ST MARK'S HOSPITAL FOUNDATION

A future free from the fear of bowel disease

How St Mark's Hospital & St Mark's Hospital Foundation are combatting bowel disease

Successes, contributions and impact of our research

Foreword from the Clinical Director of St Mark's Hospital and the Chairman of St Mark's Hospital Foundation

St Mark's Hospital in London is at an exciting stage in its development as the UK's national bowel hospital for the treatment of complex diseases requiring an especially high level of expertise and specialism.

More than 60% of the patients treated at St Mark's are referred by other UK hospitals. Our national reach is well established. The expertise that exists at St Mark's is primarily built on innovative research that drives clinical improvements and the development of new services.

In this brochure, we are delighted to share details of some of the research programmes at St Mark's, which include:

- HIPEC, a novel way to deliver chemotherapy at the time of surgery for advanced cancer patients.
- BiCyCLe, a programme to boost a person's immune system to fight cancer.
- PERFECTS, a project which aims to narrow the UK-wide skills gap in CT colonography or 'virtual colonoscopy' through a training and accreditation programme.
- PROGRESS, a project which is trying to understand why some polyps (growths) become cancerous, with a view to being able to personalise bowel cancer screening and surveillance in the future.

You will also read about promising new treatments for people with Inflammatory Bowel Disease (IBD), and our ground-breaking Surgical Robotics Research Programme which aims to take surgery for colorectal and anorectal cancers, inherited cancer syndromes and IBD to a new level.

Pushing the frontiers of treatment for complex bowel diseases requires philanthropic funders willing to invest in exciting, transformational research. After reading this brochure, we hope you will intensify your support or will wish to join us in a partnership to create a future free from the fear of bowel disease.

Professor Omar Faiz
Clinical Director
St Mark's Hospital

Sir Tom Troubridge
Chairman
St Mark's Hospital Foundation

Professor Omar Faiz

Sir Tom Troubridge

ST MARK'S HOSPITAL FOUNDATION

A future free from the fear of bowel disease

Table of Contents

Section 1

History of St Mark's and why fighting bowel disease is so important

St Mark's Hospital #1 in the world

In 1835, St Mark's Hospital opened in London as the world's first specialist bowel disease hospital for the relief of poor people affected by bowel disease. Nothing like St Mark's had existed before.

St Mark's is an extraordinary hospital, with extraordinary people. One of its first governors was the author, Charles Dickens, who donated ten guineas in gratitude to the hospital following successful treatment for a painful condition.

From its inception, St Mark's Hospital has been dedicated to researching and developing new and more effective ways of treating, managing and curing bowel disease.

For almost 200 years, there has been an unbroken chain of world leading experts at St Mark's building their knowledge and skills through research that translates into improved clinical practice and patient benefits. Each generation of experts has passed on their skills and expertise to the next generation of doctors. This makes St Mark's unique in the world. It is what enables St Mark's to be the national and international referral centre for people with complex bowel diseases that others cannot treat: more than 60% of the patients treated at St Mark's are referred by other UK hospitals.

Mr Philip Tozer, a Consultant Colorectal Surgeon at St Mark's, laying flowers at the grave of Frederick Salmon on the 150th anniversary of his passing. Mr Salmon was a surgeon and the founder of St Mark's.

The need to continue to invest to maintain and build St Mark's as a world centre of excellence

As you read through this brochure, you will discover the monumental strides that have been achieved in the field of bowel disease, for example, the survival rate from bowel cancer has increased as a result of surgical and medical research from 2% in the 1950s without surgery to over 52% with surgery today. St Mark's has played a pivotal role in the field, making major contributions that have deepened understanding of bowel diseases, and developing new procedures and techniques that have helped patients to avoid major surgery.

The medical and surgical treatment of Crohn's disease and ulcerative colitis, which are collectively known as Inflammatory Bowel Disease (IBD), has improved significantly and IBD can often be managed and controlled well for long periods. You will also read that there are currently no cures for these chronic conditions and that people can struggle for decades with debilitating symptoms. In this brochure, we are proud to describe the variety of research projects St Mark's is undertaking in order to redress this situation.

Why supporting St Mark's fight against bowel disease is of paramount importance

We know, and appreciate, that there are many calls on the philanthropic giving of generous donors. There are however good reasons why we believe you may consider supporting St Mark's or intensifying the support you are already giving.

Bowel disease: the numbers

Bowel cancer is the second highest cause of cancer fatalities in the UK and the western world, claiming more than 630,000 lives every year. If new and more effective treatments are not developed, more than six million people will lose their lives to bowel cancer over the next ten years.

Crohn's disease and ulcerative colitis impact the lives of at least 300,000 people in the UK and millions worldwide.

Crohn's disease commonly affects young people, manifesting between the ages of 15 and 40. People can live with the challenging and debilitating symptoms of Crohn's disease for more than 70 years. The health challenges of the disease include flare-ups where the bowel becomes inflamed, painful and ulcerated. Crohn's disease can also cause strictures or blockages of the bowel, and result in severe weight loss. 70% of patients require surgery at least

once during their lifetime for their disease and they may lose large parts of their bowel. This can lead to short bowel syndrome, which describes when nutrients can no longer be absorbed from food and individuals must be fed artificially by a tube inserted into a vein near the heart. Called total parenteral nutrition, this process can leave patients susceptible to illness and blood infections.

15% of people with Crohn's disease are debilitated by their condition and are not able to work after 10 to 20 years from the original diagnosis.

A study published in 2017 in the prestigious medical journal, The Lancet, stated that: 'At the turn of the 21st century, IBD has become a global disease with accelerating incidence in newly industrialised countries whose societies have become more westernised. There is a need for innovations in healthcare systems to manage this complex disease.'

A Cinderella disease that has never attracted the level of philanthropic giving it deserves

Bowel disease is a Cinderella disease. It is the poor relation in the field of philanthropic giving to medical research. It has never attracted the level of popular philanthropic support of other chronic conditions, but it is affecting more people.

We hope that, after reading this brochure, you will wish to join the fight to create a future free from the fear of bowel disease or intensify the support you are already giving. We hope you will be left in no doubt that supporting St Mark's Hospital is an excellent way to create a better, healthier future for people living with complex bowel diseases.

