Welcome to the

George Pantziarka TP53 Trust

Table of contents

Welcome to the

George Pantziarka TP53 Trust

Welcome to The George Pantziarka TP53 Trust

Dedicated to supporting families with Li Fraumeni Syndrome (LFS).

We offer practical support and advice, publish information and support research aimed at reducing the cancer risks that affect the lives of LFS families.

In this folder you will find out more about us and what we can offer, plus the following information:

- What is LFS? A summary of the condition, the implications for individual health, the outlook for the future.
- Understanding the Statistics. A look at historical bias in the data, risks of developing cancer, cancers common to LFS, the changing picture.
- Red Flags. What to look out for in adults and children with LFS; when to see a doctor.
- FAQs for Young People. Aimed at teenagers; what LFS is and isn't, looking after yourself and being proactive in your own healthcare, links to organisations that can provide information and support.
- Resources. Organisations where you can get further information, get support, find out about events, join forums and establish contact with other individuals and families, young and old, who are living with LFS.

Welcome to The George Pantziarka TP53 Trust.

Welcome to the

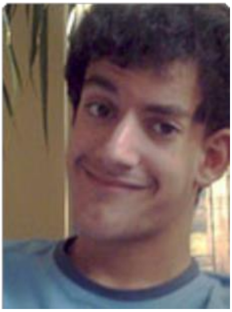
George Pantziarka TP53 Trust

First of all, a word about us

The Trust was started in 2012 by the family of George Pantziarka, a teenager from South West London who was diagnosed with LFS in 2009.

In those days, there were no national surveillance protocols, few cancer risk-reducing strategies and no organisations specifically supporting people with LFS. Basically, there was nothing to be done but try to recover from the current cancer and worry about the future possibility of another.

Knowing how devastating a diagnosis of LFS can be, George's family were determined to change the landscape.



George Pantziarka

How can the Trust help?

Each year, we host a national conference in London - which you are invited to attend free of charge. At the conference we bring together patients, families, clinicians and researchers. You can learn about the latest research advances, connect with other families, discuss important issues and talk to clinicians in an informal setting. Lunch is provided and we get together afterwards with anyone who wishes to stay.

We provide information and guidance on our website at www.tp53.co.uk, with any medical advice backed by qualified clinicians.

"Thank you everyone for making me feel welcome at my first event. Nice to meet people and the work by the medical professionals who presented is incredibly humbling - thank you for your passion and commitment."
-Lisa, 2023

"Your charity is so helpful! Your charity has really helped me."

- Aimee, 2020

Welcome to The George Pantziarka TP53 Trust.

Welcome to the

George Pantziarka TP53 Trust

What have we achieved so far?

We have campaigned for routine screening for LFS in children with cancer and for surveillance protocols to be adopted throughout the UK, including annual Whole Body MRI (WBMRI). You can find information about these on our website, or contact us for advice.

We have forged links with the medical profession and researchers and supported research that aims to be of direct benefit to people with LFS. This includes the MILI trial (Metformin in Li Fraumeni) – looking at the anti-diabetic drug metformin as cancer prevention.

We have formed a network of clinicians and researchers in LFS, to share knowledge and expertise and further improve services.

We have a begun a partnership with the University of Oxford Cancer Centre, to work together to extend and develop patient involvement in research.

How can you contact us?

You can reach out to us through our website or our Facebook page, or you can connect with us on LinkedIn and Instagram, or contact us via email.

If you'd like to speak with someone who shares similar experiences, our Trust ambassadors are available for a chat via the website.

- The George Pantziarka TP53 Trust
- The George Pantziarka TP53 Trust
- http://www.tp53.co.uk/
- georgetp53

Welcome to The George Pantziarka TP53 Trust.

A last word…

George was only diagnosed with LFS in 2009, after developing three different cancers, the first at the age of two. Tragically, George lost his battle to osteosarcoma in 2011 at the age of seventeen. A diagnosis of LFS can still be devastating, but things have changed and are continuing to change as we learn more about this condition and how to manage it more effectively.

