
  - A swap of genetic material between chromosomes (called a translocation)
  - A change in the order of the DNA

Genetics in AML

We do not know the exact causes of AML. People with AML have genetic changes in their leukaemia cells that stop the cells working properly. However, in most cases, we do not know why these genetic changes occur. They can happen by chance, or they can be inherited.

- All people with AML have some genetic changes in their cancer cells that happened by chance. These genetic changes happen during your lifetime. They are not inherited. This means you did not get them from your parents, and you cannot pass them on to any children you may have.
- Some people with AML also have genetic changes they inherited from one or both of their parents. Inherited genetic changes can be passed on to future generations.

Knowing the genetic changes in your leukaemia cells can help your haematology team work out the best treatments for you. It can also help them predict how well your AML is likely to respond to treatment. If you have AML, your haematologist should send your blood or bone marrow samples for genetic testing. They will talk to you about what the results mean.

Around 86 in every 100 people with AML only have genetic changes that happened by chance.

Around 14 in every 100 people with AML have genetic changes they inherited from one or both parents, as well as genetic changes that happened by chance.

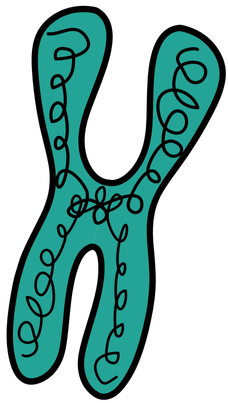
AML associated with inherited genetic changes is called familial AML because it can run in families.

Key point

People who inherit these genetic changes have a higher chance of getting AML than people without the genetic changes. However, having these changes does not mean you will definitely get AML. Some people will never get it. It is not possible to know what will happen to any one person, or when.

Summary: Genetics changes that happen by chance

- There are **many genetic changes** that can affect the way AML develops.
- In people with AML, genetic changes that happen by chance can affect either whole chromosomes or individual genes.
- There are some gene changes that are found commonly in the cancer cells of people with AML. Changes can affect more than one gene.
- Common chromosome changes found in people with AML include:
    - DNA **swapping** from **one chromosome** to another
    - DNA **swapping** from **one part** of a **chromosome** to another
    - DNA on part of a chromosome **switching order**



Genetic changes that happen by chance

People with AML have chromosome changes or gene changes in their bone marrow cells. Most of these changes have happened by chance during your lifetime. They are not due to anything you have done. These types of changes only affect some of the cells in your body. They do not affect sperm or egg cells, so they cannot be passed on to any children you may have.

Risk factors for developing genetic changes linked to AML include:

- Age: risk increases with age
- Exposure to high doses of radiation or chemicals such as benzene
- Long-term tobacco smoking
- Previous cancer treatment such as radiation therapy or chemotherapy

Your haematology team will tell you about any important genetic changes they have found. This can help with planning treatment. They will explain what your genetic changes mean for your diagnosis, treatment and outcome (prognosis).

Gene changes

Gene changes in people with AML have complicated names. They are usually named after the protein the gene codes for, or parts of it. Often these names are very long so they are shortened to their initials.

People with AML may have changes in more than one gene. Genes that often show changes in people with AML include:

- ***FLT3:*** Around 33 in every 100 people with AML have changes in this gene. They usually have treatment with a type of medicine called an *FLT3* inhibitor.

