

WHAT NEEDS TO BE DONE TO IMPROVE OUTCOMES FOR OESOPHAGEAL CANCER PATIENTS?

An expert roundtable discussion
on issues facing patients and
healthcare professionals

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OESOPHAGEAL CANCER: THE CHALLENGE

“I think there is a bit of nihilism about oesophageal cancer... we see the progress, but we need to inform others that the progress is there.”

Dr Elizabeth Smyth, Cambridge University Hospitals NHS Foundation Trust

Despite being designated by the Less Survivable Cancers Taskforce¹ and Cancer Research UK as one of their four “cancers with substantial unmet need”,² oesophageal cancer has traditionally been overlooked and underprioritised within key national policy frameworks.

In 2016, oesophageal cancer was the seventh most common cause of death in the UK³ and out of the 20 most common cancers in England and Wales, ten-year survival rates are third lowest overall at 12% for men and 13% for women (2010-2011).⁴ Reflective of this, and other high mortality cancers, the Taskforce have set the goal of doubling the survivability of six types of cancer by 2029 – including oesophageal – which together make up over half of all deaths from cancer.¹ However, for this target to be met, change is needed in several key areas and this is particularly true for oesophageal cancer.

The first step to bringing about change is to understand what current barriers to improving patient outcomes exist, by understanding the issues that are facing both patients and healthcare professionals. It is key that this takes into account a whole patient approach, covering

issues around prevention, earlier diagnosis, effective treatment and access to such treatment.

The cancer, much more common in older people (41% of new cases are diagnosed in patients over the age of 75)⁵ is commonly caused by preventable factors, including a diet that is high in salt and low in fresh fruit and vegetables, smoking, obesity, and other medical conditions.⁶ Additionally, according to England-wide data for 2006-2010, the cancer occurs nearly 60% more often in men living in deprived areas.⁷

Oesophageal cancer is an aggressive condition with high mortality rates. It has very high levels of diagnosis at late stages, with approximately a fifth of cases being diagnosed through emergency services.⁸ In fact, 70-80% of patients are diagnosed at either stage III or IV of the disease,⁹ by which point the disease is often too established for curative treatment.¹⁰ Accordingly, mortality rates have risen by over 44% since the 1970s.¹¹ There has however, been some progress, with Cancer Research UK estimating that mortality rates from oesophageal cancer have fallen by around 8% in the last decade.¹¹

“It is a challenging cancer to diagnose and treat. It is a cancer of unmet need, because the outcomes, in terms of survival, are poor and haven’t changed that much over the last five, ten years.”

Professor Tom Crosby, (Chair), National Cancer Clinical Director for Wales

Late stage diagnosis is often linked with lack of early stage symptom awareness, such as heartburn, before the development of weight loss, difficulty swallowing, feeling full after eating small amounts, anaemia and vomiting.¹²

Moreover, following diagnosis, the patient pathway is very complex and prolonged due to the range of professionals involved in the management of the condition, including surgeons, endoscopists and palliative care specialists.¹³ This complexity is exacerbated by the complex diagnostic tests and treatments that cover a range of specialities including medical, surgical, oncological and palliative.¹⁴ Treatment of the condition requires wide-ranging procedures and extensive medication, increasing the volume of patients at fewer centres which, coupled with poor prognosis rates,¹⁵ can make the pathway intimidating for patients.

At present, surgery is one of the few curative treatment options available for a patient, often in combination with chemotherapy or chemoradiotherapy.¹⁶ However, patients need to be healthy enough to be eligible for surgery.

Oesophageal cancer can also result in significant and wide-ranging impacts on a patient's quality of life due to the long-term effects of both the disease and the treatment.¹⁷ These impacts can range from issues with eating and swallowing, to problems with speech, cachexia and fatigue^{17,18}, to the severe side effects of the toxicity of treatments¹⁹ – all of which can have devastating impacts on patients' quality of life.

