

Oesophageal and Gastric Research Newsletter

St James's Hospital Dublin



Welcome to the 2nd St James's Hospital Oesophageal and Gastric Research Newsletter. We are excited to share with you some updates from our ongoing research and clinical trials.



This newsletter contains a summary of talks given at our recent public information event, from each of our core research teams working in the areas of:

- Preparing for and recovering from surgery
- Evaluating treatment approaches
- Cancer biology

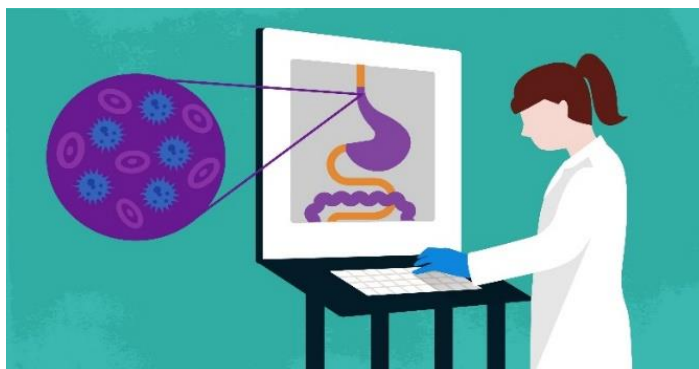
We have also included news on upcoming events from our cancer support partners. We hope you find this newsletter informative.

Sincerely,

Professor John Reynolds
National Lead, Oesophageal and Stomach cancer

Translational Cancer Research Programme

Study team leaders: Professor Jacintha O'Sullivan, Dr Joanne Lysaght, Dr Stephen Maher, Dr Graham Pigeon, Professor Maeve Lowery, Dr Margaret Dunne, Dr Niamh Lynam-Lennon, Dr Melissa Conroy



The Translational Cancer Research Programme, directed by Professors Jacintha O'Sullivan and John Reynolds, focuses on understanding how and why oesophageal and gastric cancer develops. The main questions our team aim to answer are:

- What is the role of the body's immune system in cancer development?
- Why do people have different responses to treatments such as chemotherapy and radiation?
- Can we predict response to treatments such as chemotherapy and radiation therapy by measuring certain biological markers?
- Can we target these markers using new drugs?

By developing a better understanding of the factors influencing cancer development and treatment response, we aim to develop new and improved treatment approaches and ways to predict who will respond best to certain treatments. This is so-called personalised oncology. We are particularly interested in identifying people who are less likely to benefit from standard treatment approaches, for whom alternative strategies may be more suitable.

All of this progress is only achieved thanks to patients and healthy volunteers kindly consenting to donate their biological samples to our research "biobanks", invaluable specimen and data repositories, and to charities such as CROSS and the Oesophageal Cancer Fund who fund biobanking activities. Discoveries from this research will help to improve future prevention and treatment programmes for patients with oesophageal and gastric cancers. You can follow our research progress and future public involvement events online at www.crosscharity.ie.

Translational Research Focus study: Cachexia

Study leaders: Dr Joanne Lysaght, Dr Melissa Conroy

Marked involuntary muscle loss, a condition known as cachexia, is a debilitating consequence of cancer and affects a high percentage of patients with cancer of the oesophageal or stomach. Cachexia can lead to impaired muscle function and strength, reduced treatment efficacy and diminished quality of life. However, there is evidence to suggest that identifying cachexia in its early stages and implementing interventional treatments may improve management of this condition and lead to better outcomes for cancer patients.

Currently, diagnosis of cachexia relies on identifying muscle loss via PET-CT scans. Our study proposes to find a way to diagnose cachexia earlier and by a simpler method of routine blood testing. One area of our research aims to identify the best set of markers in blood to diagnose cachexia. Earlier diagnosis will mean interventions can be performed before cachexia has fully developed, which will limit and hopefully reverse the process.

Exercise Oncology Research Group

Study team: Professor Juliette Hussey, Dr Emer Guinan, Dr Linda O'Neill, Dr Gráinne Sheill, Dr Kate Devenney and colleagues

The Exercise Oncology Research Group is led by Professor Juliette Hussey and Dr Emer Guinan, Department of Physiotherapy at Trinity College Dublin. Much of the work focuses on an understanding of how exercise and other rehabilitative interventions can help people with oesophageal and gastric cancer through their treatment and recovery, and into survivorship.

Recently the group has been awarded approximately €1.3 million in funding by the Health Research Board (HRB), Medical Research Charities Group (MRCG), and the Irish Cancer Society to support this important work. In Spring 2020 we will be starting two large studies investigating the impact of exercise before and after surgery.



The PRE-HIIT study will examine if a special high intensity exercise programme performed for at least two weeks before surgery can improve physical fitness before surgery for oesophageal or lung cancer.