Section 2

Contributions, breakthroughs and impact

Why St Mark's is a world centre of excellence - highlights of St Mark's Hospital's contributions, breakthroughs and impact

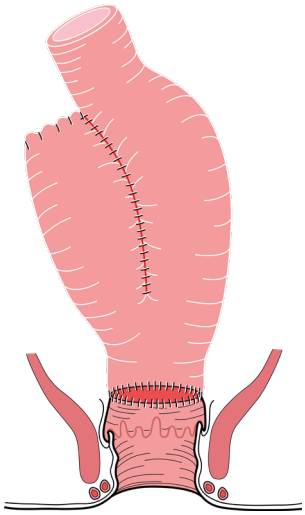
Inflammatory Bowel Disease:

What follows is a brief summary of some of the breakthroughs and impact of St Mark's Hospital in the fight against Inflammatory Bowel Disease (IBD). Crohn's disease and ulcerative colitis are types of IBD which commonly affect young people. They are chronic, lifelong conditions which are associated with symptoms that, together, can have a significant and detrimental impact on personal and social development.

- **First description of 'colonic Crohn's disease'**. Crohn's disease is not a single disease. There are five types of Crohn's disease, with ileo-colonic Crohn's disease being the most prevalent. The identification of colonic Crohn's disease was a major breakthrough in establishing the different types of Crohn's disease and, importantly, different treatments for different types of Crohn's disease.

- **First trial of amino salicylates and steroids for IBD.** These drugs are used to keep Crohn's disease patients in remission and to avoid flare-ups. As a result of St Mark's Hospital carrying out a successful large-scale drugs trial of amino salicylates and steroids, the path was laid for hundreds of thousands of patients to receive effective relief from the symptoms of Crohn's disease flare-ups. These drugs however are not a cure; they can have side-effects, such as thinning and weakening of bones (osteoporosis), and are not effective in controlling flare-ups in all patients.

- **First widespread use of the drug azathioprine for maintaining disease remission.** Crohn's disease behaves like an autoimmune disease, like arthritis and multiple sclerosis. The body is not able to distinguish between good and bad foreign bodies and attacks its own immune system to cause inflammation which damages healthy tissue. Azathioprine is an immunosuppressant, and like all drugs of this type, it dampens the immune system to stop it attacking itself. This compromises the ability to fight infections. St Mark's was the first hospital to provide widespread treatment of Crohn's disease flare-ups with azathioprine. Today, hundreds of thousands of patients benefit from azathioprine to prevent flare-ups or keep them controlled. However, it is also not a cure and is not effective for everyone with Crohn's disease.



In the 1970s, surgeons Sir Alan Parks and Professor John Nicholls from St Mark's developed the operation of choice for ulcerative colitis. This procedure, known as the ileo-anal pouch, or j-pouch, has been performed in more than 25,000 patients worldwide, helping to alleviate the pain caused by ulceration of the colon.

First controlled trial of a biologic drug for Crohn's disease. Biologics, including infliximab and adalimumab, are immunosuppressant medications like azathioprine which block the body's immune system from attacking the lining of the gut. Whilst biologic therapy has brought about a major leap forward in the treatment, management and control of Crohn's disease and can lead to relief from symptoms, like azathioprine, it is not effective in all patients, stops working in others and can cause extra-intestinal manifestations such as skin problems. Whilst biologic therapy represents an additional option in the medical arsenal of Crohn's disease treatment, it does not offer a cure but rather a way to manage disease.

IBD & surgery

Patients with IBD are often diagnosed much later than when they first developed symptoms. This can reduce the effectiveness of medical therapy and make surgery necessary to manage and control symptoms.

70% of Crohn's disease patients will require surgery at least once in their lifetime for their disease. The way surgery is used to control Crohn's disease today has radically changed. Surgery is employed as part of a multi-faceted treatment regime which, at St Mark's Hospital, may include a care pathway that begins with an accurate diagnosis, followed by genetic profiling, endoscopic examination of the colon and various scans. Patients will then be prescribed the medication that fits the profile of their disease. A patient will be escalated up the drug pathway to more potent drugs if their disease shows signs of becoming aggressive. In the most severe cases, which involve frequent flare-ups, ulceration and damage to the gut, surgery can be the most effective solution, bringing relief from painful symptoms.

Patient receiving biologic medication to control their inflammatory bowel disease.

Crohn's disease can impact severely on a teenager's physical development. For a teenager at a stage in life of forming identity, friendships and relationships it can be devastating.

Bowel cancer:

- **The development of the adenoma-to-carcinoma sequence** that underpins the medical profession's understanding and treatment of bowel cancer. It is widely accepted in the medical profession that the adenoma-to-carcinoma sequence represents the process by which most, if not all, colorectal cancers arise. Understanding this sequence established the need to remove pre-cancerous polyps (adenomas) before they grow and develop into life threatening cancerous growths (carcinomas). The contribution of leading doctors at St Mark's, such as Sir Basil Morson and Dr H Bussey, to the discovery of this sequence has influenced the treatment of bowel cancer worldwide. This discovery focussed the medical world sharply on developing the 'prevention is better than cure' regime, establishing it as a universal treatment. This work also established the need for regular surveillance, as adenomas can return.

- **The creation of the world's first staging system for cancer that determines future treatment.** Sir Cuthbert Dukes' research at St Mark's established the world's first method of defining the stage that a patient's cancer has reached. Staging establishes how big the tumour is and how widely spread it is in the body, which in turn determines the appropriate treatment regime. For cancer that has spread, the Dukes stage alerts doctors to the need to provide chemotherapy and radiotherapy as well as advanced surgery. While there have been developments in cancer staging since Sir Cuthbert founded TNM (Tumour, Node, Metastasis) staging, his method is still the most widely practiced staging method and much of this follow-on work owes a debt of gratitude to Sir Cuthbert's ground-breaking work.

- **The establishment of the world's first registry of inherited bowel cancer.** Since the days of Cuthbert Dukes and Basil Morson, the documentation of patient records and specific information pertaining to their disease has been fundamental to enabling high quality clinical research and improving our understanding of the different genetic factors that influence the development of colorectal cancer.

- **St Mark's Hospital was instrumental in identifying the gene that causes familial adenomatous polyposis (FAP) and bowel cancer.** This and other important genes in the development of colorectal cancer have been identified through our ability to access this information and tissue from patients with cancer and precancerous conditions.