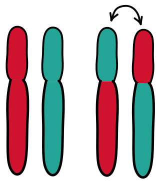
- ***NPM1:*** Around 33 in every 100 people with AML have changes in this gene. They usually respond well to treatment.
- ***IDH1/2:*** This is a family of two closely related genes. People with changes to the *IDH2* gene may respond better to treatment than people with changes in the *IDH1* gene.
- ***DNMT3A:*** Around 20 to 25 in every 100 people with AML have changes in this gene. Changes in the *DNMT3A* gene are more common in older people. How well AML responds to treatment depends on what other gene changes are found. People with *DNMT3A* changes alongside *CEBPA* or *NPM1* gene changes may respond better to treatment than people with *DNMT3A* gene changes alongside *FLT3-ITD* gene changes.
- ***ASXL1:*** Changes in this gene are much more common in people over 60. AML in people with this genetic change can be harder to treat. Knowing you have a change in this gene can help with planning treatment.
- ***RUNX1:*** Around 10 to 15 in every 100 people with AML have changes in this gene. They can happen by chance or be inherited. People with AML and *RUNX1* gene changes may not respond as well to some treatments as people with other genetic changes. Knowing about this can help with planning treatment.
- ***CEBPA:*** Changes to this gene can happen by chance or be inherited. People with AML who have changes to the *CEBPA* gene usually respond well to treatment.
- ***TP53:*** Changes to this gene affect fewer than 10 in every 100 people diagnosed with AML. They are more common in older people. AML in people with this genetic change can be harder to treat. Knowing you have a change in this gene can help with planning treatment.

If you want to know about your gene changes, ask your haematology team. They can explain what the changes are and what they mean for you.

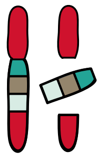
Chromosome changes

In humans, chromosomes are numbered from 1 to 23. Chromosome changes are named based on which ones they affect.

Common types of chromosome changes found in people with AML are:



- **Translocations:** This is when part of a chromosome swaps over with part of the same or a different chromosome. This results in a reordering of the genes.



- **Inversions:** This is when a chromosome breaks in two places. The broken piece of DNA is reversed and re-inserted back into the chromosome. This also results in a reordering of the genes.

The most common chromosome changes found in people with AML include:

- A translocation between chromosome 8 and chromosome 21. Scientists write this as t(8;21). This chromosome change makes two genes stick together to make an abnormal 'fusion' gene called *RUNX1-RUNX1T1*. People with this type of chromosome change generally respond well to treatment.
- A translocation between one chromosome 16 and the other. Scientists write this as t(16;16). It makes two genes stick together to make an abnormal 'fusion' gene called *CBFB-MYH11*. People with AML and this chromosome change usually respond well to treatment.
- A chromosome 16 inversion. Scientists write this as inv(16). This also makes the abnormal gene called *CBFB-MYH11*. People with AML and this chromosome change usually respond well to treatment.
- A translocation between chromosome 9 and chromosome 11. Scientists write this as t(9;11). It leads to changes in a gene called *KMT2A*. AML in people with this type of chromosome change can be harder to treat.

Summary: Inherited genetic changes

- **Genetic changes in egg or sperm cells** can be passed from parent to child. These genetic changes can be inherited.
- AML associated with inherited genetic changes is called **familial AML**.
- **People with familial AML do not inherit AML directly.** They inherit a changed gene that can increase their chance of getting it in the future.
- Inherited genetic changes can affect a number of different genes. Knowing which gene is affected can help with planning treatment.

Inherited genetic changes

Genetic changes in egg or sperm cells can be passed from parent to child. These genetic changes can be inherited.

AML associated with inherited genetic changes is called 'familial AML'.

Familial AML

Familial AML is a rare type of AML that can be passed through families.

People with familial AML do not inherit AML directly. They inherit a changed gene that can increase their chance of getting it in the future. It means they may develop AML later in life. It does not mean they will definitely get AML.

Inherited genetic changes linked to AML

Inherited genetic changes that increase the chance of getting AML are seen with the following genes:

- ***CEBPA:*** Changes to this gene can happen by chance or be inherited. An inherited change in this gene can lead to familial AML. In general, AML affects older adults. But in familial AML associated with a changed *CEBPA* gene, AML can affect younger people, including children. People with familial AML who have changes to the *CEBPA* gene usually respond well to treatment.
- ***DDX41:*** Inherited changes to this gene can increase a person's chance of developing AML and some other blood cancers. The genetic change can be passed to males or females, but males have a higher chance of getting AML. We do not know why this is. AML associated with *DDX41* usually develops in later adulthood (60s) but can affect younger people. People with familial AML who have changes to the *DDX41* gene usually have a good response to treatment.

