Symposium Meeting Report: AllCaN Oesophageal Symposium 2024, October 23, 2024.

Location: Durkan Lecture Theatre, Trinity Translational Medicine Institute, Trinity College Dublin, St. James's Hospital, Dublin, Ireland.

Overview and introductions

The All-Ireland Cancer Network (AllCaN) Oesophageal Symposium took place to foster collaboration and exchange insights amongst clinicians, scientists and patient advocates from across the island of Ireland. The symposium aimed to address challenges and advancements in understanding, preventing, diagnosing, and treating Barrett's oesophagus and oesophageal cancer. As a joint initiative across Northern Ireland and the Republic of Ireland, AllCaN Oesophageal strives to unify research and clinical practices in oncology, with a particular focus on patient-centred solutions. The symposium structured discussions around AllCaN Oesophageal's four core work packages: Prevention, Intervention, Targeted Diagnostics, and Novel Therapeutics, providing a comprehensive look at current research and development efforts in Barretts Oesophagus oesophageal cancer care.

In the morning session, **Prof. Jacintha O'Sullivan**, the AllCaN Oesophageal Leader, welcomed attendees and outlined the symposium's objectives. **Prof. Maeve Lowery**, Academic Director of the Trinity Centre Cancer Institute, followed with a presentation on the significance of AllCaN Oesophageal's efforts in enhancing patient management for oesophageal disease. Tomas Adell, Director of Elective Care and Cancer Policy from the Department of Health Northern Ireland, highlighted governmental support and policies aimed at addressing cancer care across Ireland. Finally, Orla Dolan, CEO of Breakthrough Cancer Research, expressed the organization's commitment to funding critical cancer research initiatives, underscoring the importance of cross-border collaboration in driving progress against oesophageal cancer.

Session Summaries

Session 1: Prevention and Intervention

Prevention

Prof. Helen Coleman, Co-Lead of AllCaN Oesophageal, opened the symposium and the Prevention session by emphasizing the significance of population-level strategies for reducing oesophageal cancer incidence. Key presentations included **Dr. Victoria Cairnduff** discussing her progress and plans on the North-South database on Barrett's oesophagus and dysplasia trends across Ireland, highlighting it's potential in cancer risk monitoring and prevention. **Dr. Órla Carney** presented on an innovative diagnostic tool, the Capsule Sponge, which offers an accessible method for detecting Barrett's oesophagus in primary care settings. Moreover, **Dr Carney** involved opinions and views from patients to inform her study. **Ms. Kelly Tang** explored how commonly prescribed medications might correlate with increased oesophageal cancer risk, raising awareness for possible preventive strategies in medical prescriptions. **Ms. Abigail Jeyaraj** shared her project plan into age-based disparities in Barrett's oesophagus and oesophageal adenocarcinoma, with intentions to investigate variations in treatment and survival rates. **Ms. Rachel McMenemy** presented her project plan on environmental

exposures which could be linked to oesophageal cancer, and potentially identifying novel risk factors that may inform future preventive measures.

Anticipated Deliverables for this work package:

- Report on why OAC is a male predominant disease and why there are sex disparities in risk of progression.
- Report on our All-Ireland BO incidence trends & OC survival comparisons.
- Report on the production of an All-Ireland OC histological subtype atlas.
- Report on medication exposures in BO and OAC risk and progression.
- Report on environmental exposures in BO and OAC risk.
- Report on comparison of BO treatments and intervals between population-based data in NI (where healthcare is free as part of the UK NHS), with BO Registry data in the ROI.
- Report on the evaluation of potential barriers and acceptability to use risk prediction tools and screening for oesophageal neoplasms in primary care on the island of Ireland.