Establishing surveillance programmes in IBD to detect early cancer. Our research into the long-term effects of inflammatory bowel disease has contributed to the recognition of the increased risk of developing colorectal cancer once affected with inflammatory conditions of the colon. Many years of seeing patients with this condition has enabled us to define the benefits of regular surveillance to prevent these patients succumbing to a preventable cancer.

Diagnostics and non-invasive therapies: Endoscopy

St Mark's surgeons were the first to use 'lighted examination' of the colon to accurately assess the level of damage to the cells lining the rectum (called the rectal mucosa). The accuracy offered by this now well-established diagnostic procedure has greatly informed the choice of treatment, providing a more tailored and effective treatment regime. This procedure is used extensively worldwide.

The Wolfson Unit for Endoscopy at St Mark's Hospital is recognised as a world centre of excellence by the World

St Mark's Hospital surgeons have championed the adoption of minimally invasive, laparoscopic (keyhole) surgery for the treatment of bowel cancer.

Organisation of Digestive Endoscopy for its outstanding contributions to international education in endoscopy. The Unit has been at the forefront of training and innovation in endoscopic examination of the colon for more than three decades.

The development of a magnetic imager and simulator transformed training techniques and has resulted in reduced overall complications and improved outcomes from the examination. The development of minimally invasive techniques for the excision of large polyps has spared many patients from needing major surgery.

Imaging

The technique of endo anal ultrasound examination of the anal sphincter was developed by Professor Clive Bartram in the 1980s at St Mark's and as a result transformed the understanding of the cause of incontinence in elderly women, identifying the impact of childbirth in causing tears in the anal sphincter muscles which would not reveal themselves until women reached an older age. This in turn led to a whole new approach to the repair of tears experienced during childbirth and has dramatically changed the incidence of incontinence in women.

In addition to commercially supported research, St Mark's Hospital Foundation supports a number of research programmes at St Mark's Hospital and is fundamental to helping this historic institution continue the research and education that maintains St Mark's as a world leader.

We summarise in the following sections some of the research activity that St Mark's is currently undertaking, to demonstrate that St Mark's is a centre of excellence both for research into and the clinical treatment of bowel disease.

Section 3

Colorectal cancer research

Mr Danilo Miskovic (centre, back) is a Consultant Surgeon at St Mark's Hospital and the Surgical Robotics Research Programme Lead. Here he is pictured with some of the theatre staff that are integral to the successful delivery of the Programme

Surgical robotics - to achieve the next quantum leap in surgical innovation for colorectal and anorectal surgery

The issue

Keyhole (minimally-invasive) surgery has been shown to improve results in almost all areas of abdominal surgery and is now the operation of choice (shorter length of hospital stay, less pain, quicker return to normal function). However, it can be difficult to learn and functional limitations can make the technique restrictive for certain types of bowel surgery.

There is a need to continue research and build experience in robotic colorectal surgery. Minimally invasive robotic surgery aims to remove cancer while preserving a patient's health-related quality of life.

Our response

St Mark's prioritises the quality of life of its patients as much as their survival so they can lead full and active lives after surgery. We believe the introduction of robotic surgery is an important milestone to reduce the risk of recurrent disease and provide good short- and long-term quality of life. Initial experience with robotic colorectal surgery is promising, especially for patients that are overweight, or where access to certain parts of the body may be difficult.

The Surgical Robotics Research Programme at St Mark's Hospital launched in 2018 to develop the next generation of minimally invasive surgery for colorectal and anorectal operations.

Programme objectives:

1]. To introduce a functioning robotic programme for bowel cancer at St Mark's Hospital.

2]. To become an educational hub for robotic colorectal surgery in the UK and Europe.

3]. To contribute to the evidence on the effectiveness of robotic surgery in other colorectal diseases such as the inflammatory bowel diseases (IBD), Crohn's disease and ulcerative colitis.

Patient benefits of robotic technology:

- Less tissue loss.
- Less blood loss, which helps to keep more healthy tissue alive.
- Avoidance of the need for open surgery and its associated complications: infections, hernias and leakages from the surgical join, which can all be life threatening.
- Avoidance of incontinence and the loss of organ function.

The outcome

Since the Programme launched, the St Mark's robotics team, led by consultant surgeon and Programme Lead, Mr Danilo Miskovic, has performed robotic colorectal surgeries successfully on bowel cancer and IBD patients. It has also developed a reputation as the trainer-of-first-choice for surgeons with an interest in robotic colorectal surgery, attracting visiting surgeons from hospitals across the UK and Europe. Our robotic colorectal education credentials are being further cemented through the delivery of in-house developed courses, and a plan to develop a more robust training offering in partnership with other organisations.

St Mark's has positioned itself to be one of the few centres in the UK providing this minimally invasive technology to eligible bowel disease surgical patients.

St Mark's Hospital will work continue to work in collaboration with leading organisations in the field such as the European Society of Coloproctology, publish findings in high-impact peer reviewed journals on the technique's efficacy and contribute robot operation data to the UK robot registry.

Whilst robotic technology has been established in urology and gynaecology, it has not been widely researched for bowel disease surgery. As the world's first specialist bowel disease hospital, which has a track record of developing surgical and endoscopic innovations that have set the standard of care in colorectal and intestinal medicine, it is fitting that St Mark's is pioneering research in and establishing best practice for the robotic colorectal surgical community.

Mr Miskovic (left in raspberry scrubs) operating robotically using the Da Vinci Xi console; the patient is in the theatre in the adjoining room and is looked after by an expert team.

Mr Miskovic with the patient, who is easily accessible through the adjoining room.

Robotic colorectal education in action: The robotic fellowship programme at St Mark's will train 6 surgeons over 3 years. Each will spend 6 months under the mentorship of expert robotic colorectal surgeon, Mr Miskovic. Pictured on the left is the first robotic surgical fellow, Mr James Read.

HIPEC is an innovative treatment that pumps chemotherapy around a patient's body during open surgery to kill cancer cells.

HIPEC – a novel way to deliver chemotherapy for advanced cancer patients

The issue

When cancer spreads from its original location in the bowel lumen to other parts of the body, such as the lining of the stomach (peritoneum) and liver, the cancer can become so widespread and advanced that surgery will not save the patient. Conventional chemotherapy and radiotherapy alone are often ineffective in these cases. Currently, patients that experience cancer spread (metastasis) can only be offered end-of-life palliative care. HIPEC aims to give people with advanced cancer a greatly improved chance of survival.

