Report:

cancer trials ireland

Together, we're finding answers to cancer.

Cancer Retreat 19.05.23

A half-day event for the clinical oncology community - oncologists (medical, radiation, surgical), haematologists, researchers, research nurses, radiation therapists, teams, & patients

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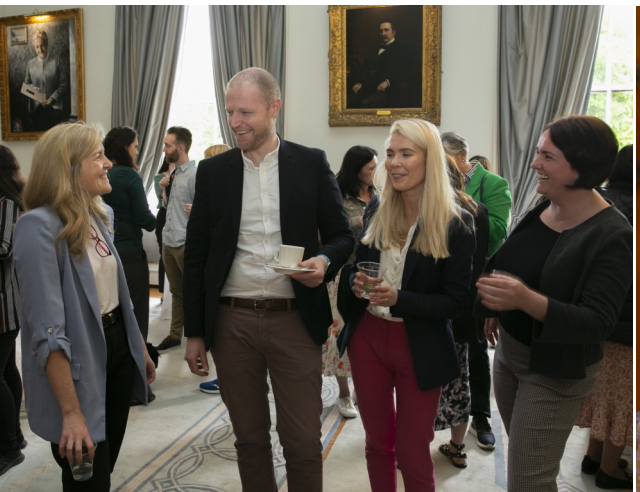
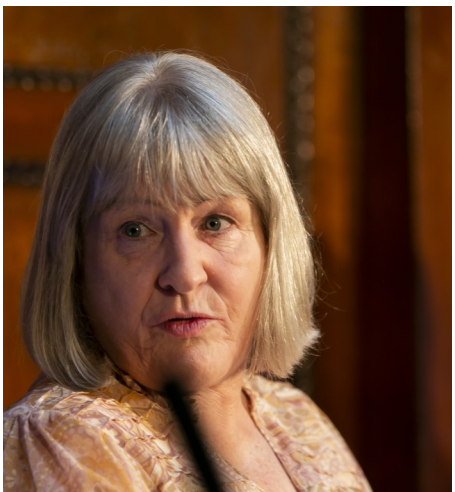
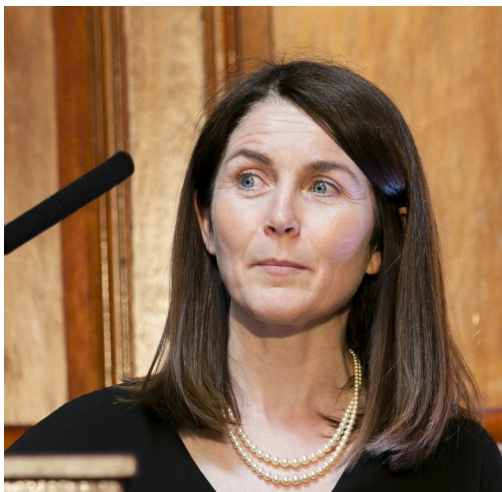






Executive Summary: Prof Seamus O'Reilly

The Cancer Retreat was established in response to the changed funding environment and also as a way of the cancer trials community coming together during the Covid pandemic. It is a focus of reflection about how we can do things better and where we are at the moment.

Cancer Trials Ireland has been hugely successful, helping more than 32,500 patients participate in trials since 2000. This is substantial coming from such a low base but there is scope to do much better. Currently there are 642 members in the organisation and 111 trials open for accrual nationally today, with almost 500 patients enrolled in interventional clinical trials and over 800 in non-interventional trials such as translational studies. The latter are important because they provide the source for the clinical trials of the future. I also want to recognise the new cohort of motivated and ambitious clinical leaders among the DSSGs.

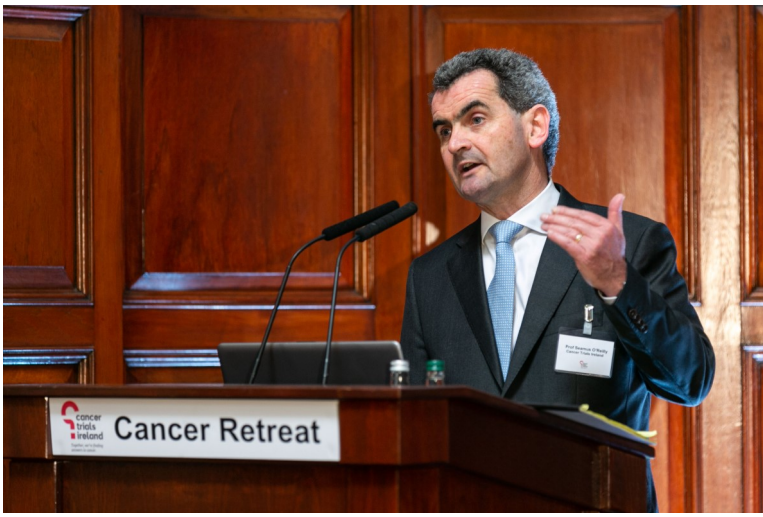
Cancer Trials Ireland enjoys a "strong global footprint", with its global network built up over the past three decades having led to practice-changing clinical outcomes. For example the POSITIVE trial impacts on our conversations with patients every week in the clinic where we are discussing if it is safe to have a baby or not or stop their treatment. Before the POSITIVE trial we didn't have that same degree of certainty for our patients.

The genesis of successful cancer trials takes place over decades, not months. When we look to the future we need to invest in staff, careers and relationships, which will ultimately deliver in our communities but it's not an immediate return on investment. ,The biggest challenge remains access - currently, 19 out of 20 patients cannot enrol on a clinical trial. Our challenge is to make that number smaller.

Barriers include trial logistics, such as data protection and ethics, as well as funding, recruitment and retention of staff, relevance to patients, protected time and succession. On the latter point, the next generation of leaders in Cancer Trials Ireland need to be cultivated and protected. Clinical staff are needed to provide care but also facilitate clinical trials. According to the World Health Organisation, there will be a shortage of 18 million healthcare workers by the year 2030.

Data protection issues continue to impede access to clinical trials and this has a direct impact on access to care. There are 27 data protection offices that each must review clinical trial protocols. The process must be harmonised so that a single review is carried out, said the professor.

Cancer Trials Ireland is spearheading a number of initiatives to address these challenges, such as our involvement with NREC. NREC has shown how centralisation and resourcing can transform clinical trial processes. The national survey of the clinical



trials experience is also an important element of this. We need data to advocate at higher levels to change things to make it more attractive for people to stay in Ireland. Nurturing the next generation of researchers is critical, as the research shows that young scientists are more innovative.

The appointment of a PPI coordinator in Cancer Trials Ireland was a big but necessary step, because it emphasises the importance of quality engagement with patients around clinical trials. Clinical trial accrual and retention improved by 10 per cent in Canada due to the involvement of patients. Patient involvement in any quality improvement project in healthcare is known to increase that improvement four-fold.

Healthcare and climate change must also be a consideration and measuring the carbon footprint of trials is now being explored; "you can't manage what you haven't monitored." This is the beginning of embedding carbon awareness in our system, Prof O'Reilly said.

Collaboration is the engine of change and will lead to better outcomes for patients. Patients must have access to all of the new developments coming down the tracks in oncology over the next decade, not least in the area of AI, where computing power has increased by one million fold in the last ten years. What can that do in a positive way for cancer patients?

Prof Seamus O'Reilly
Vice-Clinical Lead

Seamus O'Reilly

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Together, we're finding answers to cancer.