Intervention

Dr. Emer Guinan provided an overview of the Intervention work package, focusing on post-diagnosis care and lifestyle interventions. Presentations for this work package included **Dr. Linda O'Neill** who discussed the Upper GI Cancer Survivorship Biobank, developed from the ReStOre II trial, which aims to gather critical long-term data for survivors of upper GI cancers. ReStOre is a 12-week programme comprising exercise prescription, dietary advice, and psychosocial support, developed through an iterative process of stakeholder engagement, and evaluated by a pilot feasibility study, randomised controlled trial as a virtually delivered programme and is currently being evaluated as a definitive intervention. **Ms. Pousali Chatterjee** highlighted how the interplay between the metabolic microenvironment and inflammation may influence oesophageal cancer progression, a project which will also link into the ReStOre II trial (this will be done using the innovative Agilent 6490 targeted mass spectrometer). **Ms. Diana Cooke** outlined her project plan which involves understanding the preferences, barriers and facilitators for exercise in people with Barrett's Oesophagus. With this data she will work with patient representatives to co design an exercise intervention.

Anticipated Deliverables for this work package:

- Report using proteomic biomarker profiling to improve identification of survivors who require dietary support (personalised biomarkers).
- Report on how visceral adiposity or dietary saturated fatty acids augments progression.
- Report on the patterns, barriers & enablers to physical activity in people with BO.
- Report on an intervention for risk factor management in people with BO.

Symposium Discussion 1: Prevention and Intervention Panel

The first main symposium discussion session featured a panel of experts with different backgrounds: **Mr. John Clarke** (AllCaN Oesophageal PPI Panel Representative), **Mr. Peter Browne** (AllCaN Oesophageal PPI Panel Representative), **Ms. Carmel Doyle** (CEO, The Oesophageal Cancer Fund), **Dr. Louise Mullen** (National Cancer Control Programme), **Dr. Damien Bennett** (AllCaN Oesophageal

Collaborator), and **Dr. Frances Drummond** (Research Manager, Breakthrough Cancer Research). They discussed approaches to integrating prevention and early intervention strategies in healthcare settings. Key topics included the importance of public awareness in oesophageal cancer prevention, addressing age and environmental risk factors, and the impact of personalized patient management on early intervention. Patient and public involvement (PPI) was underscored as critical for aligning research objectives with the needs of the community. Questions that came from this discussion session included; we have included draft responses.

- **Do the studies cover Squamous Cell Oesophageal Cancer?** *The current AllCaN structure does not include squamous cell disease, however, this can be incorporated into our wider network structure. However, ReStOre II includes patients following surgical resection for oesophageal cancer and a number had squamous cell oesophageal carcinoma (approximately 14% of total).*

- **Are there any plans to look at calcium channel blockers and their relationship with oesophageal cancer?** *There are no specific plans to do this yet, but the relationship between calcium channel blockers and oesophageal cancer seems to be an interesting area to explore. We will certainly consider it as we continue to refine the network.*

- **Have you any strategies on how you are going to deal with missing data in the registries and quality control?** *Both the Northern Ireland Barrett's register and National Barrett's register Ireland have standard operating procedures in place which trained personnel use to extract core data items from pathology reports (Northern Ireland Barrett's register) or medical notes (National Barrett's register Ireland). Quality checks of the extracted information are carried out a regular basis to ensure data quality. For data items that are not as well recorded within routine pathology reports and medical notes it would be important to explore the cause of missing data to assess if is missing completely at random, missing at random or missing not at random and therefore if techniques to deal with missing data such as multiple imputation would be appropriate. It will also be important to monitor the availability of core data items within medical notes over time.*

- **Can your study Orla be rolled out with GPS in south of Ireland?** *Yes, this will be rolled out in ROI.*

- **Do you think the current clinical guidelines are suitable for selecting patients for capsule sponge testing?** *Based on the current BEST4 trial inclusion criteria- those suitable for capsule sponge testing are Males: 55-79, Females 65-79 with dyspepsia and regular use of PPI or other anti-reflux medications. From a primary care standpoint, if we were offering this test as a screening tool, we would need to clarify those being offered the test would be the same as the trial criterion. From initial interviews by Dr Orla Carney, GPs have mentioned that it is actually quite difficult to gatekeep a test within primary care for example restricting its use for specific age groups. For example- PSA testing is not recommended in men under the age of 55. However, with the recent publicity regarding Sir Chris Hoy's prostate cancer diagnosis, we are having many more young men presenting who want to be tested and these conversations can be very difficult if the guidelines are limiting testing based on age. Use of capsule sponge is*

currently not included in NICE guidelines/NICAN (NI cancer guidelines) or Scottish Cancer Referral Guidelines. If the test was to be implemented in primary care, we would likely need a revision of clinical guidelines to highlight where/when capsule sponge can be used and who would be eligible.