Our response

St Mark's Hospital is one of only a handful of centres in the UK to offer HIPEC treatment to advanced cancer patients. The process involves chemotherapy being administered at the time of surgery, helping it to reach the areas affected by cancer. Bathing the abdominal cavity in hot chemotherapy also means that cancer cells that break off during surgery are not given the chance to embed and grow. The early results of HIPEC are encouraging and lives have already been saved.

The outcome

St Mark's is collecting data to demonstrate that HIPEC is an effective treatment for patients with advanced cancer who, otherwise, would have little or no chance of survival.

A programme of research to improve our understanding of the body's defence mechanisms to fight cancer

The issue

The purpose of the BiCyCLe research programme is to find a way to prevent muscle wastage in people with bowel cancer. Two million people – that is 20% of all cancer patients - die every year around the world because of cancer-related muscle wastage, with no clear understanding of why it happens. Muscle is not just body tissue it is an organ that significantly supports the immune system to fight infection. BiCyCLe research may lead to solutions to combat muscle wasting in bowel cancer as well as other types of cancer, with the potential to save many lives.

Our response

BiCyCLe is carrying out research in key areas:

1]. The role of the body's white blood cells in cancer-related muscle wastage.

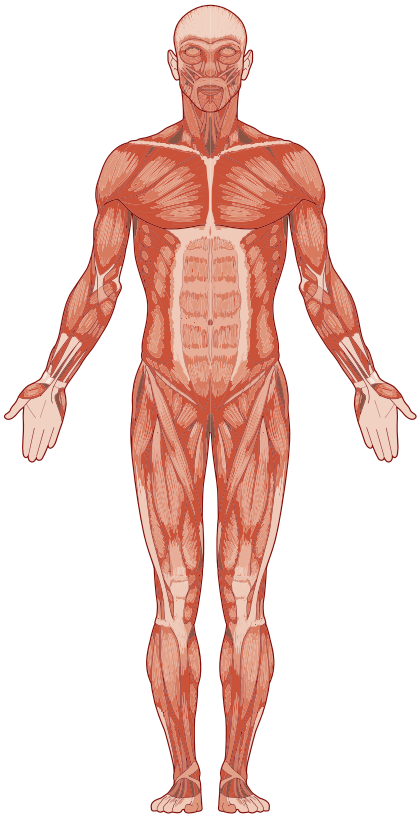
Current thinking about cancer is that it may be treated medically like an infection. The body's white blood cells play an essential role in fighting and killing infection. BiCyCLe research has been looking at a particular type of white blood cell, called a dendritic cell. In anorectal cancer, it can be seen that dendritic cells absorb fat and as a result, become ineffective at helping to fight cancer. Through our highly innovative BiCyCLe research, we aim to identify ways of making dendritic cells tough and impervious to absorbing fat by stopping the process that makes them fatty, and thus preserve their strength to fight infection and stop muscle wasting.

2]. The role of inflammation caused by bowel cancer.

BiCyCLe research is examining the levels and types of inflammation found in cancer tumour cells. This will enable us to identify biomarkers (living organisms, chemicals, or genes) that can be targeted with drugs and chemicals to fight inflammation and thus control cancer.

3]. The role of the bacteria to be found within the gut.

BiCyCLe research is analysing the types of bacteria found in the gut and the role they play in cancer development. If we can identify the ideal bacterial mix for a healthy gut, we can use this information to control the bacteria with drugs, as well as investigate the possibility of implanting good bacteria.



Muscle is an essential part of the immune system and helps to fight cancer. Through the BiCyCLe research programme, we aim to improve the quality of patients' lean muscle to help them fight cancer more effectively.

4]. Boosting a person's lean muscle bulk to help them fight cancer.

BiCyCLe is using a powerful version of the electrical stimulation machines that can be bought for general exercise of the muscle to help patients who are losing muscle bulk due to their illness, to build up their lean muscles to help them fight cancer.

5]. A novel pre-surgical intervention to preserve or increase muscle mass in bowel cancer patients to improve surgical outcomes.

The BiCyCLe research group hypothesises that muscle wastage in cancer patients can be successfully treated with enhanced nutrition, a home-based resistance exercise programme and vitamin D optimisation. Surgical outcomes will be improved in this group of patients by preserving or increasing muscle mass. If the intervention shows favourable post-surgical outcomes for bowel cancer patients, a potential future outcome of this work is hospital trusts making provision for its cost as part of patients' pre-operative care.

The outcomes

The BiCyCle programme of research is developing a range of interventions designed to boost a patient's immune system, both physiologically and physically, to make the immune system strong and efficient at fighting cancer cells and mitigate the life-threatening symptoms of bowel cancer-related weight loss.

The Lynch Syndrome Cancer Prevention Study (the LynC Study)

The issue

Colorectal cancer is the third most common cancer worldwide, with around 1 in 30 of cases occurring due to a hereditary (genetic) disease called Lynch syndrome (LS). LS is not a rare disease; indeed the World Health Organisation estimates that around 1 in 125 people have it (about half a million people in the UK). However 90-95% of people with LS are not aware they have the condition, although they may have a family history of cancer.

Most people with LS are well, but they have a 40-70% chance of developing bowel cancer, and women also have a similar risk of cancer of the womb. All people with LS have an increased risk of many other types of cancer.

The genetic mutations which cause LS can be passed on from one generation to the next, with a 50% risk of the child inheriting the condition. At St Mark's Hospital we have the UK's first LS clinic, with 4,700 families with a family history of

cancer, and 600 people thus far confirmed to have LS. This is a unique resource to develop new preventative strategies and treatments for these patients.

Our response

We believe there are many discrete clinical projects which could be rapidly scaled-up into medical practice for the benefit of people with LS.

The LynC Study encompasses three projects which have the following aims:

1]. Effective diagnosis and identification of people with LS in the UK.

2]. Improved understanding of the biological mechanism of cancer development in people with LS.

3]. Development of more tests which facilitate the prevention and early diagnosis of cancer in people with LS.

4]. Reduction in variation and improvement in access to care for people with LS in the UK.