Please do get in touch; visit our website; come to our conference; sign up for our quarterly newsletter.

We are here to support you. You are not alone.

George Pantziarka TP53 Trust

What is Li-Fraumeni Syndrome?

What is Li-Fraumeni Syndrome?

Li-Fraumeni Syndrome (LFS) is a rare cancer predisposition syndrome*. It is a genetic condition that increases the risk of getting cancer. In this sheet we will explain what LFS is, what the implications are of having it and what is being done to keep those who have it healthy.

- LFS is a genetic condition – it can be inherited from parents and passed on to children.
- Genes contain the instructions for cells to build the proteins which are needed for us to live.
- LFS is associated with a gene called TP53, which creates an anti-cancer protein called p53.

Normally, when a cell starts to become cancerous the p53 protein kicks in and stops this process so that cancer does not form. However, in people born with a fault in the TP53 gene – sometimes called a ‘mutation’ or ‘pathogenic variant’* – the protein is also faulty and cannot stop cancer developing. This means that people with LFS are at high risk of developing cancer over their lifetime.

- Sometimes a person is born with LFS without either parent having the condition. This is called ‘de novo’. It occurs when the fault in the TP53 gene happens in the foetus and not from the mum or dad.
- A person with LFS has a 50% chance of passing it onto their child.

Mostly, families with LFS have many cases of cancer in their family, across generations. In some families, no fault in the TP53 gene is detected, but they have very similar family histories of cancer. They may be given a diagnosis of LFS by their doctors if certain clinical criteria are reached.

**Cancer predisposition syndrome - A condition that means you are more likely to get cancer.*
**Pathogenic variant - Change in a gene, causing a disease e.g. cancer.*

George Pantziarka TP53 Trust

What is Li-Fraumeni Syndrome?

What does having LFS mean for my family?

If you are the first person in your family to be diagnosed with LFS, then all your first-degree relatives (parents, siblings and children) should consider being tested. It may be difficult to share this information with your relatives, but strategies for doing this will be discussed with you in detail by your cancer genetics team. Not everyone may choose to be tested, but it is important that every adult who may have the TP53 variant is informed of the risk in order to make their own decision. Decisions about testing children obviously require great care.

What does having LFS mean for my health?

LFS is not a cancer, but it increases the risk of developing it. People with LFS are prone to some types of cancer more than others, e.g. sarcomas (bone or soft tissue cancer) or early onset breast cancer. These cancers may occur in children and adolescents as well as in older adults. When a cancer develops it is diagnosed and treated, but currently there is no treatment for LFS itself.

Surveillance, also called screening, is extremely important for people with LFS, to catch cancer early so that it can be treated effectively. This means regular check-ups, including whole-body MRIs and physical examinations from childhood onwards. The management of LFS is based on a clear protocol (plan) that all people diagnosed with LFS should receive [https://www.tp53.co.uk/uk-screening-recommendations/].

Because of the high risk of breast cancer, women with LFS may be offered risk-reducing mastectomy (surgery to remove breast tissue), to lower the chance of developing breast cancer. People with LFS are also advised to live a healthy lifestyle – eat a varied diet, exercise, avoid smoking and try to reduce stress. Currently there are no studies which show that specific diets or lifestyles reduce the risk of cancer in someone with LFS.

It is important to remember not everyone with LFS becomes ill – there are some who live to old age without once getting cancer.

The future?

When you are first diagnosed with LFS you are faced with a barrage of information, particularly if you are diagnosed whilst you are being treated for cancer. LFS is rare and you may feel that you and your family are the only ones affected. But you are not alone. There is a whole community of people who have been through this and are willing and able to share.

- We are learning more about LFS and the risks for different TP53 variants. It is possible that different variants are associated with different cancer risks and types.
- Scientists are studying LFS to understand how it leads to cancer and how to reduce the risks.
- The first clinical trial is testing a drug to reduce the risk of a person with LFS getting cancer.
- There is a hive of activity involving a broad range of doctors, scientists and people with LFS to improve long-term health so that people with LFS can live unburdened by fear, worry and the threat of cancer.

