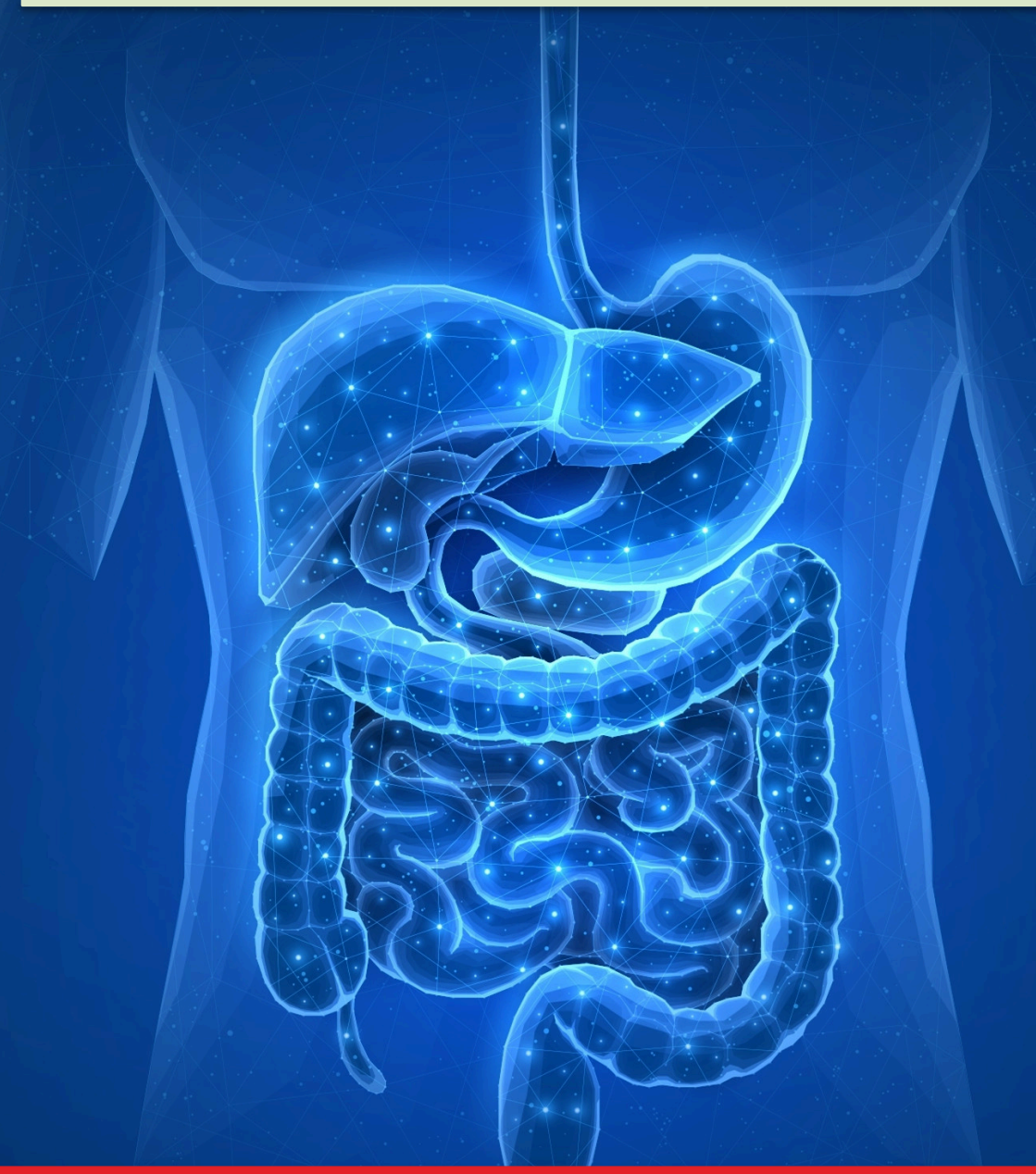
Marfan Trust
Supporting Research into Inherited Aortic and Related Disorders

Loeys Dietz

CONNECTING THE UNCONNECTED AND STRENGTHENING LIVES

# The Gastrointestinal Manifestations of Marfan & Loeys-Dietz Syndromes



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# What Are Marfan & Loeys-Dietz Syndromes?

Marfan and Loeys-Dietz syndromes are inherited genetic disorders of the body's connective tissue, affecting any gender, race or ethnic group. Connective tissue helps provide structure to the body, binding skin to muscle and muscle to bone. It also supports the internal organs.

Connective tissue is made of fine fibres and 'glue'. One fibre is called fibrillin. In Marfan syndrome (MFS), a change in the fibrillin-producing gene, fibrillin-1, means that this protein is deficient in connective tissue throughout the body, creating an unusual stretchiness and weakness of tissues. This has far-reaching implications and can affect the eyes, lungs, gut, nervous system, skeleton and, most dangerously, the cardiovascular system. Symptoms can vary widely from person to person with people experiencing mild to severe manifestations. MFS affects roughly 1 in 3,000 people which means that approximately 18,000 people in the UK have MFS. We estimate that half remain undiagnosed.

75% of patients inherit the condition whilst 25% develop it as a result of a spontaneous (new) gene change. Each child of an affected parent has a 50% chance of inheriting Marfan syndrome.

Every year, on average in the UK there are over 200 new cases of Marfan Syndrome diagnosed.

Marfan syndrome was first described by a French paediatrician, Dr Antoine Marfan, in 1896. It is caused by a change in the gene for fibrillin-1 on Chromosome 15.


Patients with Loeys-Dietz syndrome (LDS), were once thought to have Marfan syndrome, such are the similarities between the two conditions.