The need to develop more tests which facilitate the prevention and early diagnosis of cancer in people with LS has become more acute in the Covid-19 era. At present, the screening guidelines for LS patients involve the requirement of up to 20 or more colonoscopies throughout one's lifetime, which is both resource-intensive and invasive for patients. Identifying other types of screening which are effective at diagnosing bowel cancer and pre-cancerous changes in LS patients, in an era where traditional colonoscopy services are facing increasing pressures, will be essential going forward and can be used to supplement colonoscopies.

During the Covid-19 pandemic, St Mark's has spearheaded a national project to improve access to colonoscopy for high risk patients by using a stool FIT test to identify those whose need is greatest. At a time when access to colonoscopy is limited, this test is used to identify patients who should be prioritised.

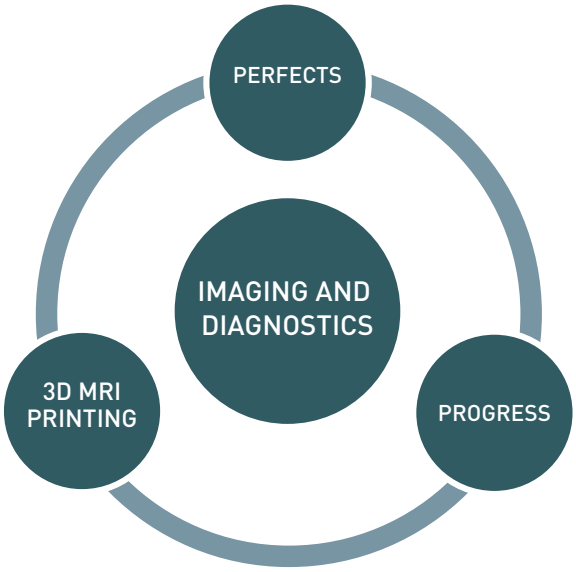
The outcomes

Across the three projects, we can develop a new paradigm in LS cancer prevention, built over a decade of three interconnected projects led by the Lynch Syndrome Clinic at St Mark's Hospital in collaboration with other hospitals and research centres across the UK.

Pictured is Dr Kevin Monahan, a Consultant Gastroenterologist in the Lynch Syndrome and Family Cancer Clinic at St Mark's Hospital, who is the site lead for the LynC Study.

Section 4

Imaging and diagnostics research



PERFECTS – improving the skill level of radiologists to increase the lives saved from bowel cancer

The issue

Bowel cancer screening saves lives. Since the national bowel cancer screening programme was introduced in the UK in 2006, it has saved thousands of lives by identifying people at the pre-cancerous and early stages of bowel cancer when it is 100% treatable. If bowel cancer is detected later when it has spread, it is much harder to treat. Currently, the most effective form of screening is colonoscopy, which involves a camera being inserted into the rectum. This provides the endoscopist with a view of the bowel lumen to see if there are cancerous growths or growths with the potential to become cancerous. However, colonoscopy is not suitable for all patients.

Our response

An alternative to colonoscopy is a negligibly invasive procedure called CT Colonography (CTC) or 'virtual colonoscopy' which is where a three-dimensional (3D) picture of the entire bowel is created using a non-invasive radiological scan. The radiologist can see the entire 3D image of a patient's bowel on a computer screen and identify what is normal and what is cancerous.

When performed skilfully, CTC is as effective as colonoscopy at identifying bowel and other cancers. St Mark's Hospital's radiology department has amassed an expert level of skill in CTC scan interpretation over several years. However, it is recognised that there are UK-wide variations in the skill levels of radiologists reporting CTC scans: diagnostic accuracy of bowel cancer through CTC scan reporting is as low as 14% in

some hospitals compared to over 90% at St Mark's Hospital and other proficient hospitals. This means that pre-cancerous and early stage bowel cancers are being missed.

The PERFECTS training and accreditation programme, which is a collaborative project between St Mark's Hospital and University College London Hospital radiology faculty, aims to narrow the UK-wide skills gap by providing one-to-one personalised training via workshops for radiologists practicing CTC. The training will teach them how to spot bowel cancers, including complex ones that can easily be missed. PERFECTS will impact international colorectal cancer policy.

More than 70 radiologists from 60+ NHS hospital trusts in the UK have taken part in our training programme and their results imply that a single day of training can improve experienced radiologist CTC reporting performance; something that is sustained for almost one year. In addition, some of the PERFECTS team were invited to be faculty members at an annual European Society of Gastrointestinal and Abdominal Radiology CTC workshop in Dublin. They were part of a group of international faculty who provided training on how to perform and interpret CTC to 70 international delegates. Therefore, in addition to the 70+ radiologists in the UK who have received structured CTC training through the PERFECTS training programme, a further 70 CTC-practicing radiologists have also benefitted from the novel model of CTC-training led by the PERFECTS team.

The outcome

UK-wide endoscopy services, which include colonoscopy, were pressured before the Covid-19 pandemic, and now they will

St Mark's Hospital is a national training hub for CTC, with training delivered by expert radiologists.

have to operate at reduced capacity for an indefinite period. This is where CTC may be used as a first line investigation instead of colonoscopy to help inform treatment plans based on cancer diagnosis.

As the value of CTC becomes more important in the wake of Covid-19, by association, it will become urgent that radiologists practising this technique are proficient at interpreting scans. The value of PERFECTS has increased significantly in the Covid-19 era.

PROGRESS – a project to improve understanding of how cancer develops to refine the bowel cancer surveillance programme and save more lives

The issue

A polyp is a growth that is at risk of becoming cancerous. Patients who have polyps removed at colonoscopy are entered into a surveillance programme which involves having repeat colonoscopies in the future.

Although the surveillance programme for patients that have had polyps removed has become refined, there is a need for further refinement to ensure that scarce endoscopic resources are targeted to patients at greatest risk of developing bowel cancer.

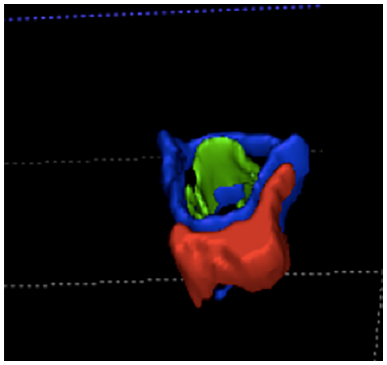
Currently, the markers of future cancer risk are the size and number of polyps that a patient has removed, but not all patients have the same risk of developing bowel cancer. This means that high risk patients may not be receiving the intensive surveillance they require, and low-risk patients are not being spared from unnecessary, invasive procedures.