Keynote: **Prof Risteárd Ó'Laoide, National Director, HSE NCCP**

"Every role is important"

The keynote address of the Retreat was delivered by a warmly-welcomed Professor Risteárd Ó'Laoide, National Director of the HSE National Cancer Control Programme (NCCP). He opened by emphasising how the NCCP is a "strong supporter" of Cancer Trials Ireland research and clinical trials. "Improving access to clinical trials is something for which we all strive." The professor outlined the key work done by the NCCP in "bolstering" staffing levels in recent years, something he said has not only enhanced the service delivery system but has also allowed many clinicians across various disciplines to carve out protected time for clinical trials activity.

For example, as a result of funding provided in 2021 and 2022, the NCCP allocated an additional 400 posts to frontline services, of which more than 60 were consultant posts including 18 medical oncology posts, 10 new haematology posts and seven radiation oncology posts, as well as nursing posts across multiple grades and other allied health professionals such as pharmacists. Importantly, he noted, 48 of these posts were in psycho oncology and survivorship. The NCCP has also endeavoured to support and facilitate the development of academic positions in oncology in cancer centres, which was possible with the support of the academic institutions.

This investment has also allowed the NCCP to develop new programmes aimed at implementing key aspects of the national cancer strategy such as survivorship and cancer genetics and genomics, while strengthening existing services in areas such as prevention. The National Cancer Information System is now in place in 11 hospitals, including four cancer centres, and will hopefully be in situ in six of the eight cancer centres by the end of the year. A number of clinical trial regimens have been built into NCIS, he added, and there has been engagement with Cancer Trials Ireland around the possibility of capturing trial participation information in NCIS.

"But despite all the progress we have made, there remain many challenges and areas for development," said Prof Ó'Laoide. The effect of the Covid pandemic on delayed diagnosis may not be fully clear yet and the research conducted in this area is particularly important, he noted. This is in addition to the demographic impacts of cancer incidence and prevalence. "The key priority for me is to try and improve the dedicated infrastructure and capacity for cancer services." An important aspect of this will be incorporating the necessary infrastructure for research and clinical trials, and the professor said he is working closely with his colleagues at a senior level in the HSE and the Department of Health to try to address the deficits in this infrastructure. Prof Ó'Laoide noted that the NCCP needs to provide more focus on research "in its broadest sense", and expressed pleasure at the recent appointment of Prof Donal Brennan as the national clinical lead for research in the NCCP. "This clinical research leadership will help direct the NCCP's role in supporting cancer research and drive the implementation of the recommendations of the national strategy related to research and clinical trials," he said.

A national cancer research group is now in place in the NCCP and will be chaired by Prof Brennan; the group has representation from the Department of Health, Department of Higher Education, the HSE, the National Cancer Research Institute (NCRI) and the All-Ireland Cancer Research Institute. Key funders of cancer research including the HRB, SFI, and the Irish Cancer Society are also represented, and Prof Ó'Laoide noted there are currently efforts ongoing to collect data on current funding for cancer research in order to identify gaps in this funding, and prioritise activities on this basis.

The professor also noted that recommendation 47 of the National Cancer Strategy calls for the integration of clinical cancer research and the staff who deliver it into cancer services. "The NCCP and the HSE have a role to play in this… we would like to see it progressed both for the cancer patients and also for the highly skilled staff delivering clinical trials and research - every role is important," he told the audience. "These staff need to be supported and facilitated to maximise the benefit of their expertise." He welcomed the survey currently underway with clinical trials staff, noting that the results will be helpful in understanding "how all of us can work together".

Prof Ó'Laoide concluded by saying he believed collaboration will be necessary to maximise Ireland's participation in wider developments at European level, such as the EU Mission on Cancer, which sees proposed implementation of the national cancer mission hubs across the countries of Europe including Ireland. "There is an opportunity for the NCCP and Cancer Trials Ireland to work more closely together in a way that can enhance clinical trials."

CEO: Eibhlin Mulroe

We want to be indispensable to everyone who works in cancer clinical trials in this country and also outside the country

- Eibhlin Mulroe,

CEO, Cancer Trials Ireland

The theme of partnership and collaboration with patients was continued by Eibhlín Mulroe, CEO of Cancer Trials Ireland. She noted that developing the Cancer Trials Ireland strategy 2022-2027 was set buy the Board and a truly inclusive process, finalised only after significant time - of engaging with and listening to patients and stakeholders. The mission of the organisation is to maximise cancer trials access and outcome to prolong patient lives and expand cancer research in Ireland and its vision is an indispensable all-island hub for cancer trials globally recognised for excellence in governance, collaboration and innovation in clinical research. Ms Mulroe emphasised the use of the word "indispensable"; "We want to be indispensable to everyone who works in cancer clinical trials in this country and also outside the country." She noted the increasing level of international cooperation, with Cancer Trials Ireland working with many international research groups. "Very often we are the go-to organisation to run academic trials in Ireland for Europe."

Mulroe also noted that the patients are the most important voice, with patients no longer seen as passive trial participants but as collaborators, bringing their experience as a patient to the scientific process; there have been multiple applications already to the PPI patient consultant committee.

Ms Mulroe told the audience that funding from the Irish Cancer Society will allow Cancer Trials Ireland not only to meet its own trial targets but continue to grow, and importantly, "to stop saying no". "The reality is that the public want more clinical trials and there are many people now fundraising specifically for cancer trials." She also noted the tangible impact of lobbying and advocating for clinical trials infrastructure; for example, the HSE recently approved specific roles in contract management and data protection for health research.

Indeed, there are many positives to reflect on - the numbers of doctors in all disciplines have dramatically increased, and with it their protected time for clinical research, meaning more activity in cancer clinical trials will be seen as a result. The converse of that is that there is more cancer to treat. By 2040 it is projected that there will be 40,000 annual diagnoses of cancer - currently it is 24,000. "We are going to need more trials; we are going to need more research so we are very conscious of that."

STRATEGIC OBJECTIVES:

- *Maximise contribution to National Cancer Strategy*
- *Optimal, stable and scalable talent to serve growth*
- *Position clinical research as a integral part of cancer care through thought leadership, advocacy, and influence*
- *Deliver a compelling "All-Ireland" cancer trial proposition*
- *Financially sustainable and funded for growth*

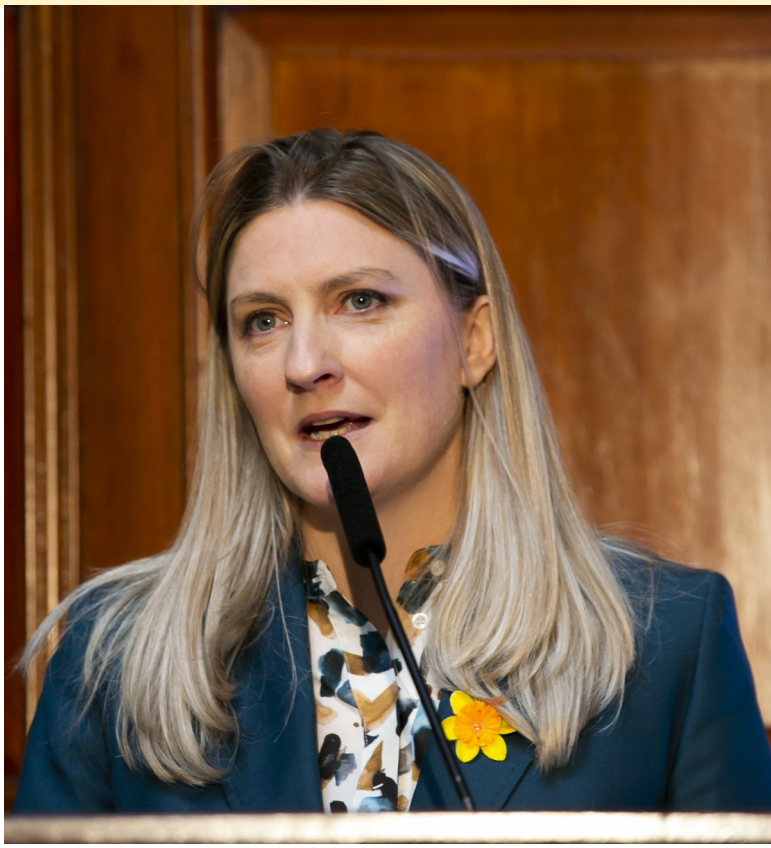
Funding: Averil Power, CEO, Irish Cancer Society

The Irish Cancer Society is passionate about cancer research and trials because research means new discoveries and new treatments, better odds and lives saved, said Averil Power, its CEO. Irish cancer research and global cancer research lost valuable time during Covid, she noted. “It’s really important that we come together now to catch up on that time and deliver maximum benefit for patients… we need to do everything we can to ensure people affected by cancer in Ireland have access to world class cancer research, trials and expertise.”