ReStOre II
Rehabilitation Strategies following
Oesophago-gastric and
Hepatopancreaticobiliary Cancer

The ReStOre II study will examine if a programme of exercise, dietary advice, and multidisciplinary education can aid recovery following surgery for cancer of the oesophagus, stomach, pancreas, or liver. We hope that the results of the PRE-HIIT and ReStOre II studies will help inform the development of rehabilitative services for patients with upper gastrointestinal cancer. If you would like further information regarding our programme of research, please email us on exerciseoncology@tcd.ie.

The Oesophageal Cancer Survivorship Clinic

Study team: Professor John Reynolds, Professor Narayanasamy Ravi, Professor Carel le Roux, Dr Jessie Elliott, Dr Conor Murphy, Ms Michelle Fanning

The survivorship journey after oesophageal cancer surgery is a difficult one for many patients. A significant amount of research at St James's has explored the impact of surgery on weight and nutrition as well as the potential underlying factors. We have learned that gut hormones, which are released when we eat, may have a role in nutritional issues and quality of life after oesophagectomy.

To expand on this research and drive our clinical survivorship services forward, we established the 'Upper GI Nutrition & Quality of Life clinic' at St James's. The approach is patient-centred with the ultimate goal of improving quality of life. We also aim to continue bringing research and clinical practice in oesophageal cancer survivorship closer together to accelerate progress in both. Based on our knowledge of the major and common difficulties that can occur in this context, the clinic has a main focus on nutrition, but also links with other services to ensure a multi-disciplinary approach to care. Finally, as each survivorship journey is unique, we emphasise a personalised approach in order to best deal with the concerns of each individual. Moving forward, we aim to continue developing research projects that improve our understanding of the issues that occur after cancer surgery of the oesophagus or stomach.

Frequently asked questions

Is oesophageal cancer hereditary?

No, the majority of Barrett's oesophagus and oesophageal cancer cases arise sporadically. This may be as a result of long-term damage to the oesophagus caused by gastroesophageal reflux disease (GORD) or tobacco, and diet and obesity may be relevant, but it is not as a result of a defined genetic abnormality. Only small number of cases (approximately 7%) are thought to be linked with genetics. Overall, no specific genetic predisposition has been identified for oesophageal cancer, so it is very unlikely you can pass it on to family members. Most oesophageal cancer like cancer in general is just bad luck.

How is the 5-year overall survival rate calculated?

The five-year survival rate is the percentage of people still alive five years after their diagnosis. This percentage is calculated based on the survival times of many cancer patients, with all stages grouped together. It does not take into account whether the patient has become cancer-free (in remission) or if the cancer still remains. Your doctor will be able to give you more specific information based on your cancer stage and your individual health background.

What causes weight loss in cancer?

Cachexia (extreme weight loss) is characterised by involuntary muscle loss. Many patients, particularly those with gastrointestinal cancers, have reduced food intake which contributes to weight and muscle loss. However, cachexia is a complex condition and is not caused by reduced food intake alone, and we are only starting to understand what factors control it. Chronic inflammation and altered metabolism are also noted in cachexia, which themselves have multiple driving factors. Abnormal levels of several inflammatory and muscle proteins have been identified in cancer patients with cachexia and it is believed that these proteins contribute to the condition. Research is ongoing to explain the exact role of these factors in the progression of cachexia. Visit this website for more information on weight loss: <https://www.ocf.ie/dietandnutrition/>

Can muscle loss be reversed?

Yes, certainly in most but not all patients. It is possible to manage muscle loss and ideally interventions should start as early as possible. Such interventions would include treating the symptoms that are reducing food intake e.g. administering an appetite stimulant or increasing caloric intake, or starting exercise interventions. However, a big

challenge in the management of muscle loss is reliably detecting it. Currently, muscle loss can only be diagnosed by PET/CT scans. New tests are urgently needed to facilitate monitoring and earlier diagnosis of cachexia. This will allow for greater success in managing cachexia and preventing its progression.

How can I put on weight?

Gaining weight after an oesophagectomy is normally challenging for many patients. Weight gain can be difficult because you may not be able to eat the same amount of food after your surgery, and the way your body takes nutrients from the food you do eat may be less efficient. The focus after surgery is usually to help patients maintain the weight they have. If patients are obese then it is reasonable to allow some weight loss and maintain a healthy weight based on muscle mass. Visit this website for more information on high calorie diets: <https://www.breakthroughcancerresearch.ie/books-new/>

Why do I feel tired immediately after eating?

It is normal to feel a little tired after eating, due to our body increasing blood flow towards the digestive system and reducing blood flow to muscles. This makes digestion more efficient, so our body temporarily slows down some of its other functions while it breaks down the food we've eaten. If you've had an oesophagectomy and you feel tired after eating, but do not experience any other symptoms (such as nausea, dizziness, or sweating), it is very likely that the reason for your tiredness is the one explained above. However, your tiredness is much greater because with an oesophagectomy, your body must work much harder to cope with the food that you've eaten. So, it's normal to feel more tired and tired for longer after eating. Speak with your doctor if you have concerns, or if you experience any unusual changes in the amount of tiredness you feel after eating.