Reviewed by Helen Hanson,
Consultant in Clinical Genetics.

George Pantziarka TP53 Trust

Understanding the Statistics

Before looking at the available statistics on LFS and cancer risk, it’s important to understand that the published numbers, which are widely quoted, suffer from a number of drawbacks.

Historical Data and Bias

Firstly, the statistics on cancer risk have been mostly collected from historical cases of LFS, when genetic testing was expensive and not performed routinely. Most of the people diagnosed with LFS had already suffered one or more cancers or had very strong family histories of cancer. Consequently, the cancer risk appears very high as anyone with LFS, but without cancer, would not have been counted (technically known as ascertainment bias), and it has the effect of inflating the apparent cancer risk for people with LFS. As time goes on and more people without cancer are diagnosed with LFS, it is expected that we will develop a better understanding of cancer risk for people with LFS.

Different TP53 Variants

Secondly, there are a wide range of TP53 variants in people with LFS. Some variants may be more associated with cancer risk or with specific cancer types than others. It is important to bear in mind that the statistics for LFS apply to the group as a whole and cannot be applied to any one individual or variant. Even within families that share the same TP53 variant there are differences in the types of cancer and age of diagnosis, with some affected individuals not getting cancer at all and some developing it early.

Ongoing Research and Better Understanding

Finally, it is important to be aware that our understanding of LFS is constantly expanding. We are learning much more about how different TP53 variants impact cancer risk, how cancers form and develop and how best to manage LFS. We are even exploring ways to reduce the risk of cancer ever starting. The published statistics, even when we understand ascertainment bias, can be frightening/daunting, but they do not paint the whole picture of life with LFS.

Despite this, you will see a range of figures quoted on the internet. The most commonly quoted figure is the life-time risk of developing one or more cancers by the age of 70, with a historical figure of 70% in men and 80%-90% in women (due to their increased risk of breast cancer). The risk of a second cancer is around 40%-50%. The age of cancer incidence varies, with a peak in adolescence/early adulthood.

One figure that is not in doubt is that each time a parent has a child, there is a 50% chance of passing it on. However, some people are born with LFS despite neither parent having it. Known as ‘de novo’ mutation, it occurs at conception. It is believed that between 7% - 20% of LFS cases are de novo, and they will also have a 50% chance of passing it on to their own children. If someone with LFS wants to avoid passing on a TP53 variant to children, there are options available including a type of IVF that can be used to screen embryos.

The most commonly seen cancers in people with LFS are breast, brain, soft tissue or bone sarcoma, leukaemia, and adrenocortical carcinomas, although the risk of developing any type of cancer is greater than in the general population. Currently it is not possible to say whether a given TP53 variant makes one type of cancer more likely than another. Even within families sharing the same variant, different individuals may be affected by different cancers or none at all.

Figures on average life-expectancy for LFS suffer from even greater levels of bias and are not usually listed. Again, this is because the statistics apply to historical cases – when cancer diagnosis and treatments were very different. What we can say is that even with the historical cases, there were some rare individuals with LFS who never developed a cancer and who lived a normal lifespan. Furthermore, with LFS surveillance protocols in place cancers are increasingly being caught early when they are most treatable.

Over time we fully expect that the headline statistics for cancer risks in people with LFS will change, for the better. But for now, treat the figures that are published as worse case scenarios from historical records.

Red Flags in Adults with LFS

Not every cough or twinge of pain is a signal of cancer, but it is important to monitor your own health when you have LFS. Knowing what to look for can help reduce unnecessary worries and also help to identify the real warning signs that mean you should go to the doctor. The following list is a guideline only. The fact is that you know your own body better than anyone – and if something really does not feel right then get it checked out – you have the right to be reassured. You don’t have to deal with it alone.