The Irish Cancer Society is a committed partner to Cancer Trials Ireland and its three year funding and partnership agreement will see the Society invest €1 million this year and for each of the next three years, having increased this contribution from €500,000. “We are passionate about Irish patients having access to cutting edge studies which centre on improvements in their cancer care and quality of life,” said Ms Power, citing the happy case of a breast cancer patient who participated in the POSITIVE trial, which looked at the impact of stopping hormone therapy treatment to attempt pregnancy, and who has now given birth to a baby girl.

As the largest voluntary funder of cancer research in Ireland, the Irish Cancer Society understands the real difference that it makes for patients and their families and the hope that it provides for them, she continued. This is why they also take an important role in advocacy in clinical trials and Ms Power stressed the importance of working together in order to streamline the national cancer trials regulation process. “We don’t want Irish patients missing out in potentially lifesaving international trials as a result of a lengthy approval process,” she said. Central to this is advocating for strategies to improve the recruitment and retention of our clinical trials workforce, and she noted that in 2017 the Irish Cancer Society took the lead in funding protected time for clinician research and this is something they continue to advocate for and support.

Demystifying clinical research for the public is key, and driving wider public awareness and understanding of the potential benefits of clinical trials will help in fundraising efforts. “By making people more aware of the impact our investment in trials is having, we can keep raising money and support CTI more in the years to come,” said Ms Power. This also helps with patient and public involvement (PPI) in cancer research, and she spoke of the need to ensure that the patient voice is “front and centre in everything we do”. “People affected by cancer should be our partners.”



People affected by cancer should be our partners

- Averil Power,

CEO, Irish Cancer Society

Irish Cancer Society

CANCER & CANCER TRIALS IN IRELAND BY THE NUMBERS

€6.9M

In HRB funding over 5 years from Jan 2022

€6.5M

What Cancer Trials Ireland saves government annually in drug costs

40,000

Projected annual diagnoses by 2040

35,000

Patients on trials on the island of Ireland since 2000

24,000+*

Number of people diagnosed with cancer annually

*24,871 - 2019 stats from NCRI

650+

Members

623

Trials since 2000

194

CTI affiliated articles published in peer reviewed journals like NEJM since 2006

82

Practising Haematologists

71

Medical Oncs – 100 needed by 2028

50+

Staff in Cancer Trials Ireland

34

Radiation Oncologists

23

Collab group relationships studies

8

Cancer Trial Groups we work with in Ireland

5

Key Strategic Objectives

€3

What Cancer Trials can attract in investment for every €1 of gov funding**

Figures above current as of May 2023; 24,000 sourced from NCRI where latest figures available were for 2019.

** https://www.cancertrials.ie/wp-content/uploads/2017/01/2016-05-18-DKM-Economic-Impact-of-Cancer-Research-Final-Report-Final.pdf Page 7

PANEL 1

Dr Laia Raigal, Project Manager with the UCC Cancer Trials Group, presented the preliminary results from the survey of cancer trials units, which explored activity and staffing at a hospital level. The survey, which finished recruiting at the end of May, was designed to gather valuable information about clinical trial staff, satisfaction, training needs, perspective and staff retention. "The purpose of this survey was to identify areas for improvements and make changes that can improve the experience of staff in clinical trials in Ireland," Dr Raigal explained.

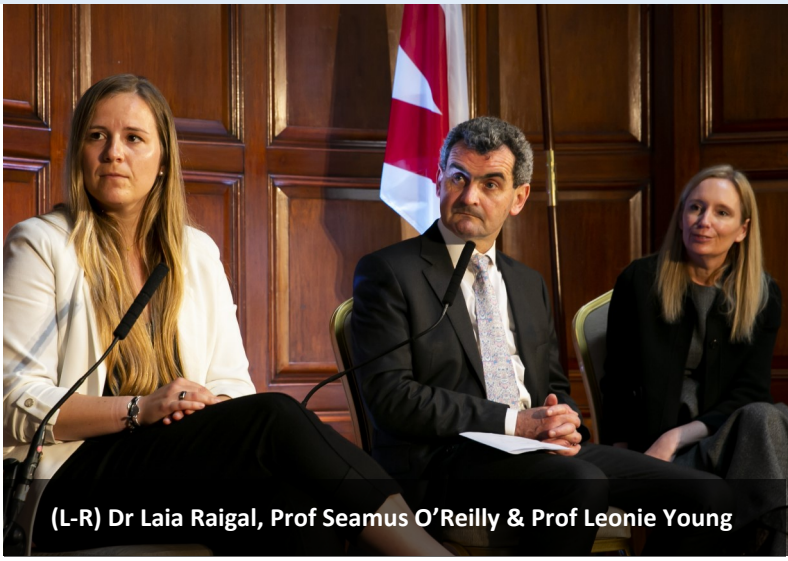
A total of 135 participants had completed the survey so far, although it was due to remain open for another two weeks. One-quarter of the respondents were research nurses and 15 per cent were medical oncologists - some 80% of respondents were hospital-based.

Participants were first asked to rate their motivation - the mean score was 7.1 out of 10, where 10 is "fully motivated". 11% of respondents scored less than 5 and 50% scored between 8 and 10. More than half said they had been promoted in their role, and the main reason was via a promotional pathway in their own organisation but for those who had not experienced a promotion, most attributed the lack of a defined career pathway within their organisation.

In terms of training interests, the most common answers given were clinical trials specific training, IT training and project management. Attending relevant training courses was the number one priority for respondents in terms of their career development needs. Main training hurdles were lack of time, cost and timing/location issues, with most participants saying they preferred a mix of face-to-face and elearning - notably, just five per cent said they preferred to have solely e-learning options.

When asked what were the biggest barriers to staff recruitment and retention, almost a quarter cited the lack of career progression, while 22.34% said non-permanent contracts were to blame. Staffing levels were also a big consideration, with 21% saying this posed a barrier. In terms of barriers to opening trials, almost 29% believed the prompt for staffing was the main barrier, while 17% highlighted ethics decisions as the biggest impediment.

A panel discussion followed the results presentation, with Prof Seamus O'Reilly, Vice Clinical Lead, Cancer Trials Ireland, Prof Leonie Young, RCSI University of Medicine and Health Sciences (Host Institution), and Deirdre Hyland, Senior Research Nurse/Director of Research Nurse Education, RCSI, joining Dr Raigal on stage.



(L-R) Dr Laia Raigal, Prof Seamus O'Reilly & Prof Leonie Young

The results were interesting and somewhat surprising, admitted Prof O'Reilly. Noting that the lack of career progression and non permanent contracts were consistently highlighted by respondents, he admitted he didn't realise these were as big an issue as they clearly were. He also welcomed the huge interest in career development and training, not just in terms of learning the biology behind the cancer but all aspects of clinical trials. The average motivation score was reassuring, in that it showed most people working within cancer clinical trials do like their job, although he expressed concern about the people who scored their motivation as less than 5. The professor also noted that the survey did not necessarily capture the voices of staff who had already left the clinical trials network and doing so would help to provide a broader picture of what improvements are needed. Dr Raigal highlighted the general enthusiasm for the survey - the response in just a week was immediate and huge, with over half of the respondents taking part in the first five days.