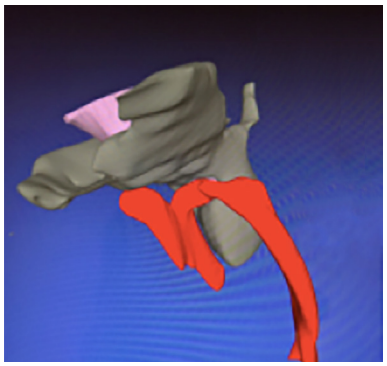
Our response

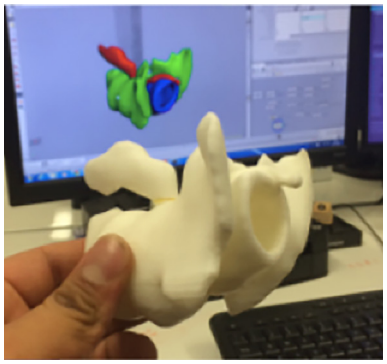
We are collaborating with renowned organisations in the UK, including Barts Cancer Institute in London, to be able to study the behaviour of polyps on a molecular level to understand why some develop into bowel cancer. This will make it possible to identify high risk patients in need of intensive monitoring and surveillance by colonoscopy. Concurrently, low risk patients will not have to undergo more procedures than necessary.

A linked goal to the above is to alleviate the growing pressures on clinical services such as colonoscopy; overuse of colonoscopies is a recognised problem. For example, with an ageing UK population, there are more people eligible to be enrolled into Bowel Cancer Screening Programmes. However, we have

Professor Siwan Thomas-Gibson, a Consultant Gastroenterologist and Endoscopist at St Mark's Hospital, is a world leading proponent of bowel cancer screening.







Novel use of MRI and 3D printing will help surgeons to understand complex fistula anatomy, helping them to navigate the area and avoid patients becoming incontinent.

explained that not all these patients will have the same risk of developing bowel cancer, and therefore the PROGRESS project is our attempt to understand the pathology that leads some polyps to develop into bowel cancer, in order to prevent all patients from entering the same monitoring and surveillance system; this is not only resource-intensive, it is invasive for patients.

The outcomes

This research has the potential to influence national and international guidelines of colonoscopic surveillance based on knowledge of how polyps grow and evolve to a cancerous state. This offers the endoscopy profession enormous potential to offer patients personalised treatment based on their risk level of developing bowel cancer, using scarce NHS endoscopic resources more efficiently. In the Covid-19 era, the need to make clinical services more efficient has become even more critical.

Novel use of MRI and 3D modelling for perianal fistulae

The issue

One in three patients with Crohn's disease, a type of Inflammatory Bowel Disease (IBD), will develop a perianal fistula. A perianal fistula is a small tunnel that develops between the end of the bowel and the skin near the anus. They are notoriously difficult to treat and heal completely and the symptoms can be debilitating, significantly impacting on social interactions and quality of life.

The surgical treatment of complex perianal fistulae presents considerable difficulties. For the surgeon, fistula anatomy can be difficult to visualise, making surgery more challenging. For the patient, the involvement of the sphincter muscles means that the risk of incontinence during surgery is high.

Our response

This research is using MRI technology in a novel way to assess the volume of fistula tracts over a specific time period. This will help us to understand how many fistula tracts are present and how complex they are. Moreover, the results would show whether or not patients are responding to medical therapy, helping gastroenterologists to make informed decisions about whether to stop or switch a patient's treatment.

This project will create 3D models of complex fistula anatomy as an aid to surgical planning, which will help surgeons to know the location of the healthy tissue and muscle they need to navigate around.

The 3D models will also be used as educational tools for surgeons whose work involves complex fistula surgery, but also to help prepare patients and support the consent process for surgery.

The outcomes

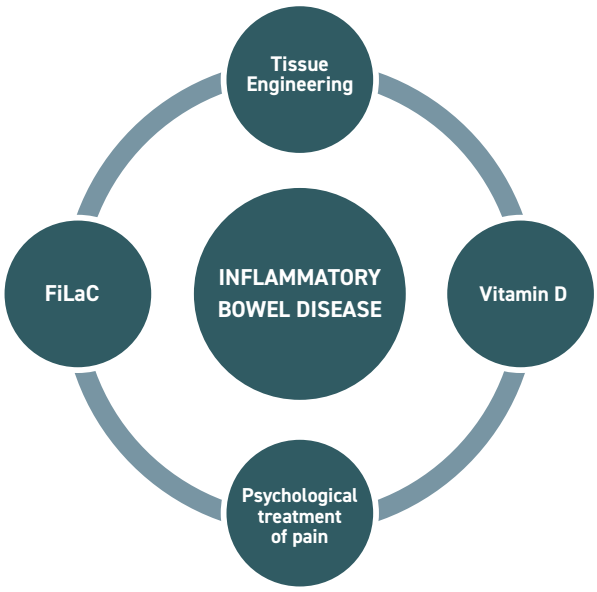
As proof of concept, we have shown that it is feasible to generate objective fistula volume measurements from MRI studies using computerised software. MRI volumes have been calculated for patients before and after medical therapy over a one-year time period. We have learned that MRI volume measurements can provide an accurate assessment tool alongside radiology reports and clinical follow-up.

The James Lind Alliance, a national Priority Setting Partnerships group of patients and clinicians, identified perianal Crohn's disease, and specifically the factors that influence treatment strategies and outcomes, as one of the top 10 unanswered questions in the field of IBD. The Association of Coloproctologists of Great Britain and Ireland also identified that improving the management of patients with perianal Crohn's disease was one of the top priorities for future research.

This project has the potential to develop an objective radiological measure of response to treatment, supporting the goals to offer personalised medicine in the future and improve surgery for and education in the treatment of complex fistulae.

Section 5

Inflammatory bowel disease research



Tissue engineering - growing the world's first replacement bowel for people with short bowel syndrome from their own cells

The issue

Individuals who lose large amounts of their bowel through trauma or conditions such as Crohn's disease develop short bowel syndrome, which means they can no longer absorb nutrition from food and must receive nutrients artificially into a vein near their heart. This process of feeding is known as total parenteral nutrition (TPN). There are approximately 1,000 adults on TPN in the UK.