LDS was first described in 2005 by Drs Bart Loeys and Harry Dietz. It is caused by a variant in one of the genes in the transforming growth factor-beta signalling pathway, TGF-β. The genes that cause LDS are: TGFβR1, TGFβR2, SMAD3, TGFβ3 and TGFβ2. TGF-β is a crucial signalling pathway involved in various cellular processes, including cell growth and immune responses. It is a key player in development and tissue repair. When a gene change occurs, it has implications for many systems of the body. Whilst symptoms vary from patient to patient, with some being similar to those of Marfan syndrome, the most characteristic are: arterial tortuosity, aortic enlargement, bifid uvula, curvature of the spine, high-arched palate and over-crowded teeth.

This pamphlet is intended for patients with both Marfan and Loeys-Dietz syndromes.

Loeys-Dietz syndrome is much rarer than MFS and the incidence is currently gauged to be 1 in 100,000 although this is probably an underestimation.

# Gastrointestinal Symptoms in Marfan syndrome

Gastrointestinal (GI) disorders in the MFS/LDS population have not been well studied so far. They are not a 'characteristic trait' of MFS that is included in the Ghent nosology (the diagnostic criteria). GI problems are common in the general population and some are more common in people with connective tissue disorders. The treatments and investigations used are the same or very similar to those that would be used in the general population.

Research has demonstrated a link between connective tissue disorders and functional gastrointestinal disorders (FGIDs). A large amount of this research is in the Ehlers-Danlos populations (EDS). More work is needed in the MFS/LDS populations as these are symptoms that are often described by our members and require investigation by their medical specialists.

## What is a Functional Gastrointestinal Disorder (FGID)?

A group of disorders characterised by chronic gastrointestinal (GI) symptoms in the absence of obvious, demonstrable pathology. This means that often, despite tests and investigations some patients do not find a cause for their symptoms. There are a wide range of symptoms that can fall under this umbrella term of FGID. This list is not exhaustive:

- Irritable Bowel syndrome (IBS)
- Functional dyspepsia (pain or discomfort in the upper abdomen)
- Postprandial distress (feeling of early fullness or satiety)
- Heartburn (similar to dyspepsia, pain or discomfort behind the breastbone)
- Dysphagia (difficulty swallowing)
- Bloating
- Nausea and Vomiting
- Constipation
- Diarrhoea

More information can be found at **https://www.nhs.uk/conditions/irritable-bowel-syndrome-ibs/**

## How to Manage Symptoms

- Consult your GP if you are concerned about symptoms and ensure tests have been done to rule out any obvious cause for them
- Try changing/improving the diet, swap out unhealthy options for healthier alternatives
- Try to limit the amount of fatty, processed food that you eat
- Reduce the amount of caffeine you consume
- Try a probiotic
- Keep a food and symptoms diary to see if there are specific foods that seem to trigger your symptoms
- Stay well hydrated


You need to seek additional help from a dietician or GI specialist if dietary changes or over the counter remedies are not helping and your symptoms are affecting your quality of life and ability to carry out your daily activities. Your GP can make a referral.

Any significant change in bowel habit should be discussed with the GP who can arrange appropriate investigations. There may be structural causes for the symptoms that require treatment and these can be diagnosed with tests such as blood tests, colonoscopy, gastroscopy. This leaflet is mainly concerned with the range of symptoms that are described as Functional Gastrointestinal Disorders (FGIDs).

## Other Information

As well as the FGIDs, some rare complications, caused by issues with the structure of the bowel have been reported in MFS. These are usually reports of single cases as MFS is a rare condition and in these circumstances, it is difficult to accrue sufficient numbers of patients to find trends and attribute cause. However, it is important that doctors are aware that these conditions are reported in the MFS population as GI symptoms need to be thoroughly investigated.

- Midgut volvulus (bowel becomes twisted)
- Small bowel diverticulosis (sacs or pouches can form at weak spots in the bowel wall and cause inflammation)
- Upper gastrointestinal bleeding
- Various types of hernia

Individuals with LDS are more prone to allergies to environmental triggers and food, this can cause certain types of inflammatory GI problems, and it is important that your GI doctor knows that you have LDS when considering the possible causes of your symptoms.

## Weight

People with Marfan syndrome may experience difficulty gaining weight. This tends to be more common in younger individuals, particularly children, though the exact cause is not well understood. Similarly, those with Loeys-Dietz syndrome (LDS) can also struggle to gain weight. In LDS, however, there is a higher likelihood of food and environmental allergies, eczema, and asthma. These inflammatory conditions can increase calorie needs or interfere with calorie absorption. In some cases, nutritional supplements are recommended to help boost calorie intake, especially if surgery is planned.

## Red Flag symptoms - need to be reported to the GP for further investigation

- Bleeding from the rectum
- Weight loss of more than half a stone without trying
- Any persistent change in bowel habit (more than a month) for no obvious reason like change to diet, new medication, stress
- Persistent fevers or tiredness

## Current research

Lee et al (2019) reported results from approximately 2400 patients (around 1800 with EDS and 600 with MFS). All GI symptoms were significantly worse in EDS. In this study the prevalence of GI symptoms was around the same in MFS as in the general population. In MFS 27% patients had IBS, 25% patients had functional dyspepsia, reports of bloating were higher in MFS than in EDS (16.8% v 12.4%. Women with MFS experienced all types of FGID more commonly than men with MFS.

Inayet et al (2018) looked at 90 patients with MFS/EDS and 90 controls. When the results from MFS/EDS were combined and compared to the controls, nearly all the GI symptoms were more prevalent in the group with connective tissue disorder. When just the MFS group were compared to controls the only symptom that was significantly more common was that of abdominal pain.

Scoones (2016) looked at 270 patients and compared MFS to controls. In this study, 40% of MFS patients reported IBS symptoms as compared to 15% of controls.

## References

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# How you can help

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