Prof Young agreed that the survey provided insight into what is needed to do better and what's working well. On the positive side, she noted the "transformative collegiality" of recent years - "we are organising ourselves as cancer centres like we have never done before", and said that collaborations and partnerships between hospitals and universities is "key to achieving our ambitions in this regard". The "clear aim" of six per cent of all cancer patients on clinical trials is a big ambition, she said, and the hospitals and Cancer Trials Ireland cannot do it alone. Universities will be key players, she said. "All of our hospitals are associated with universities - they have infrastructure and power." Prof Young also spoke of the need to look beyond the traditional interventional clinical trials and look outside that box towards radia-

tion and surgery, while observational studies are also crucial. She echoed Prof O'Reilly by saying data is essential. "We need to ask our patients what they need."

Ms Hyland welcomed the insights provided by the survey, saying the same issues in research nursing are reflected worldwide - this is not solely an Irish problem. The Irish Research Nurses and Midwives Network has been funded by the HRB to carry out research into the problems facing their members. Their report published in 2019 showed that of 143 respondents, just a quarter were working on HSE contracts in permanent posts with increments, and it was assumed that these were the oncology nurses. "The group that were employed in HSE contracts had greater job security and that was very different from the rest of the research nursing and midwifery workforce." She noted, however, that when it came to satisfaction with career progression and education and training, "they were all the same because the same challenges applied to all cohorts". The HRB has now provided funding for follow-up research, and this will be a larger project looking at roles and responsibilities, job descriptions and skills and competencies, and ultimately working with all stakeholders to address some of the challenges that exist. "The key challenges for research nurses and midwives are ad hoc contracts and temporary contracts," said Ms Hyland. While cancer clinical trials units are running for up to 20 years - of their respondents, less than 30 per cent were in post longer than five years. "They have to move between posts the whole time because there aren't permanent posts… we are bleeding skills and experience from the service the whole time." Ultimately it is hoped that the research will find solutions to some of these issues. She also agreed that motivation isn't lacking: "The research has shown that people love the job, love the challenge and find it a very exciting area of practice."

{Cancer Trials Ireland's Deepti Sharma] noted the lack of an MSc programme for nursing in clinical research, either with UCD or Trinity, and asked the panel how this lack of further education opportunities affects career progression and the lack of permanent contracts. Hyland responded that while she would love to see an MSc - even in clinical trial management as this would be transferable across all disciplines - this is a niche area, and building the business case for such an MSc is "quite challenging". While there are a number of MSc in clinical trials or research in universities around the country, they are not tailored specifically to the competencies of clinical research nurses and other clinical trials staff. Some short modules at the RCSI are ongoing in all aspects of clinical research management but they are not linked to an MSc currently - perhaps this could be developed and linked to other existing programmes. Prof O'Reilly agreed that there is a clearly a need for something like this, and suggested that perhaps one centre could take the lead on this and provide online learning rather than cannibalising resources across the country.

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- Deirdre Hyland

Senior Research Nurse/Director of Research Nurse Education, RCSI

Prof Risteard O'Laoide welcomed the survey results and said the NCCP is keen to work with the research team on addressing their findings. Recruitment and retention and what contracts are available is a "complicated but crucial issue" and it requires more stakeholders such as the HSE and the universities working together to address it. An online comment noted that the response to the survey was "fast and honest" because it represented a unique opportunity for staff on the ground to have their voice heard.

The Irish Cancer Society's former director of research Dr Rob O'Connor noted that he was troubled by the significant geographic disparity in the findings and this is reflected in what he said has been called "apartheid" in terms of patient outcomes. "We need to ensure we can raise all boats." It was noted that more responses overall are needed to address the current imbalance in where they come from. Ms Mulroe also noted that hospitals in the west of Ireland are working hard "through a difficult period" to ensure that patients there have access to trials.

Young made the point that it is time for the universities to "step up and use their organisational capacity through education nationally". Collaboration is key, she said, and she agreed that there is no point in having bespoke training opportunities in a single university when this is a common problem - the solutions will come from collaboration.

In conclusion, Prof O'Reilly noted that the pandemic has provided the oncology community a "watershed" and a time to reflect and build better. The trials of the pandemic illustrated "the unity of purpose within healthcare" and he cautioned that this window of opportunity should not be missed.

The second panel of the session explored issues faced by team leaders and trail managers on the ground. The panel was facilitated by Eibhlín Mulroe, CEO, Cancer Trials Ireland, and included: Jo Ballot, Team Leader, Cancer Clinical Research Trust, St Vincent's University Hospital; Erica Bennett, Radiotherapy Operations Manager, UPMC / Bon Secours Cork; and Maureen O'Grady, Trial Unit Manager, University Hospital Limerick

As the discussion begun, Ms Mulroe emphasised the "key role" of the team leader in running clinical trials, and said this important role must be adequately resourced and trained. Ms Ballot noted the unique situation in SVUH in that they have a local research charity so they are able to advertise, interview and hire within their own HR network. While this makes it easier in some ways, it also invites difficulties in terms of career pathways and succession. With a small team of 12 people, they can offer a good starting point for research assistants but cannot offer a long career pathway, she noted, while for research nurses, because they aren't part of the HSE, they can't offer the same career pathway with the same security such as permanence and pension etc. "For future planning, we need to embed ourselves within the hospital structure in order to provide that career pathway and ensure staff retention," said Ms Ballot.

In response, Ms Mulroe asked the question: Who should be funding the nurses working on clinical trials - the HSE or HRB? Ms Ballot explained that they work on studies that are reimbursed by pharma, which represents guaranteed funding to a certain extent. The HRB also offers this, but she admitted that it is an "awful lot of work to procure the HRB funding, as transformative as it has been". She noted, however, that the HRB funding encouraged them to collaborate with the Mater Hospital and while they were initially reticent, this has been hugely beneficial.

As UHL is a HSE hospital, Ms O'Grady noted that the HSE process is "very different", with the entire unit funded by the HSE. The concern with a HRB-funded post is that it is not a guaranteed post past five years, as the HRB funding is based on performance indications. "When you have lots of issues that are not within your power to resolve, it can impact your application," she said. Thus retaining staff can be difficult.

Ms Mulroe suggested that the HRB network could be more embedded within the HSE structures that exist so that people can see the defined career pathway of a clinical research nurse; "this could be a learning from today." Ms O'Grady elaborated on this by suggesting that the title should be standardised across institutions - it would help people applying for these roles to recognise what their exact job will be. For example, a post may be advertised as a CNM2 when really that is just used to indicate a salary level, and it is more akin to a CNS role.

Ms Bennett then offered the private sector perspective. Having worked 15 years in the public sector before joining the private sector, however, she said the challenges of radiation therapists are much more fundamental, as they are not traditionally viewed as being involved in cancer research. Some 50 per cent of cancer patients will need radiation but there are just 12 radiation therapists in Ireland involved in cancer trials, and of those 12 there are only six who are full time equivalents in those roles. "There is a huge mismatch between the patient demand for the service and what we can offer them," said Ms Bennett. It is an area that is massively under-resourced and staffed, and there needs to be advocacy for each profession within the cancer trials community, not only at a local level but at an organisational and executive level too. While Ms Mulroe pointed out that private hospitals see the value in running radiotherapy clinical trials, Ms Bennett noted that in the future, more trials will involve immunotherapies combined with radiation therapy and that will help resourcing. There is a need to focus on the recruitment and retention of highly trained radiation therapists and Ms Bennett said that being involved in clinical trials allows for longer engagement with patients throughout their cancer trajectory.