- ***GATA2:*** Inherited changes to this gene increase a person's chance of developing AML. It is also associated with a weakened immune system and swelling caused by a build-up of fluid in the lymph system. Other health problems such as lung disease and deafness can occur.
- ***RUNX1:*** Changes to this gene can happen by chance or be inherited. People who inherit this gene change usually have low platelet levels throughout their life. They have an increased chance of getting AML and certain other blood cancers. These can occur either in childhood or later on in life. They may also have an increased chance of getting skin problems. People with AML and *RUNX1* gene changes may not respond as well to certain treatment as people with other genetic changes.
- ***ANKRD26:*** People who inherit this gene change usually have low platelet levels throughout their life. They also have a higher chance than other people of developing AML and chronic myeloid leukaemia (CML).
- ***ETV6:*** People who inherit this gene change usually have low platelet levels throughout their life. They also have a higher chance than other people of developing some blood cancers, including AML. These can develop in childhood or later in life.

The UK Cancer Genetics Group has patient leaflets about these gene changes. Scan the QR code and scroll to the section on 'haematological malignancy'.

Tests for you and your relatives

If your initial test results show you have any of these gene changes, your haematologist may recommend more tests to confirm whether they are inherited. This usually involves taking a small sample of your skin, which can be tested for inherited gene changes as it does not contain cancer cells.

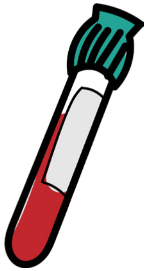
If the results of the extra tests show your genetic change is inherited, other close members of your family might also have it. This means they may have a higher chance of getting AML than people without the genetic change. It does not mean they will definitely get AML.

You should be offered genetic counselling to learn more about what this means for you and your family. You may be advised to tell close family members such as parents, adult children, brothers and sisters. They should also be offered genetic counselling to help them decide if they want to be tested for the genetic change.

If you have familial AML and you need a stem cell transplant from a family donor, they may be offered genetic testing to make sure they do not have the inherited genetic change. This is because it could affect how successful the transplant is, even if they are a 'match'. Your family member should have genetic counselling to help them decide whether to have the test.

Summary: Information for family members

- Finding out a close family member has leukaemia can be upsetting. Realising you might also have an increased chance of getting it can be a shock.
- If your family member has AML linked to an inherited genetic change, you will be offered **genetic counselling and genetic testing** to find out if you also have the genetic change.
- It is **your choice** whether or not to be tested.



- Genetic tests are usually performed using a blood sample or a small amount of saliva. Results may take several weeks to come back.
- If your tests show you do **not** have the inherited genetic change, it means you are unlikely to have a higher chance of getting AML than other people.
- If your tests show you **do** have the inherited genetic change, **it does not mean you will definitely get AML**. It means you have a higher chance of getting AML in the future than people without the genetic change.
- If you do have the inherited genetic change, you can be made aware of symptoms and signs of AML to look out for. This will make sure that if you do develop AML, you can be diagnosed early and you get the most suitable treatment promptly.
- If you do have the genetic change, you may be able to **access screening tests** to check blood counts.

Information for family members

Finding out a close member of your family has acute myeloid leukaemia (AML) can be upsetting. Discovering that you might also have a higher chance of getting it can be a shock. The emotional impact can be very distressing. You might experience a number of emotions. People react in diverse ways. It is normal to feel fear, anger and confusion.

If you need support, please contact us on our freephone helpline **08088 010 444** or email **support@leukaemiacare.org.uk**. Alternatively, scan the QR code to access our support services.

Leukaemia is a type of blood cancer. There are many different types. Acute myeloid leukaemia (AML) is a fast-growing type of blood cancer that starts in blood-forming cells in your bone marrow called myeloid stem cells.

People with AML have genetic changes in their leukaemia cells that stop the cells working the way they should. Many of these changes happen by chance during the person's lifetime and cannot be passed on to any children. However, some people with AML have inherited genetic changes. These can be passed on. Inheriting these genetic changes does not mean you will definitely get AML. It means you have a higher chance of getting it than people without the genetic changes.