Do patients need to volunteer for clinical trials?

Teams involved in recruiting patients to clinical trials try to ensure that all possible eligible patients are approached to consider becoming involved. However, your doctor will always welcome any questions you have regarding clinical trials and will consider your suitability depending on your cancer type, stage, health history and previous treatment. Not all patients are eligible for available trials. If you are eligible, you may choose not to participate, and this will not affect your future care. For more information, see: www.cancertrials.ie or call Cancer Nurseline Freephone 1800 200 700.

Clinical Trials update



Cancer Trials Ireland, the nation's leading cancer trials network, is sponsoring 2 academic investigator-led trials, currently enrolling:

- CTRIAL-IE 10-14 NeoAEGIS, compares standard chemotherapy with chemoradiation therapy for oesophagus and oesophago-gastric cancer.
- CTRIAL-IE 11-32 Lithium Autophagy Study, evaluates the achievable dose of Lithium added to standard chemotherapy of oxaliplatin and capecitabine for advanced oesophago-gastric or colorectal cancer.

In addition, there are two industry-sponsored trials open:

- CTRIAL-IE 18-12 MK3475-811/KEYNOTE-81, evaluates the outcome of Trastuzumab plus Chemotherapy and Pembrolizumab versus standard therapy in HER2 positive metastatic gastric or gastro-oesophageal cancer.
- CTRIAL-IE 18-30 MK3475-859, evaluates the outcome of pembrolizumab plus chemotherapy versus standard therapy in previously untreated, HER2 negative advanced gastric or gastro-oesophageal cancer.

For further details, please visit: www.cancertrials.ie

Oesophageal Cancer Fund



WE'RE BRINGING
THE GOOD FIGHT
TO A BAD CANCER

The Oesophageal Cancer Fund (OCF) supports research at Trinity College/St James's Hospital

through funding vital supports like biobanking facilities, clinical trial supports (Neo-AEGIS trial) and acting as an important link between researchers and those affected by oesophageal cancer. The OCF has funded the National Barrett's Oesophagus Registry, which has registered 7,210 patients, and stored biopsy samples for research from over 400. This is a unique database and collaborative network involving St James' Hospital, Mercy University Hospital Cork, Beaumont Hospital, St Vincent's University Hospital, the Mater Misericordiae University Hospital and Galway University Hospital. Find out more at: www.ocf.ie

CROSS charity



The CROSS charity supports Cancer Research of the Oesophagus and Stomach at St James's Hospital, funding education, training and vital

equipment and biobanking supports for the Dept of Surgery's Translational Oncology research team. Find out more about our latest research at www.crosscharity.ie



Irish Cancer Society

The Irish Cancer Society is Ireland's national cancer charity supporting those affected by cancer with information, advice and advocacy.

We are the largest voluntary funder of cancer research in Ireland, committed to improving the lives of cancer patients through research. In 2019, the public donations that make our research possible have allowed us to fund the work of over 100 talented professionals in research priority areas including prevention, early detection, better treatments, clinical trials and survivorship. In 2019 we increased our Public and Patient Involvement (PPI) in research activity, training 30 volunteers to review the PPI sections of our research applications. We would like to express our gratitude to all our researchers and PPI reviewers for their hard work and dedication to improving the lives of those affected by cancer, we very much appreciate your contributions. Please keep an eye out for more PPI reviewer opportunities in the future! For more information, visit: www.cancer.ie or call our Nurseline on 1800 200 700.

Breakthrough Cancer



Breakthrough Cancer is an Irish medical research charity. We fund research into poor prognosis

cancers, facilitate collaboration between scientists and clinicians across Ireland and internationally, and accelerate the translation of lab discoveries into new effective treatments. Investment is intended to also enhance facilities with state-of-the-art equipment and ensure that all cancer patients in Ireland can access the most up to date and effective treatment for their disease. Consultant physicians and surgeons collaborate with us across Ireland, voluntarily giving their time to research with the aim of improving the care and treatment of Irish patients. We work with dieticians, researchers and oncologists to create evidence-based cookbooks available for cancer patients who are experiencing cancer-induced weight loss. To order a free copy, visit: www.breakthroughcancerresearch.ie/

ARC Cancer Support



ARC Cancer Support Centres offer a holistic approach to people affected by cancer. Located near the major

centres of excellence for cancer care in Dublin: the Mater Hospital, Beaumont Hospital, St James's Hospital and St Vincent's Hospital, clients are offered psychological, educational and practical support, complementary therapies and counselling services. All services are provided by professional staff and trained volunteers, available to anyone in Ireland and are completely free of charge. See: www.arccancersupport.ie