Ms Simone Walsh from the IRNM commented that "the want for change is real" and explained that she has been appointed as the first programme manager to the IRNM, funded by the HRB. The goal now is to take this data and be a catalyst for change, working on an all-Ireland basis and also liaising with international colleagues to look at the titles and language that is used around research nursing. "This has already begun and is moving ahead quickly."

Ms O'Grady concluded by emphasising the importance of training for research staff in the core competencies of clinical trials, which is a "brand new language". Ms Ballot highlighted the need for a career pathway for the next generation. The panel noted that Irish patients are getting the opportunity to access both homegrown and international studies over the past two decades and there is widespread enthusiasm among the patient community who have shown they are willing to travel to participate in trials.

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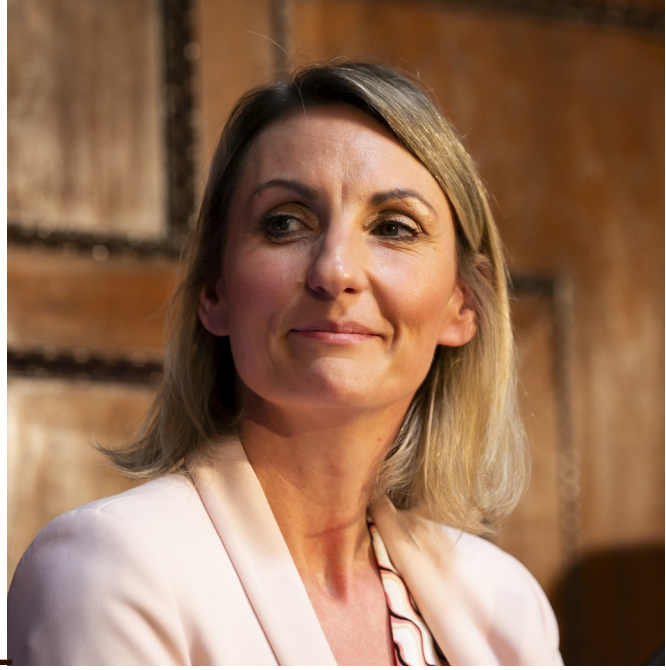
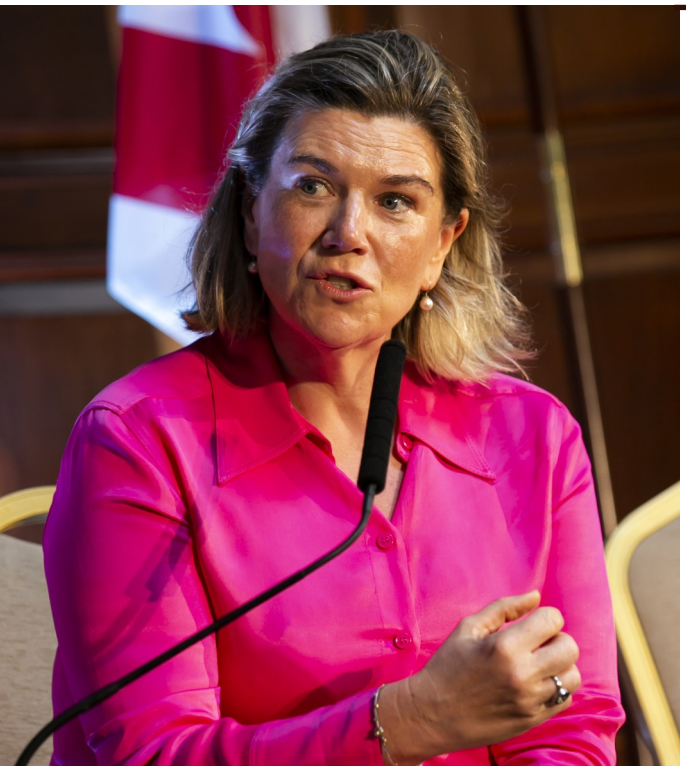
- Erica Bennett, Radiotherapy Operations Manager, UPMC / Bon Secours Cork





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- Jo Ballot, Team Leader, Cancer Clinical Research Trust, St Vincent's Hospital

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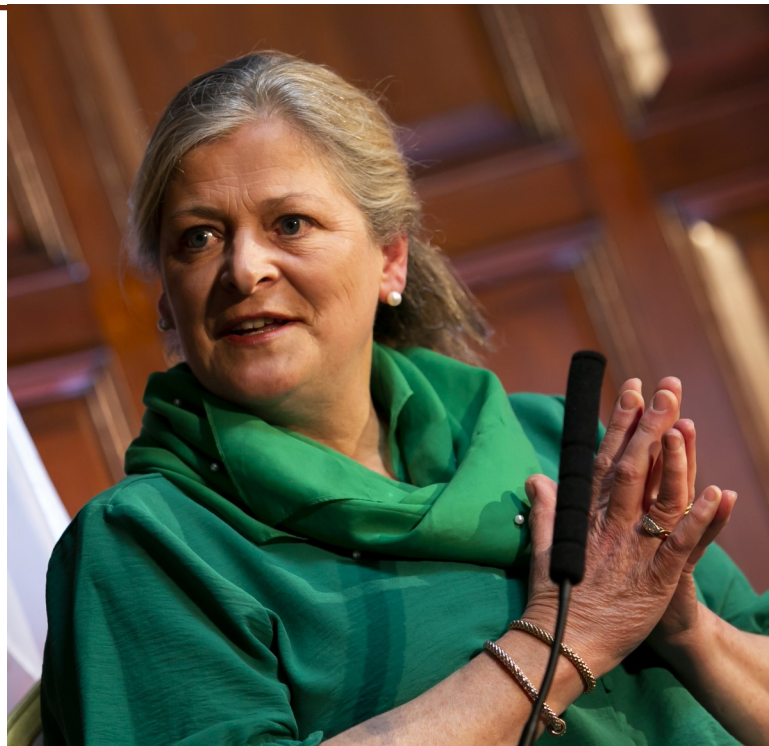
- Maureen O'Grady, Trial Unit Manager, University Hospital Limerick



Professor Ray McDermott, Clinical Lead, Cancer Trials Ireland, facilitated Part 1 of this session, which focused on investigator-led trials. Speakers included: Oonagh Ward, Head of Research and Innovation Infrastructures at Health Research Board; Dr Gavin Dowling, Beaumont Hospital, Dr Stuart McIntosh, Queen's University Belfast; and Professor Peter O'Gorman, consultant haematologist at the Mater Hospital.

People are at the centre of the core functions of the HRB, said Ms Ward as she opened the session, and she noted that this has been a theme of the meeting, in that everyone is working towards meeting patients' needs. The importance of clinical trials is a key element of the HRB's research centre strategy 2021-2025 and it is understood that the appropriate environment and partnerships are needed for this to be able to work. The HRB have taken a leading role in this over the last 20 years, funding a significant amount of clinical trials infrastructure. By connecting hospitals with academic institutions, Ms Ward said, this has provided the expertise and support needed to conduct a clinical trial. "Clinical trial networks are critical to providing the critical mass of expertise and provide a strategic approach to clinical trials within any one disease area."

The HRB also endeavours to support those infrastructures with opportunities to do clinical trials to provide high quality evidence on health interventions. This is the HRB's Definitive Intervention and Feasibility Award (DIFA) scheme, the aim of which is to provide tangible benefits to patients, people's health, and health services through the support of studies. To date, four rounds of funding have given 45 awards totalling €32.5 million.