- **Is there any way to look at microplastic consumption and its relation to OAC?** *Due to limitations regarding available methods for quantifying individual microplastic exposure, as well as the difficulty of longitudinal measurement, designing a study to explore any associations between microplastic consumption and OAC risk is challenging. Microplastic exposure has likely seen a rise in recent decades, as has OAC incidence, so a reasonable approach would be to compare trends in their respective levels and see whether there is an overlap. Investigating the presence of microplastics in archived oesophageal tissue samples vs healthy controls may be another approach that could be considered. However, the problem with microplastics is that they are so ubiquitous that determining exposed and unexposed groups could be difficult. There is certainly a lot more work to be done on microplastics and cancer risk and In vitro and animal studies may be a starting point to explore any potential relationship.*

- **Can practice nurses perform the sponge test?** *In theory, practice nurses are able to perform the test. According to capsule sponge manufacturers, training can be completed in one clinic session with 8-10 patients for nurses with no experience of capsule sponge testing. However, treatment room nurses can be employed in one of two ways- either employed by the Health Care Trust and then deployed to a treatment room or directly by the GP practice. Nurses employed by the Health Care Trust often have specific duties that they are employed to do and will not be allowed to perform duties outside of this list. For example, Health Care Trust nurses are not allowed to give flu vaccines as this is not on their list of duties. Therefore, a Health Care Trust would have to agree that performing capsule sponge test would be included in their job plan. Furthermore, trust employed nurses may not always work in the same practice and there can be rotation of nurses within GP practices and so it would be important to consider if a trained nurse would be available regularly or whether there would need to be specific capsule sponge testing clinics. There is more flexibility with GP practice employed nurses. If the GP partners felt this was an appropriate test, they would have to arrange for the nurse to undergo appropriate training and facilitate the testing. The benefit here would be that the same nurse works in the same practice regularly.*

- **RESTORE looks at exercise after surgery but how important is exercise/nutrition before surgery and for patients for whom surgery is not possible?** *Yes exercise/nutrition is important pre surgery and for those in whom surgery is not possible. The PRE- HIIT trial compared a two-week high intensity interval training (HIIT) programme to standard care for patients scheduled for oesophageal or lung resection surgery. The trial is now complete and the data is being analysed for submission to an international conference. Once the results have been published a link to the paper will be provided by the website.*

- **Regarding cytosponge, patients with GORD symptoms may order test and get result privately if don't get from their GP. Are there plans for how to manage these patients?** *GPs in the UK do not usually get involved in private testing results. Guidance from RCGP is that patients who opt to go for private investigations should be advised that all results and treatment required as a result of this should be followed up privately and that patients should be told that that they would need to pay for this. Patients regularly contact their GPs with private test results and there is a lot of discontent in primary regarding this. There is variation between GPs practically about what is done. Some GPs will refer/ treat patients with private testing, but they are under no obligation to do so. With current pressures on primary care, many GPs are taking a hard-line approach and will not accept any private results at all. It's a really difficult area to manage, especially when patients come with concerning results and state that they cannot pay for further investigations/ tests. Overall though, private testing should be followed up and managed within the private sector.*

- **Can exercise cause Barrett's symptoms to get worse?** *Possibly, we must design prescribed exercise regimes that do not make reflux symptoms worse. This is why informed workshops with Barrett's patients will inform this design to positively impact Barrett's patients. We also believe that certain types of exercise performed after eating may increase symptoms and hence why we are doing an extensive, in-depth study of exercise preferences, barriers etc so we can advise on the types of exercise that do not lead to increased symptoms. While typically exercise is extremely beneficial for people with Barrett's, certain types of physical activity can aggravate gastroesophageal reflux disease GERD. High-impact activities like running, jumping, or vigorous aerobics can increase intra-abdominal pressure, potentially triggering acid reflux and causing discomfort. Similarly, exercises that involve bending or intense core engagement, such as certain yoga poses or abdominal workouts, can push stomach contents upward, leading to reflux symptoms. Weightlifting, especially with heavy loads, may also contribute to reflux episodes due to increased abdominal strain. However, low-impact exercises like walking, swimming, and cycling are generally safer and less likely to trigger symptoms. To minimize discomfort, it's recommended to exercise at least 2–3 hours after eating, stay upright during workouts, and wear loose clothing to reduce pressure on the abdomen.*