There is also an issue with lack of effectiveness of treatment options in oesophageal cancer, with oesophageal considered one of the hardest forms of cancer to treat.²⁰ Systemic treatments such as chemotherapy are unlikely to cure oesophageal cancer and as mentioned above, usually need to be used in conjunction with surgery, which commonly leads to side effects such as low blood pressure, myelosuppression,²¹ infection risk and fatigue,²² as well as lung complications including pneumonia.²³ Beyond this, the broad classification of oesophageal cancer treats the disease as a single entity, when in reality the majority of cases are adenocarcinoma or squamous cell carcinoma, which are each quite distinct in terms of risk factors and treatment sensitivities, further complicating patient's experience.

The roundtable therefore provided a forum to discuss systemic issues around patient experience and quality of life, as well as challenges in diagnosis and treatment, with the core objective being to facilitate discussion between key experts working in the oesophago-gastric field to gain their perspectives on the solutions required to improve patient outcomes and experience. It encouraged open discussions on the current barriers in patient care and looked to identify solutions and recommendations to overcome these.

The content and recommendations outlined in this report are based on discussions held during a roundtable focusing on improving outcomes for oesophageal cancer patients. The meeting brought together a broad range of experts

to discuss some of the current challenges facing patients and health professionals across the oesophageal cancer pathway.

A full list of expert roundtable contributors is included as an appendix to the report. This report, and roundtable, was initiated, organised and produced by Bristol-Myers Squibb, with the discussion chaired by Professor Tom Crosby, Medical Director, National Cancer Clinical Director for Wales.

RECOMMENDATIONS

- 1. Diagnostic services are fragile and precarious, with a fifth of patients in England diagnosed through emergency services,²⁴ but are critical in improving patient outcomes.**
 - A significant increase in diagnostic capacity is required in order to introduce a standardised patient pathway. This can only be achieved through recruitment and training of radiologists, pathologists and histopathologists, improved diagnostic infrastructure (such as scanners and endoscopy facilities) and developing more streamlined diagnostic and treatment pathways.
 - Early diagnosis must be prioritised. This will require raising awareness of the disease and a shift to primary care-based tests as well as endoscopy and pathology services.
- 2. Dyspepsia and heartburn should not be ignored and can mask symptoms of oesophageal cancer.²⁵**
 - A targeted health campaign could reach out to those most at risk of the disease. Evaluation regarding the methodology and outcomes for such awareness campaigns are very important. Restrictions/healthcare advice warnings should be placed on the sale of proton-pump inhibitors (PPIs).
- 3. Patient pathways are disjointed and variable, dictated by regional specialties and access to treatments, leading to substantial regional and demographic variation in survival.²⁶**
 - Standardising the pathway would improve access to consistent, holistic needs support and give patient access to care plans, including nutritional support, that can make patients fitter and better able to tolerate treatment. All patients should have access to high-quality treatments and an appropriate standard of care.
- 4. New, effective treatments are emerging, but patients' ability to access them varies regionally or based on patients with a particular need.²⁷**
 - There is a need for a more cohesive system, where patients are able to access treatments and specialists based on what their condition warrants and what could benefit them.
- 5. The hospital referral system does not take into account the variety of patients presenting with oesophageal cancer or the different types of oesophageal cancer.²⁸**
 - Patients are not risk-stratified effectively, hospital appointments are not allocated efficiently. Patients should be triaged as soon as possible to more accurately reflect the differing needs of patients.
- 6. The uniform way of measuring success and successful outcomes is through survival, which is not appropriate for all patients.²⁹**
 - Other outcomes should be prioritised alongside survival. Treatments have high toxicities and can seriously impact patients' quality of life post-treatment. Patients must be stratified post-treatment if effectiveness of treatments is to be properly assessed.
- 7. The current links between primary and secondary care can be disordered. Inconsistent referral advice and referral management schemes from NICE can lead to varying referral patterns, and can damage the quality of the referral process.³⁰**
 - Nurse-led cancer care is important to support patients' holistic needs as well as their physical needs. Increasing access to nurse-led care would provide consistency for patients and reduce the risks of patients receiving inaccurate information from external sources. GPs need to be kept informed on what treatments their patients are receiving so that they can modify the care they provide accordingly.