Definitive intervention trials are offered €1.2 million over a five-year period to conduct a trial which provides a definitive assessment of a proposed therapy or intervention, assessing its efficacy, cost and broad impact. This can be any intervention, from a medical device to a drug to a surgical procedure, that will prevent and treat disease and improve healthcare. Feasibility studies must be done in preparation for the main trial, and outline the likelihood that such an intervention will work, and these are also funded under the DIFA scheme.

When it comes to deciding on who to award funding to, the DIFA panel wants to see the feasibility study for a definitive intervention trial, or clear plans to progress to a definitive intervention if it's a feasibility study, Ms Ward explained. They also have some key assessment criteria: a relevant research question; evidence of public and patient involvement (PPI); appropriate methodology; a strong research team, the capability to successfully conduct the research, and the potential impact of the study.

As the HRB considers its next strategy, Ms Ward said, they will make strategic choices based on the future of investigator-led clinical trials to provide greater funding opportunities. Based on feedback from the clinical research community, the goal is to ensure a greater pipeline of activity from the development of interventions, feasibility, evaluation, and implementation but also as part of predictable funding cycles. The HRB also wants to support novel trial designs, as well as trials utilising real world data, and ensure open and equitable access for diverse populations. EU funding partnerships will also be of increasing importance - the ERA4Health is exploring mechanisms to support multinational clinical trials.

Ms Ward also took the opportunity to announce additional funding from the Department of Health and other stakeholders, which will provide a call for University Hospital Limerick and University Hospital Galway to apply for funding. This so-called "enhancement award" aims to bring them to a level where they can be competitive at the next round of HRB funding, she said. "Access to clinical trials and building up that expertise at a national level is extremely important."

The **SHAMROCK** trial was outlined by Dr Gavin Dowling, who is working with Professor Bryan Hennessy at Beaumont Hospital on investigating a standard chemotherapy-sparing approach to curative-intent treatment. The SHAMROCK trial involves neoadjuvant trastuzumab deruxtecan (T-DXd) being given as response-directed definitive therapy in early stage HER2-positive breast cancer. An antibody drug conjugate of trastuzumab and deruxtecan, T-DXd has a higher drug to antibody ratio of most other conjugates and thus an increased antitumoural efficacy. The pivotal DESTINY-Breast trials demonstrated durable antitumour activity and an increase in progression-free survival and overall survival when T-DXd was given over standard chemotherapy options.

The RNA Disruption Index (RDI) Score will be employed in the SHAMROCK study; a high RDI score essentially correlates with a good response to neoadjuvant chemotherapy, as has been explored in other clinical trials. SHAMROCK will take place across five sites in Ireland: SVUH, CUH, Beaumont, Limerick and Galway and the aim is to accrue 80 patients in total. The primary objective is to evaluate the efficacy of T-DXd in the neoadjuvant treatment of HER2-positive breast cancer using pathological complete response (pCR) as the primary endpoint. Patients will be divided into two outcome groups; those who are successfully treated i.e., achieve pCR at surgery and avoid cytotoxic chemothera-

py, or those patients treated with other systemic therapy in addition to T-Dxd. The study currently has conditional approval from HPRA and NREC, however it also requires approval from the HPRA medical devices unit.

Dr Stuart McIntosh, consultant breast surgeon and researcher at Queen's University Belfast, described the **SMALL** trial, which aims to compare surgery versus vacuum assisted excision for small, early breast cancers. Mammographic screening identifies a significant number of small breast tumours with favourable biology; Dr McIntosh explained that many of these will never progress and would never have been diagnosed without a screening mammogram. It is not a problem of overdiagnosis, he maintained, but "a problem of overtreatment". Research has shown that for every breast cancer death prevented by mammographic screening, a further three patients were overdiagnosed and overtreated. Standard treatment of surgery and adjuvant radiotherapy can be associated with significant complications, and few potential benefits, he said. "There is a need for better, less invasive ways of treating screen-detected breast cancer."

The SMALL trial aims to do this, and is a Phase III, multicentre randomised control trial evaluating whether minimally invasive vacuum-assisted excision (VAE) is an acceptable alternative to standard surgery for screen-detected small cancers (up to 15mm). Patients are randomised to either standard surgery or VAE followed by a radiological assessment and a mammogram, with a real-time second opinion service also available.

It is hoped to recruit 800 patients but the study has experienced extensive delays due to the cessation of screening programmes during the pandemic, as well as global supply chain issues, and is currently at almost 300 patients over 36 sites. Almost all eligible patients are being approached, with a 46 per cent consent rate, "which for a surgical de-escalation study like this is very good", noted Dr McIntosh. Minimally invasive approaches for good prognosis disease are increasingly being investigated but level 1 randomised evidence will be required to change practice, he said. There is already evidence from the SMALL trial that the VAE approach is acceptable to both patients and clinicians with widespread clinician support for de-escalation approaches. In the Q&A, Dr McIntosh noted that the main reasons for decline are the desire to have the standard surgical treatment or surgical staging carried out, and the aim is to carry out patient accept/decline interviews which will further explore these decisions.

Consultant haematologist at the Mater Hospital, Professor Peter O'Gorman, discussed the **Isa-RVD** trial, which is currently accruing. Multiple myeloma is the second most common haematological malignancy, with around 340 cases diagnosed each year in Ireland. The plasma cell disorder is incurable but response rates and survival times have been steadily improving, with a move towards a "functional cure" where the patient receives ongoing treatment but has long-term survival.

New treatments have been emerging, including immunomodulatory treatments, and bispecific antibodies and CAR-T have been approved most recently. Prof O'Gorman explained that the original RVD trial had evaluated the efficacy and safety of a combination of lenalidomide, bortezomib, and dexamethasone in patients with newly diagnosed multiple myeloma; this demonstrated a 93% overall response rate and has since become the standard of care in these patients globally. The Isa-RVD trial will now look at the combination regimen of isatuximab, lenalidomide, bortezomib, and dexamethasone in patients with newly diagnosed multiple myeloma. Isatuximab is an anti-CD38 antibody - this protein is preferentially expressed on plasma cells making it a relatively targeted therapy. The trial is being run in conjunction with the Dana-Farber institute - there are six sites in Ireland and one Danish site, and it is accruing well, with 23 patients recruited in Ireland and 25 in the US so far, with accrual hoped to be completed before the end of 2023.

Sinead Noonan highlighted the rapid pace of accrual in this trial and asked how this could be achieved or replicated elsewhere. Prof O'Gorman cited a focused multiple myeloma group in Ireland that has enjoyed good leadership and support from within the community. He also emphasised the need to choose the sites well and choose the lead investigator well. Elements of the trial can also make it attractive such as drug availability or convenience of therapy or single-arm trials, he added.

During the Q&A, Professor Liam Gallagher, who is co-lead for the All-Island Cancer Research Institute, commented that international best practice in cancer research "closes the loop between basic and clinical research" - while there is investment for interventional trials, there is no funding for translational research and particularly biobanking which is under-serving research and also patients. What is the vision for supporting translational research infrastructure at a national level? Ms Ward said they see the value of this research but made the strategic decision to focus on interventional trials. There will eventually be national plans, however; for example, a national research group is currently looking at what types of trials have been funded to date so that the gaps can be identified. Other funders that should be in this space will also be identified. She also agreed biobanking is critical, particularly as genomics becomes more important in oncology - the HRB has funded the first national biobank in the area of Covid-19 research, which will provide key learnings but she doesn't think the HRB can fund national biobanking alone - a number of different stakeholders will need to be involved.