Significant health complications can result from TPN, such as infection of the line that is used for feeding, and the five-year survival rate is poor. The current solution to coming off TPN is a bowel transplant. However, this relies on a suitable donor becoming available and there is a shortage of organ donors. This situation may improve with the passing of a new organ donation law in the UK in 2020, which now automatically enrols people as organ donors unless they have specifically opted out. However, with organ donation, recipients face a lifetime on immunosuppressant medication to prevent organ rejection, which can lead to complications.

Our response

A group of renowned scientists which now includes Dr Karin Greco, Head of Research at The Griffin Institute (formerly Northwick Park Institute of Medical Research), and Dr Simon Gabe, a consultant gastroenterologist at St Mark's Hospital, are working on an exciting area of research.

The world's first tissue engineered bowel scaffold, grown at St Mark's Hospital in conjunction with its research partner, The Griffin Institute.

Their work aims to improve the lives of people with Inflammatory Bowel Disease (IBD) by generating an alternative healthy bowel tissue to replace that lost by disease. This novel approach would avoid the need for organ donation because the stem cells used to grow new bowel would come from the patient themselves.

The Griffin Institute and St Mark's Hospital have been working collaboratively on this novel research for a decade, using innovative solutions to, first, create a scaffold, and then identify the right source of stem cells to integrate with the scaffold. The third step will be to try to grow functional and clinically relevant lengths of tissue so that patients can absorb the vitamins and minerals they need through food and can potentially be weaned off parenteral nutrition, with the future goal being implantation into patients.

The outcome

This research offers the hope of an alternative to parenteral nutrition for thousands of patients that have lost large amounts of bowel due to disease or trauma, and represents collaboration at its best between The Griffin Institute and St Mark's, organisations with complementary expertise.

St Mark's aims to be the first centre in the world to grow a fully functional, tissue engineered bowel.

Vitamin D as an additional therapy to conventional medical therapy for Inflammatory Bowel Disease

The issue

The medical arsenal for the treatment of Inflammatory Bowel Disease (IBD) is growing. However, as we have explained in this document, these drugs are not suitable for all patients and do not achieve complete healing in others as loss of response is common. In addition, the drugs are associated with complications, such as extra-intestinal manifestations (e.g. skin problems), a compromised ability to fight infections and a higher risk of developing lymphoma (cancer of the body's lymphatic system). There is therefore a need to identify natural treatments which have the benefit of no side effects that can be used alongside conventional medical therapies, which may help to reduce the chronic inflammation caused by IBD.

IBD shares similar characteristics with other autoimmune conditions, whereby the immune system attacks itself by behaving hyperactively to cause inflammation. Vitamin D

has been shown to be an effective treatment for rickets and is showing great promise as an additional treatment for tuberculosis and multiple sclerosis.

Our response

For over a decade, researchers at St Mark's have been studying the immunomodulatory effects of vitamin D for the treatment of IBD, hypothesising that vitamin D supplementation reduces the number of bacteria that cause inflammation and increases numbers of bacteria with anti-inflammatory properties.

St Mark's Hospital has focussed some of its research time on looking at the administration of super-high doses of Vitamin D to investigate if it improves the efficacy of the conventional drugs that are used for IBD. Furthermore, the effectiveness of vitamin D to reduce inflammation may mean that dosages of existing drug therapies could be lowered.

The results from our research support the hypothesis that vitamin D supplementation may reduce disease activity in patients with active IBD.

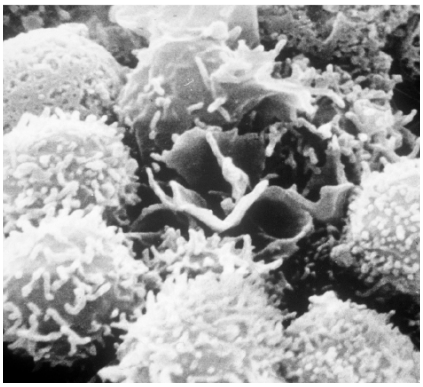
The outcome

Information arising from this area of work will add to our knowledge of environmental factors; vitamin D that is provided naturally in ample amounts by the sun in sunny climates may modify the types of bacteria in the bowel of patients with IBD.

More widely, recognition of the role of the gut bacteria in other diseases means that the potential modification of the gut bacteria with vitamin D supplementation may have wider therapeutic implications in conditions like diabetes, heart disease and other autoimmune conditions.

We continue to collect data and investigate whether vitamin D is an effective addition to conventional medical therapy and if it could be used to reduce dosages of existing IBD drugs.

Professor Ailsa Hart, the Inflammatory Bowel Disease Department Lead at St Mark's Hospital pictured with former St Mark's research fellows.



There is a growing body of research on vitamin D and its immunomodulatory effects in IBD. This is an image of dendritic cells, which are known to play an important role in this process.

Psychological treatment of chronic abdominal pain (PTCAP) programme

The issue

The gut is one of the most innervated organs - that is, furnished by nerves - in the body, yet not all the information from the gut goes to the brain as this would cause sensory overload. There is a 'gate' which prevents this overload, but for many gastrointestinal patients, this gate opens and they feel more abdominal pain. These are commonly patients that have had bowel surgery or bowel infection and inflammation, and also patients who faced and could not process a severe emotional trauma and are chronically anxious.

Chronic abdominal pain is one of the most common clinical problems seen in St Mark's patients. It is a severe and enduring symptom of nearly all gastrointestinal diseases and disorders which are treated by St Mark's physicians and surgeons.

There has been a constant stream of growing evidence that mind-body therapies are effective at significantly helping patients to cope better with pain, improve the quality of their life and reduce the need for painkillers. However, no comprehensive comparative research has been carried out to test the efficacy of psychological treatments or to explore how they can be integrated with conventional medical therapies.

Our response

Our pioneering Psychological Treatment of Chronic Abdominal Pain (PTCAP) programme will research whether Acceptance and Commitment Therapy (ACT) is effective at helping people with chronic abdominal pain to cope and manage their pain better.

Within the scope of this project, there may be potential to consolidate our results in a larger group of people if the results from the first phase of online-based ACT are encouraging and positive, or to explore the feasibility of hypnotherapy to improve the functioning of people with chronic abdominal pain.