If a family member has AML and their tests have found a genetic change that runs in families, you will be offered genetic counselling and genetic testing to find out if you also have it. Both medical and psychological support should be available.

Do I have to have the test?

Finding out you have a genetic change that increases your chance of getting AML can be very worrying. Some people prefer not to know, especially as they might never develop AML. It's your choice whether or not to have the test. You should be offered genetic counselling to help you decide. Talking to others in the same position can help. It can be difficult to talk to loved ones so you might prefer to talk to someone independent.

If you need support, call our freephone helpline on **08088 010 444** or email support@leukaemiacare.org.uk. Alternatively, scan the QR code to access our support services.

Why might I want to find out?

If you do have a genetic change that increases your chance of getting AML, you and your doctor can be aware of signs and symptoms of AML to look out for. This means that if you do develop AML, you may be diagnosed earlier. It can also help ensure you get the most appropriate treatment as soon as possible.

Symptoms of AML

- Pale skin
- Tiredness
- Breathlessness
- A high temperature (fever)
- Excessive sweating
- Weight loss
- Frequent infections
- Unusual and frequent bleeding, such as bleeding gums, nosebleeds or abnormal bruising
- Wounds that do not heal as quickly as usual

What does testing involve?

Genetic tests are usually done using a blood sample, or occasionally a small amount of saliva. This goes to a lab for specialised tests. Results can take several weeks to come back.

Waiting for the results can be an anxious time. If you need support, please contact us on our freephone helpline by calling **08088 010 444**.

What could the results show?

- Your test could show that you do not have the inherited genetic change. This means you are unlikely to have a higher chance than other people of getting AML.
- Your test could show that you do have the inherited genetic change. This does not mean you will definitely get AML. It means you have a higher chance of getting it than people who do not have the genetic change.

What happens then?

Knowing you have the genetic change that increases your chance of getting AML means you and your doctor can check for any symptoms or signs of leukaemia. You might also have regular blood tests. An increase in the number of your white blood cells may be a sign of AML.

If you do develop any symptoms of AML, your doctor can make sure you get the tests you need quickly. This should help you get an earlier diagnosis and start treatment as soon as possible.

If you or your partner are pregnant, or you think you might want to have children in the future, talk to your genetics doctor or genetic counsellor. They can explain your personal chance of passing on the genetic change. They can also talk to you about different testing or reproductive options you could consider.

Glossary of medical terms

Acute myeloid leukaemia (AML)

A fast-growing type of blood cancer that starts in blood-forming cells in your bone marrow called myeloid stem cells.

Bone marrow

Spongy tissue in the cavities of bones where blood cells are made.

Cancer

The uncontrolled growth of abnormal cells.

Chemotherapy

Drugs that kill cancer cells or stop them dividing and multiplying.

Chromosomes

Long, coiled strands of DNA that sit in the nucleus of your cells. Each chromosome contains lots of different genes.

DNA

The genetic code that tells your cells how to grow and behave.

Familial

A condition that may affect several members of the same family.

Gene

A section of DNA that tells your cells how to make a particular protein.

Genetic

Relating to genes.

Haematology

The branch of medicine that deals with diseases of the blood and bone marrow.

Immune system

The cells and systems in your body that protect you from infection.

Inversion

When a chromosome breaks in two places and the broken piece is reversed and goes back into the chromosome back-to-front.

Leukaemia

A group of cancers that usually start in the bone marrow and result in high numbers of abnormal blood cells.

Myeloid

Relating to bone marrow.

Platelet

A type of blood cell that helps your blood clot and stops bleeding.

Prognosis

The expected outcome of a condition in a particular person, based on their individual characteristics.

Radiation therapy

Treatment that uses high doses of radiation to kill cancer cells.

Stem cell transplant

Treatment that kills abnormal blood-forming cells in your bone marrow and replaces them with healthy ones.

Translocation

When part of a chromosome swaps over with part of the same or a different chromosome.