PANEL 3

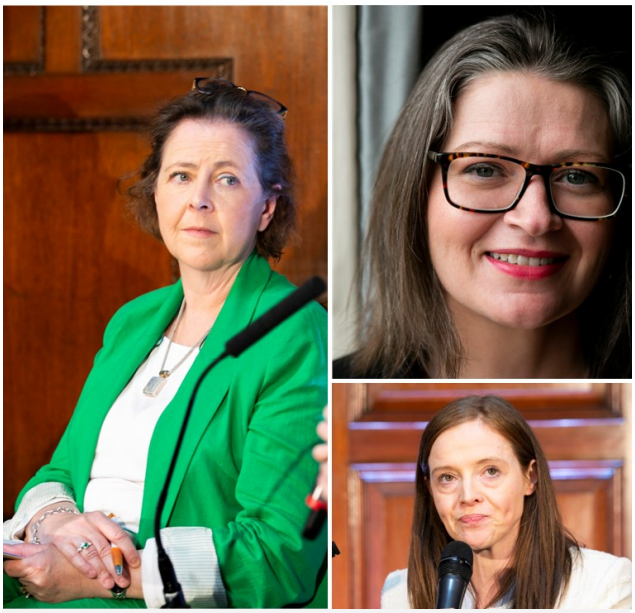
Part 2 of the session focused on public & patient involvement (PPI) in cancer clinical trials. The panel discussion was facilitated by Dr Sarah McLoughlin, PPI Co-ordinator with Cancer Trials Ireland, and the other panellists were Dr Grainne O'Kane, GI DSSG Co-Chair with Cancer Trials Ireland and consultant medical oncologist at St James's Hospital, and Siobhan Gaynor of the Patient Consultants Committee in Cancer Trials Ireland.

The value of PPI in cancer clinical research had been a recurring motif throughout the meeting, and Dr Sarah McLoughlin opened the panel discussion by noting its positive impact on trials but also its growing importance in terms of achieving funding, given that it is now one of the HRB criteria in its grant applications.

The Cancer Retreat had offered an opportunity to reflect on the core values of clinical research, said Dr Grainne O'Kane. She praised the vision for Cancer Trials Ireland, especially the specific focus on governance. Innovation and collaboration with patients is at the core of that. Dr O'Kane also added that she would love to see translational research embedded more in our cancer trials infrastructure, as translational research can ultimately lead to changes in clinical practice.

Her time in Canada had offered her important learnings from working within a different healthcare system, she told the audience. Grant applications in Canada also required a patient partner, and this taught her some significant lessons about the value of PPI. "You can get bogged down in what you are trying to achieve, and you have to always come back to the patient." She admitted that doctors are not good at writing lay summaries, for example, while having the patient perspective on protocol is crucial when it comes to how it will affect them. "The patient being able to live that live protocol is very important," she said. PPI is now integral to every protocol and every trial, and this is wholly appropriate.

PPI can lead to bigger, systemic changes, and Dr O'Kane recalled a memorable patient who passed away from a rare, large liver tumour within four months of diagnosis. His family's request that his tumour was sequenced led them to develop a new signature that they believe is common in patients with both inflammatory bowel disease (IBD) and certain rare liver tumours. The family have since raised significant money - over $1m in Canadian dollars - to create awareness of the need for this research, and were integrally involved in devising protocols for this research. They also sought access to trials for patients with IBD who are often excluded from trials with immunotherapies. Dr O'Kane spoke of how this one patient and his family had made such



Siobhan Gaynor, Patient Advocate, member of the Cancer Trials Ireland Patient Consultants Committee (left); Sarah McLoughlin, PPI Co-ordinator, Cancer Trials Ireland (top); Dr Grainne O'Kane, Medical Oncologist, St James's Hospital (bottom right)

a lasting impression on the trials landscape, despite her initial hesitancy. Dr McLoughlin agreed that many clinicians and researchers can identify with being nervous when working closely with patients as it represents a shift in the relationship. Dr O'Kane said it is often outside the doctor's comfort zone; "it isn't always easy but the benefits are obvious". They agreed that patients are no longer passive - they are organising themselves on social media, and are very motivated and empowered, educating themselves about clinical trials and research. "We change practice for our patients every single day but doctors also need to change and be more open to what patients actually want," Dr O'Kane stated. The Cancer Trials Ireland Patient Consultants Committee is "of huge value", she said and creates a bridge from patients to physicians. Yet she stressed that these groups should represent all patients including very vulnerable groups of patients, and disparities around the country should also be addressed. "It's about supporting people to be around the table and broaden it and bring a wider range of voices to the table."

Living with metastatic breast cancer is a patient-led research project spearheaded by Siobhan Gaynor, who is herself living with Stage 4 metastatic breast cancer. With a background in biomedical research, she could immediately identify "a mismatch between what we think as researchers and what we experience as patients" and realised that she

was potentially in a good position to address these gaps. Yet we need the data to support where the gaps are, and this data is often lacking, particularly in the stage 4 cancer area, as these patients were traditionally excluded from clinical trials. With newer treatments, she and other patients are living longer, and it is not known what is needed to support them at this part of their journey. Ms Gaynor decided that she would collect this data and with the support of Cancer Trials Ireland, she established a patient-led survey focusing on metastatic breast cancer. This was chosen not because it is "her" disease, but rather because it is the most prevalent of stage 4 cancers and has a higher unmet need - it is hoped the survey will be rolled out to other cancers eventually. Various patient groups were brought together to develop the survey questions - the protocol is now completed and it was announced at the meeting that the study had received ethical approval from the RCSI.

This is the first patient-led research project within Cancer Trials Ireland, said Dr McLoughlin, and it is hoped that it will be a model for other patient-led studies. She also noted the support available for PPI, not only from Cancer Trials Ireland but from the PPI-IGNITE Network.

"Innovation happens because there's a need - you have to ask patients what they need and give them the space to give their answers," commented Ms Gaynor. "The reality is that the patient partnership is to enhance what we do and make sure we are doing it in the most efficient way for the best possible output," said Prof O'Kane.

In the past there was a certain amount of cynicism regarding PPI and "tokenistic behaviour", said Ms Gaynor; "but you can be surprised by what patients can deliver for you."

"We change practice for our patients every single day but doctors also need to change and be more open to what patients actually want,"

- Dr Grainne O'Kane, Medical Oncologist, St James's Hospital & Chair of the GI DSSG

Patients are keen to engage in research and bring their own skills and talents to the table, as well as their knowledge of their disease, she added.

Ms Mulroe highlighted the involvement of patients in closed discussions, and how they may need a certain level of confidence to question clinicians on protocols in DSSGs, for example. Ms Gaynor pointed out that patients who become involved are a "self-selecting group - it is not the meek and mild that come forward." Dr O'Kane emphasised the importance of simply offering patients the opportunity to speak at these meetings, while Dr McLoughlin noted that having at least two patients in the room makes a big difference - "providing that peer support can really empower somebody." One mechanism they have recently introduced to gynae and breast DSSGs is a preliminary meeting where they discuss what a trial really means for the patient - this has been an effective tool for introducing the patient voice as they are forewarned and forearmed with their questions.

In the ensuing Q&A, Ashley Bazin, team leader at Tallaght University Hospital commented how "inspirational" it is what Ms Gaynor has achieved. She explained that as it is often the research nurses who approach the patients about getting involved in PPI, sometimes even she is not sure what exactly they are asking them to do. The terminology can be "harsh and brutal" - by discussing progression-free survival etc - the sensitivity around it is lacking sometimes and she worries for these patients. Patients are educated and empowered, replied Ms Gaynor, and it can be surprising what patients already know but agreed the patient commitment could possibly be better mapped out. Dr O'Kane agreed, saying it is clear that patients really do want to know more. She spoke of the implementation of a patient portal in Canada where patients received real time results from their scans. She believed it would not work in practice, but it was "the best thing that ever happened for these patients". The patients who did not want to know, just did not look at the scan results, but those that did came to their next clinic visit prepared and armed with the questions they wanted to ask. Dr McLoughlin noted that Cancer Trials Ireland is developing information on what PPI actually entails and this will be available soon.