- **Will intervention include Barrett's patients undergoing RFA treatments?** *Yes, these can also be included. We have yet to design the intervention but at this point expect that patients who have had RFA treatment will be included (but not in the early post procedure timeframe).*

- **What advice would you give to researchers working in other cancer sites who would like to initiate more North-South collaborative working?** *Construct a multidisciplinary team you know will work well together, collaboration is key, so joint trainee supervision structures are key. You must also build on string foundations so you can bring this into the network at the start.*

- **On socioeconomic patterning of cancer, how/where do members of the panel think we can best address this?** *It would involve a multifaceted approach that considers various factors contributing to disparities in cancer incidence, diagnosis and outcomes. Firstly, we need to*

continue developing research studies and data collection techniques that help us to better understand how socioeconomic factors influence cancer risk and outcomes. Then, a collaborative approach is needed to address any disparities found, working with community organizations, healthcare providers, policy makers and patient groups to co-design public health interventions that meet the needs of high-risk populations, including awareness campaigns that focus on lifestyle changes for prevention and the importance of attending regular screenings and being aware of cancer symptoms for early detection. Appropriate support services also need to be considered for cancer patients and survivors including financial assistance, counselling and peer support groups particularly for those from lower socio-economic backgrounds.

- **How can we roll out the capsule sponge but cope with the increase in endoscopy referrals once the device picks up more positives?** *Regarding increase in endoscopy referrals, I think we would need to carefully weigh up the increase in referrals for Barrett's (if we're estimating that 1-2% of the population has Barrett's then we are massively underdiagnosing cases) vs the reducing the number of patients referred for OGD due to negative capsule sponge tests. From speaking to some gastroenterology professionals, the waiting lists are already at all-time highs and they cannot see how they would cope. If we were to use capsule sponge to triage those already being referred for endoscopy then it would likely not have a negative effect on waiting lists but if it is to be used as a screening test in primary care, then I feel that endoscopy services may not be able to cope without increased funding for staff/ lists.*

- **How best do you think capsule sponge testing could be integrated into GP practice?** *Initial interviews are suggesting that GPs feel positive towards the capsule sponge. They like the idea of a practical test that can help guide management, e.g. if negative, they may feel more comfortable managing symptomatically vs referring if they have a positive test. Clear guidelines for use are important- GPs want to know who is eligible, if a capsule sponge will be required before referral (for example like a Qfit), how often we should be repeating the test for patients without concerning features but with ongoing dyspepsia and whether it will be used as a tool to reject endoscopy referrals. Money/ treatment room time/ GP time are concerns- primary care is already stretched at present and GPs are reluctant to take on anything else at a cost to them.*

- **Would all oesophageal cancer patients have had Barrett's present first?** Can we say this is 100% a fact. *This has been debated for some time. A recent study from Prof Rebecca Fitzgerald's group examined tissues spanning the gastroesophageal junction from healthy donors, and donors with Barrett's oesophagus and oesophageal adenocarcinoma using a number of molecular technologies such as single cell RNA sequencing and methylation profiles. From the results, they concluded that oesophageal adenocarcinoma likely arises from undifferentiated Barrett's oesophagus cell types even when the Barrett's oesophagus can't be detected once the cancer is present. Previous work for the Northern Ireland Barrett's register has shown that 7.3% of patients with Oesophageal adenocarcinoma diagnosed between 2003 and 2008 had received a previous diagnosis of Barrett's oesophagus and also that a previous diagnosis of Barrett's was associated with better survival. Therefore, more work is needed to*

identify more patients with Barrett's oesophagus so that they can be entered onto surveillance programme and any further changes can be picked and treated at an earlier stage.