Red flag warnings in adults:

- Headache – persistent and often worse in the morning
- Nausea or vomiting, particularly in the morning
- Unsteady when walking, poor coordination
- Loss of appetite or unexplained weight loss
- Slurred speech
- Seizures (any type)
- Changes in vision or abnormal eye movements
- Personality change
- Excessive bruising
- Bumps or lumps that appear with no explanation or apparent cause and which do not shrink and disappear
- Joint or bone pain, swelling around joints
- Swollen tummy and/or persistent constipation (new symptoms)
- Persistent and unexplained fatigue
- Unusual bleeding or discharge, for example blood when you go to the toilet
- A chronic cough that doesn't get better or hoarse voice and sore throat that doesn't improve
- Difficulty swallowing
- Night sweats or fevers

Pan Pantziarka, reviewed by Professor Sarah Blagden, University of Oxford

Red Flags in Children with LFS

As a parent of a child with LFS it is completely normal to feel apprehensive when your child appears to be feeling unwell or under the weather. But not every off-day signals something bad. Knowing what to look for can help reduce unnecessary worries, and also help to identify the warning signs that mean you should go to the doctor. The following list is a guideline only. The fact is that you know your child better than anyone, and if something really does not feel right then get it checked out – you have the right to be reassured. And remember, you don't have to deal with this alone.

Red flag warnings in children:

- Headache – persistent and often worse in the morning
- Nausea or vomiting, particularly in the morning
- Unsteady when walking, poor coordination
- Drooling and/or difficulty swallowing
- Loss of appetite (weight loss)
- Slurred speech
- Seizures (any type)
- Changes in vision or abnormal eye movements
- Personality change
- Excessive bruising (bleeding)
- Bumps or lumps that appear with no explanation or apparent cause and which do not shrink and disappear
- Joint pain or swelling around joints (children should not have back pain or hip/pelvic pain without a clear reason/injury – and should get better within a short time)
- Swollen tummy and/or persistent constipation (new symptoms)
- Signs of puberty appearing early (infants/any child under 10-years old developing acne, hair growth, redness of the face and weight gain)

Pan Pantziarka and Dr Mette Jorgensen, Paediatric Oncologist.

George Pantziarka TP53 Trust

FAQs for Young People

When you have just been diagnosed with Li Fraumeni Syndrome (LFS), you will have lots of questions as you try to make sense of what this means for you. You are not alone; everyone with LFS goes through this at some point.

And so, we have put together some answers that we hope will help. We have also included links to some organisations that can provide further information and support.

Know also that you and your family can contact us any time if you want information or advice. Here goes!

What is LFS?

- LFS is caused by a mutation in one of your genes, called TP53 – a mutation is a bit like a spelling mistake in the instructions for making a protein (chemical) that your body needs.
- It is most likely to have been inherited from one of your parents – but sometimes it can be new, and there will be nobody else in your family affected.
- There is nothing that you have done to cause this ‘spelling mistake’.
- LFS is not the same as cancer – it’s a condition that can lead to cancer but it’s not cancer itself.
- It does not mean that you will automatically get cancer. But it does mean you are at a higher risk of cancer developing because of the faulty gene. And while cancers are common among people with LFS, some people with LFS never get cancer, despite having the TP53 mutation.

Will I always have LFS?

- LFS is a lifelong condition, but it doesn’t mean you can’t carry on with your life for example school, friends, activities.
- LFS is only one part of all the things you are.

Are there any treatments?

- There is no treatment for LFS itself, but there are lots of treatments for cancer, including new treatments being developed all the time.
- New research into LFS is being carried out so that we can learn more about how it might be possible to reverse the effects of the mutation.
- There is a clinical trial, (which is a way of testing a new treatment), that is trying to see if taking a drug everyday can lower the chances of a cancer developing in people with LFS. This trial is called MILI, and it is open to people with LFS aged 16 or over.
- Catching cancer early is essential for people with LFS, so regular scans and check-ups are important and shouldn't be skipped.

What can I do to look after myself?