Prof O'Reilly concluded the meeting by praising Ms Gaynor's endeavours. "It is an exemplar that will be used across other cancer types and allow us to take better care of people… your work will have a great transgenerational impact and we are very grateful."

The Cancer Retreat had once again been a wonderful success, with much discussed and much to consider, he said. "The benefits of the networks and connections that were established here and the ideas that will come from today will continue to change and improve how we do in the community."

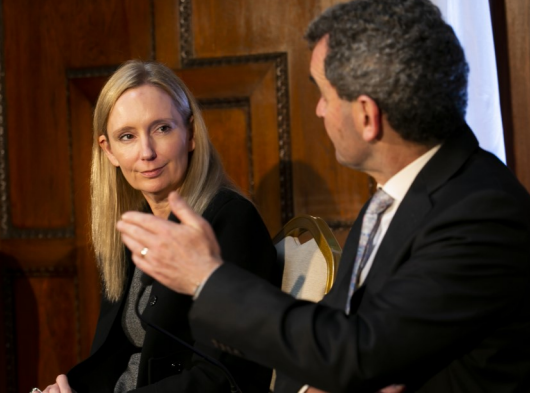
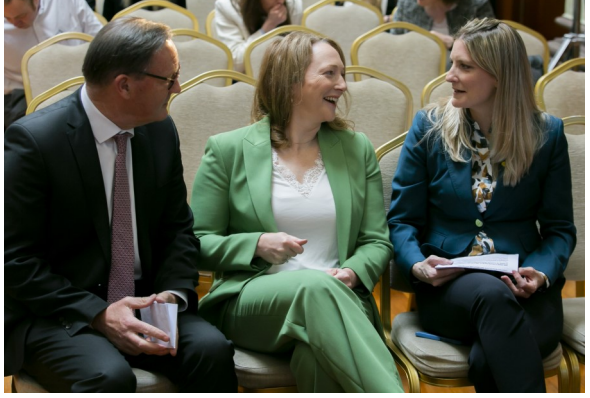
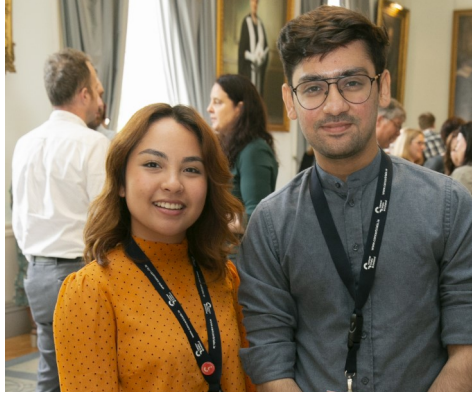
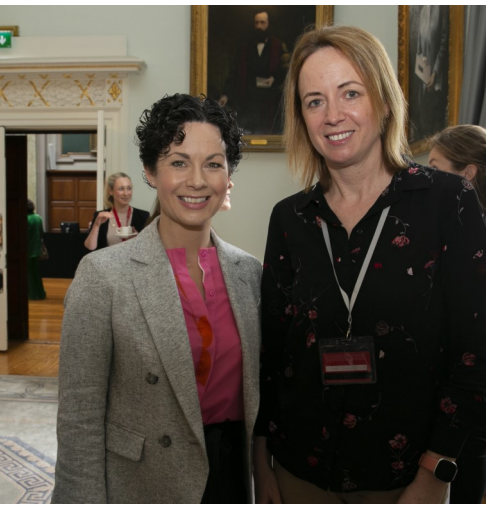
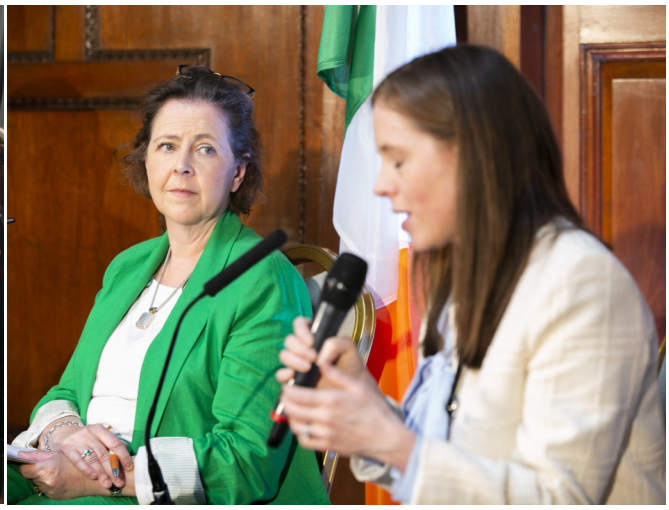
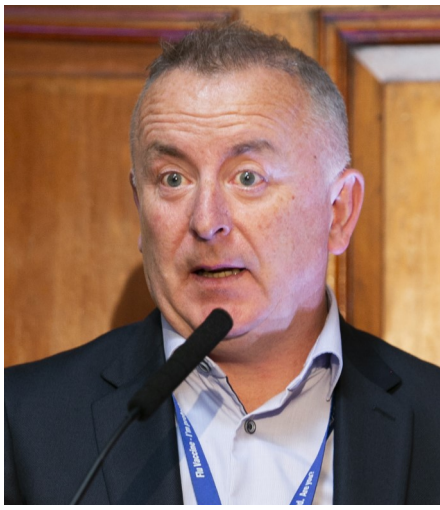
CONCLUSIONS

- **The area of cancer clinical trials has been bolstered by substantial improvements in infrastructure and enhanced staffing in recent years. New funding mechanisms have encouraged collaboration which has been hugely beneficial. Motivation is also high among those working within cancer clinical trials.**
- **Yet there are many areas for improvement. Some 19 out of 20 Irish patients cannot access a clinical trial. Recruitment and retention of staff is an ongoing issue. Inefficiencies in the approvals process mean Irish patients are being denied access to trials because of long delays.**
- **Preliminary results of the Cancer Trials Unit Survey highlight the lack of defined career pathways for many clinical trial staff, a desire for more training and education opportunities, and non permanent contracts. These results were echoed in previous research carried out by the IRNM. Suggestions included training modules provided by one centre that could then link up with other programmes, while it was also proposed that the HRB funded nurses could somehow be integrated into the HSE structures so that job security beyond five years can be offered.**
- **Public and patient involvement (PPI) now underpins all research. This may be new to some clinicians but it is now a requirement when it comes to grant funding and is of significant value. Patients are informed and empowered and wish to make a meaningful contribution to clinical research. It is hoped that the approval of the first truly patient-led research project will lead to many other similar endeavours and provide answers to questions on aspects of living with cancer that no one else is asking. The establishment of the Cancer Trials Ireland Patient Consultants Committee will serve to attract more patients into this role.**
- **A recurrent theme was the need for more translational and basic research, and appropriate funding mechanisms to allow for this. Radiation and surgery must also be considered when building clinical trials infrastructure.**
- **Cancer clinical research is transforming patient lives - whether it is helping them to start a family, saving them from unnecessary treatment or ensuring they receive the newest most effective therapies.**

There are many positives to reflect on - the numbers of doctors in all disciplines have dramatically increased, and with it their protected time for clinical research, meaning more activity in cancer clinical trials will be seen as a result. The converse of that is that there is more cancer to treat. By 2040 it is projected that there will be 40,000 annual diagnoses of cancer - currently it is 24,000. We are going to need more trials; we are going to need more research so we are very conscious of that.

- Eibhlin Mulroe

Cancer Trials Ireland

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Together, we're finding answers to cancer.

The Cancer Retreat was supported by the Cancer Trials Ireland's Just Ask campaign to raise awareness of clinical trials around International Clinical Trials Day, May 19th, 2023. The Just Ask campaign is supported by:

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