The outcome

We aim to disseminate our findings nationally, with the hope that the pain-reducing modality we identify can be offered to thousands of patients who are struggling to cope with abdominal pain by centres throughout the UK.

FiLaC - laser therapy to alleviate the pain caused by fistulae, while avoiding the risk of incontinence

The issue

Anal fistulae represent one of the most common benign conditions of the lower gastrointestinal tract. They account for the vast majority of surgical procedures performed in the region of the anus/rectum.

Evidence shows that there are more than 10,500 yearly interventions for fistulas in the UK. Furthermore, they account for a significant degree of morbidity in patients with Crohn's disease, affecting around one in three of these patients. According to Crohn's & Colitis UK, there are at least 115,000 people with Crohn's disease in the UK, and many millions worldwide.

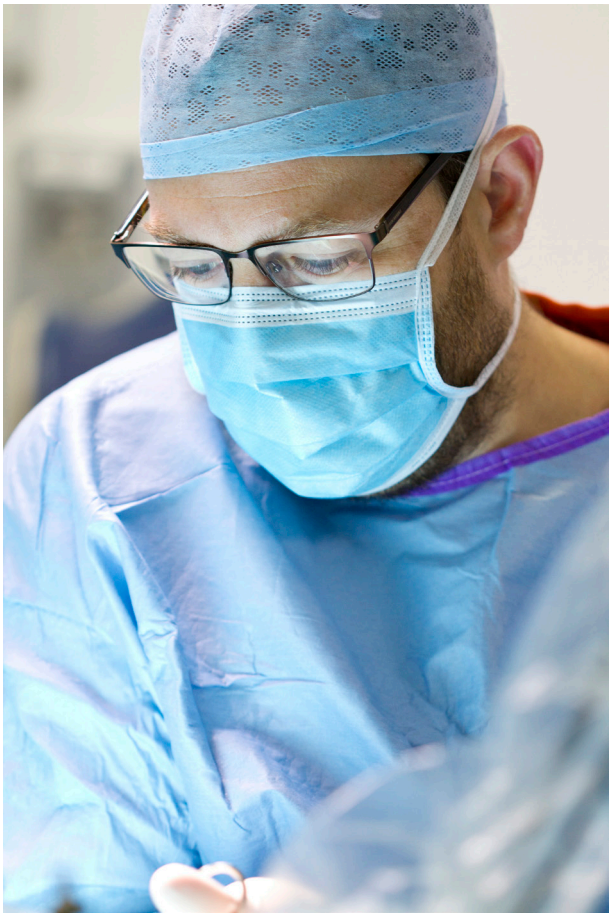
There is a need to effectively evaluate novel techniques that may offer better therapeutic options for patients with this debilitating anal condition, such as improved healing and minimal risk to the continence function.

Our response

This project is assessing the safety and feasibility of fistula tract laser closure (FiLaC) in certain patients with anal fistula. The current surgical treatment of complex fistulae which involves the sphincter muscles poses a high risk of incontinence. Laser therapy has the significant benefit of avoiding the continence issue.

Mr Philip Tozer, Consultant Colorectal Surgeon and Lead, Robin Phillips Fistula Research Unit, St Mark's Hospital.

Mr Tozer is one of our surgeons currently using FiLaC in the treatment of complex anal fistula.



The outcome

We have introduced FiLaC into clinical practice at St Mark's Hospital for the treatment of anal fistulae. The procedure involves use of a radial emitting laser probe passed through the fistula tract, with the aim of burning the internal surface of the fistula to induce healing and the formation of scar tissue. FiLaC is what is known as a sphincter-sparing procedure, meaning that there is minimal disturbance of the anal sphincter muscles and, as a result, there is no theoretical risk to continence status.

Currently, the conventional treatment for anal fistula is surgery. Our research is focused on gathering evidence to show that laser therapy is a feasible alternative that achieves long-term healing, symptomatic improvement, reduces the risk of fistulae recurrence, and can improve the health-related quality of life of the thousands of patients with this debilitating anal condition.

Over 50 patients with idiopathic fistula (of unknown cause) and Crohn's anal fistula have been treated with FiLaC to date, and we are currently in the process of assessing long-term clinical outcomes and healing in these patients.

Conclusion

St Mark's is committed to researching and developing new and more effective treatments for bowel disease, and disseminating clinical best practice worldwide through St Mark's Academic Institute. The Institute educates and trains 1,200 doctors and other healthcare professionals annually. Please support St Mark's Hospital to maintain its position as a leader, and create a healthier future for people with complex bowel diseases.

As the value of specialism in medicine increases and as complex and difficult to treat conditions are referred from general hospitals to centres of excellence, there is a need to invest in St Mark's, the UK's national bowel hospital. This investment will enable St Mark's to continue its work developing better ways to treat bowel disease, whilst it strives to cure the conditions that debilitate lives through improved knowledge and understanding about how they behave. Equally, your support will enable St Mark's to continue educating and training the world in clinical best practice for the benefit of people in need across the world.

To talk to us about sponsoring a specific research programme or making a donation in support of our work more generally, please contact the fundraising team by emailing: info@stmarkshospitalfoundation.org.uk

A final word about the most important measure of the impact of St Mark's Hospital's research

The most important measure of our work at St Mark's is the impact our research and research-driven services have on the quality of life of our 50,000 patients, but also the patients that benefit from the Hospital's sharing of best practice with the medical community. The photos opposite provide the last word about the difference our research makes to our patients' lives.

These 'before and after treatment' photos of Nancy Fahmy, a St Mark's patient, illustrate what we aim to achieve for all our patients.

A future free from the
fear of bowel disease

St Mark's Hospital Foundation

Northwick Park, Watford Road,
Harrow, Middlesex HA1 3UJ
Telephone: 020 8235 4042
Email: info@stmarkshospitalfoundation.org.uk
Website: www.stmarkshospitalfoundation.org.uk

Compiled and written by Ms. Riyah Talati, Senior Fundraising Development Manager, in conjunction with the senior management and trustees of St Mark's Hospital Foundation, and the medical personnel at St Mark's Hospital.

St Mark's Hospital Foundation is dedicated to bringing about a future free from the fear of bowel disease through research, education and dissemination of clinical excellence

Registered Charity No. 1140930