- **What is known about H pylori decreased risk?** *H pylori is associated with a decreased risk of oesophageal adenocarcinoma which is thought to be due to H pylori–induced gastric atrophy, which reduces acid production in the stomach and therefore in turn reduces acidic gastroesophageal reflux which is an established risk factor for the development of Barrett's oesophagus and oesophageal adenocarcinoma. A recent study followed 661,987 individuals up for a median of 7.8years (range 1-24 years) to explore oesophageal adenocarcinoma risk after H pylori eradication therapy. The findings showed that overall risk was not increased after eradication of H pylori and it did not increase over time after the treatment so therefore the authors concluded that eradication of H pylori is safe from a cancer perspective.*

- **For restore samples, what types of nutritional information is collected in samples?** *We collected serum, plasma, and whole blood samples at each of the three key trial timepoints. These samples may be used to look at nutritional biomarkers in the future. The samples have been collected in tandem with the nutritional information collected in ReStOre II including dietary intake obtained by a dietary interview and completion of Foodbook24, a web based dietary assessment tool. Nutrition related symptoms were also obtained by the Gastrointestinal Symptom Rating Scale (GSRS) and the Simplified Nutritional Appetite Questionnaire (SNAQ).*

- **How will you recruit patients to your lifestyle changes for Barrett's patients?** *This has yet to be decided and will probably be trough clinics. We would still also welcome your suggestions. While we are still in the early stages of developing our lifestyle intervention, we are planning a multi-method approach for recruitment. We plan to contact people on the Barrett's Registry directly as well as visiting Barrett's clinics, contacting support groups and charities and an online social media campaign to reach as many people as possible. We plan to work closely with the PPI panel to find any other method they believe would help too.*

- **Is there any serum marker(s) used to diagnose oesophageal cancer?** *There is no current biomarker that can be screened in the blood to pick up OAC.*

Session 2: Targeted Diagnostics and Novel Therapeutics

Targeted Diagnostics

Dr. Richard Turkington opened the Targeted Diagnostics session, discussing efforts to develop precise diagnostic tools for detecting oesophageal cancer at earlier stages. Subsequent to this, **Dr. Debra Higgins** from OncoAssure presented the audience with advanced oncology platforms that offer personalized diagnostics, paving the way for tailored patient care. **Dr. Ciara Durin White** of Deciphex discussed a digital pathology and AI-supported workflow aimed at improving diagnostic accuracy for gastrointestinal cancers. **Mr. Richard Murray** shared his research plan to study the malignant potential of Barrett's oesophagus using morphomolecular pathology, speculating on the use of genetic and molecular markers that could inform cancer risk assessment.

Anticipated Deliverables for this work package:

- Report on the development of a signature predictive of progression of non-dysplastic BO to HGD/OAC.
- Report evaluating if digital pathology features, analysed using artificial intelligence, can predict the development of HGD/OAC.

Novel Therapeutics

Prof. Joanne Lysaght introduced the Novel Therapeutics work package, which aims to innovate and refine treatment options for Barrett's oesophagus and oesophageal cancer. **Dr. Declan Soden** from Mirai Medical discussed Pulsed Field Ablation, a novel, less invasive treatment for Barrett's oesophagus, emphasizing its safety and precision. **Ms. Lorraine Smith** examined the effects of this electroporation technology on Barrett's tissue microenvironment, exploring its potential as a therapeutic intervention with some fantastic insights. **Mr. Sam Cahill** presented his research plan on immune checkpoint signalling in Barrett's oesophagus, with the goal of identifying targets for immunotherapy to prevent cancer progression.

Anticipated Deliverables for this work package:

- Report on the role of intrinsic immune checkpoint signalling across the BO-OAC sequence
- Report on the role of electroporation on the inflammatory tissue microenvironment and immune cell activation
- Report of the role of autophagy and calcium signalling pre and post electroporation.