- Try to eat a varied, healthy diet, to exercise and find ways to reduce stress. Keeping the body fit, healthy and strong helps us to fight all kinds of diseases, including cancer.
- Examine your body regularly for anything out of the ordinary. There is a link below, to a website that will advise on this.
- Learn to monitor your own health – you know what's normal for you and what isn't.
- Always tell someone if you do find something unusual – even if it is embarrassing. Tell a doctor or parent/carer. NEVER, NEVER ignore it and hope it will go away. It may well be nothing important, but if it is anything, it is better to catch it early.

George Pantziarka TP53 Trust

FAQs for Young People

Is there anything else I can do?

- Look after yourself generally. It's your body, your health.
- When you turn 16, you may or may not wish to be able to talk to your doctor privately. Either way, make sure you advocate for yourself, whether that's raising concerns or discussing surveillance.

What if I went through treatment for cancer as a child and I am not currently in the system for genetics?

- Don't worry – you can refer yourself to your local genetics clinic to discuss any options, concerns etc.

And remember – you are not alone! There are many people who want to help and support you, and others with LFS that you can talk to if you want.

George Pantziarka TP53 Trust

FAQs for Young People

More Information and Tips

Coppafeel

Coppafeel! Has some useful tips for young women on how to correctly check your body to keep safe.

Living LFS

Living LFS is a US organisation for people with LFS. Has lots of information on the condition, put into simple words.

Young Lives vs Cancer

Young lives vs Cancer is a UK organisation dedicated to supporting and advocating for families of young people affected by cancer in the UK.

Teenage Cancer Trust

Teenage Cancer Trust – if you or a family member is diagnosed with cancer this is a useful site to navigate the condition

The George Pantziarka TP53 Trust

The George Pantziarka TP53 Trust – that's us! The only organisation in the UK totally dedicated to people with LFS. Lots of useful info on our website!

George Pantziarka TP53 Trust

Resources

Specific information related to LFS in the UK:

The George Pantziarka TP53 Trust website provides information – as listed below – articles, blog posts and a newsletter that you can sign up to.

Specific information includes:

- Surveillance protocols
- Genetic testing
- Red Flags for GPs; a list of things to watch out for and take action on in adults and in children
- Clinical trials
- Reproductive choices, including IVF
- Double mastectomy
- Online databases of cancer drugs and clinical trials

Patient-specific information about cancer:

MyCancerNavigator; an LFS-friendly service that offers personalised, science-based information about cancer and treatments in easy-to-understand language, free of charge. www.mycancernavigator.org

Events I can take part in:

- **LFS UK** – annual, national conference run by The George Pantziarka TP53 Trust
- **LFS Awareness Day** – annual online event run by Living LFS
- **LFS Virtual support group** – quarterly online and run by Maggie's, funded by GPTP53 Trust. Contact Maggie's: 0203 982 3141 or email Maggies.royalmarsden@maggiescentres.org

Our social media

The George Pantziarka TP53 Trust

http://www.tp53.co.uk/

The George Pantziarka TP53 Trust

georgetp53

George Pantziarka TP53 Trust

Resources

Bone Cancer Research Trust

A charity dedicated to fighting primary bone cancer.

www.bcrt.org.uk

Li-Fraumeni Syndrome Association

A US organisation supporting people with LFS.

www.lfsassociation.org

Living LFS

A US charity supporting people with LFS.

www.livinglfs.org

Maggie’s

An organisation that supports people with cancer.

www.maggies.org

UK Genetics Clinics

List of UK genetics clinics.

https://tinyurl.com/2e9ckxpe

Sarcoma UK

The bone and soft tissue cancer charity.

www.sarcoma.org.uk

Coppa Feel!

Youth-focused breast cancer awareness charity.

www.coppafeel.org

Young Lives vs Cancer

An organisation that supports young cancer patients and their families.

www.younglivesvscancer.org.uk

Breast Cancer Now

A charity supporting breast cancer patients.

www.breastcancernow.org

These are places where you can find further information, get support, find out about events, join forums and establish contact with other individuals and families, young and old, who are living with LFS.

Remember – you are not alone.