White blood cells

Cells that fight infections. There are several different types of white blood cell.

Useful contacts and further support

There are a number of helpful sources to support you during your diagnosis, treatment and beyond, including:

- Your haematologist and healthcare team
- Your family and friends
- Your psychologist (ask your haematologist or CNS for a referral)
- Reliable online sources, such as Leukaemia Care
- Charitable organisations

Leukaemia Care

Helpline: 08088 010 444 (Monday to Friday, 9am to 5pm)

WhatsApp: 07500 068065 (Monday to Friday, 9am to 5pm)

www.leukaemiacare.org.uk
support@leukaemiacare.org.uk

Blood Cancer UK

Leading charity into the research of blood cancers.

0808 2080 888

www.bloodcancer.org.uk

Macmillan

Provides free practical, medical and financial support for people facing cancer.

0808 808 0000

www.macmillan.org.uk

How you can help us

If you've been affected by AML, sharing your story can help others going through a similar situation and help the public to better understand.

Scan the QR to share your story:

Alternatively, you can email our Communications team at communications@leukaemiacare.org.uk.

We are continually working to make sure our information is up to date and includes everything you need to help feel supported and empowered to advocate for yourself. With this, it is important for us to listen to any feedback you might have.

After ordering one of our booklets online, please consider leaving a review. Your feedback helps us provide better information.

Alternatively, you can email our Information team at information@leukaemiacare.org.uk, call our office line on **01905 755 977** or write a letter to our Head Office at **Leukaemia Care, One Birch Court, Blackpole East, Worcester, WR3 8SG**.

If we've helped you - here's how you can give back

Fundraising is at the core of what we do here at Leukaemia Care, and without it we wouldn't be able to provide the support we do.

Fundraising isn't all about running a marathon, and there are plenty of ways to give thanks and show your support.

You could:

- Ask your local shop or workplace to host a collection tin
- Ask your place of work about charity of the year partnerships or grants
- Take on one of our more accessible walking challenges
- Host a quiz night or get your friends together for a catch-up and a meal
- Host a bake sale at work or school, or even a coffee morning with friends
- Share information about the activities we have going on to get friends and family joining in
- Stream online from the comfort of your own home

However, if you can run a marathon or want to do a thrilling skydive, we've got you covered!

Whatever you want to do, we can support you to raise money for Leukaemia Care. Get in touch with the fundraising team by email fundraising@leukaemiacare.org.uk or calling **08088 010 444**.

You can find out more about how to get involved by scanning the QR code.

Plenty of ways to give

There are so many ways you can give in support of those affected by a leukaemia diagnosis, the possibilities are endless - find one that fits you and let's get giving!

By bank transfer

You can transfer your donation straight from your account to ours. Our bank details are:

Sort code: **20-98-61**

Account number: **80823805**

Account name: **Leukaemia Care**

By cheque

Please make your cheque payable to Leukaemia Care, and then pop it in the post to: **Leukaemia Care, One Birch Court, Blackpole East, Worcester, WR3 8SG**

Online

Simply pop onto our website at www.leukaemiacare.org.uk/donate to pay your money in. Remember to include as much information as possible to help us know it's you paying in.

By phone

You can call us to pay by debit or credit card over the phone. Simply call **01905 755977**.

You can also make a donation by scanning the QR code.

Leukaemia Care is the UK's leading leukaemia charity. For over 50 years, we have been dedicated to ensuring that everyone affected receives the best possible diagnosis, information, advice, treatment and support.

Every year, 10,000 people are diagnosed with leukaemia in the UK. We are here to support you, whether you're a patient, carer or family member.

Want to talk?

Helpline: **08088 010 444**
(free from landlines and all major mobile networks)

WhatsApp: **07500 068065**

Office Line: **01905 755977**

www.leukaemiacare.org.uk

support@leukaemiacare.org.uk

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Leukaemia Care is registered as a charity in England and Wales (no. 1183890) and Scotland (no. SC049802).

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Leukaemia Care
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