Symposium Discussion 2: Targeted Diagnostics and Novel Therapeutics Panel

The second symposium discussion brought together panellists **Mr. Mark Kelly** (AllCaN Oesophageal PPI Panel Representative), **Mr. Stewart Dickson** (AllCaN Oesophageal PPI Panel Representative), **Dr. Declan Soden** (CEO, Mirai Medical), **Dr. Aisling** Heeran (Research Lecturer, and **Dr. Oana Deac** (Clinical Panel Expert, St. James's Hospital). This discussion focused on the promise of precision diagnostics and novel therapeutic approaches for improving patient outcomes. Panellists explored challenges in implementing cutting-edge diagnostics like digital pathology and AI, and discussed the potential of immune checkpoint therapies for treating Barrett's oesophagus and preventing oesophageal cancer. The discussion emphasized the importance of expanding access to these new diagnostic and therapeutic options and highlighted the role of patient input in shaping future research directions. Questions that came from this discussion session included:

- **For industry partners, for researchers who may be naive to working with industry what advice would you have for getting started?** *Reach out and have open conversations about how you can jointly come together to work on a collaborative study to impact patients. Each side must bring expertise to the table and clear goals must be set so each party knows what are the expected deliverables.*

- **Can AI tools be used with capsule sponge samples or images or is this too much of a leap at the moment?** *AI is not currently used in routine practice to analyse capsule sponge test samples. The capsule test currently requires a pathologist to review two slides (stained with*

H&E and the immunohistochemical biomarker TFF3). Previous research has suggested that capsule sponge tests may identify up to 10 times more people with Barrett's oesophagus than current practice. Therefore, large-scale screening of at-risk individuals using the capsule sponge would represent a huge challenge for healthcare services with limited resources. Work is ongoing within the wider research community to explore how best AI models could be best used to assist pathologists in the review of pathology samples collected via capsule sponge with aim of reducing demand on the workforce, improving efficiency and freeing up more time to spend on the more complex cases.

- **Could targeted agents be delivered at time of electroporation?** *Electroporation can be administered in combination with other treatments. The idea is electroporation can make the membrane more porous, thus allowing possible better penetration of the treatments.*

- **How can we collaborate more to help speed up translation of biomarkers into clinical practice?** *Acceleration of translation must happen in partnership with industry partners.*

- **If percutaneous thermal ablation (PTA) causes less damage does it have as much effect as RFA/cryo and if so does its impact last as long?** *PFA or Irreversible electroporation which I am investigating has not yet been used on Barrett's patients. However, it is now being used regularly for cardiac ablation in the USA, where heart tissue is pulsed with electric fields to treat arrhythmias. Here, it has shown to be more effective as tissue heals better (less scaring and ulceration) and has a superior safety profile. Furthermore, the pulses can penetrate deeper into the tissue as unlike RFA, it is not limited by collagen nor fat. Initial results indicate improved lesion durability, but further preclinical and clinical studies are necessary to establish the long-term impact of IRE.*

- **What research is needed before IRE will be trialled in larger studies?** *We need to build a significant pre-clinical data package first that will then led to the structure of a clinical trial.*

- **Can AI help with the pathology diagnosis of indefinite for dysplasia?** *Yes, this is what we will be testing in AllCaN.*

- **How do you get over all Data protection regulations in doing AI on retrospective samples?** *Patients will be reconsented if they have not already agreed for their samples and data to be shared with third parties.*

Closing remarks

The symposium concluded with an address by **Prof. Jacintha O'Sullivan**, who outlined the future of the AllCaN Oesophageal network. She discussed opportunities to expand AllCaN Oesophageal's research footprint and the importance of continuing to engage clinicians, researchers, and patient representatives in collaborative research efforts. Participants were encouraged to leverage AllCaN Oesophageal's resources and maintain an open dialogue with PPI representatives to ensure that all projects remain patient-centred. **Prof. O'Sullivan** shared funding opportunities and welcomed new co-funding initiatives for all those across the network. The symposium provided an invaluable platform

for knowledge exchange and highlighted AllCaN Oesophageal's dedication to advancing oesophageal cancer care across Ireland.

This short report briefly captures the core discussions and presentations from the AllCaN Oesophageal Symposium, underlining the network's dedication to prevention, innovation, and improved patient outcomes in Barrett's oesophagus and oesophageal cancer research.