OPENING REMARKS

8. It is vitally important to raise awareness amongst oncologists that just because a cancer is not curable, that does not mean that it is not treatable.⁴⁰

— Education, engagement and awareness-raising efforts could improve knowledge amongst oncologists and standardise treatment practices.

9. Research needs to be more precise and refined, and unwarranted variation needs to be eliminated.⁴¹

— Research funding needs to be refocused to target cancers with the highest mortality rates, not those with the highest incidence. There is a need to diversify the range of clinical trials available for patients, so treatments' effectiveness can be more accurately gleaned in the real world and provide more equitable access to high quality interventional and observational research. There is also a need to develop Real World Evidence (RWE) to drive improvements in the management of this disease.



**Professor Tom Crosby, (Chair),
National Cancer Clinical Director
for Wales**

Professor Tom Crosby opened the meeting by outlining the rationale for the session taking place. He identified three main areas of difficulty with the treatment of oesophageal cancer. These were defined as:

Quality of life: Professor Crosby highlighted that quality of life not only diminishes as a result of the disease itself, but also as a consequence of the current treatment options available.³² He noted that this was transcendent across treatment options, whether endoscopic, surgical, radioscopy or chemotherapy, all of which are highly invasive and disruptive to patients' lives.

Diagnosis: With oesophageal cancer symptoms not easily identifiable and often symptomatic of a more benign condition,²⁵ the Chair highlighted concerns around the ability to diagnose the cancer early. Professor Crosby added that this in turn makes it challenging to treat the condition due to the disease progression at the point a definitive diagnosis is made. Therefore, raising awareness and screening uptake, supporting primary care and growing diagnostic capacity are crucial to improving survival by ensuring access to optimal treatments.²⁴

Treatment: Professor Crosby acknowledged the inherent problems associated with modern treatments for oesophageal cancer. Beyond the toxicity of treatment options, he noted anecdotally that less than 50% of patients are cured, less than 50% of patients respond to systemic therapies and that under half of patients are able to control the disease via radiotherapy.

PATIENT EXPERIENCE AND QUALITY OF LIFE FOR PEOPLE LIVING WITH OESOPHAGEAL CANCER

The stark reality of the challenge

Mimi McCord, Chairman, Trustee and Director of Heartburn Cancer UK, opened the discussion by sharing two patient case studies to articulate the often-poor patient experience and quality of life for people diagnosed with oesophageal cancer. Whilst distinct case studies, both highlight a number of themes that can be attributed to the cancer, particularly when diagnosed at late stage.

Ms McCord's case studies made clear that the diagnosis of patients was not handled appropriately. They highlighted that at the time of diagnosis, patients can appear and feel in good health, thus exaggerating the impact of the negative news. Furthermore, Ms McCord recounted from one case study that a patient was told to cancel future

plans as treatment would soon become the central focus of their life.

It was made clear that the shock is compounded by a tendency to source further information on the condition through the internet which often references the low five-year survival rates associated with the disease.⁴ Ms McCord highlighted the danger to patients of receiving information from such a source, which may not be accurate or relevant to their case. This is also evident during the patient transition from primary to secondary and specialist care, where the value of continuity of care can be highly valued by patients, even if it is underestimated by healthcare organisations. Responding to such concerns, Venetia Wynter-Blyth (Upper GI Cancer Nurse Specialist) advocated the importance of ensuring patients are assigned an individual Clinical Nurse Specialist (CNS)

CASE STUDY ONE

In 2002, Michael visited a locum doctor complaining of food sticking in the throat after starting to swallow, giving him hiccups, though his complaints were dismissed as only heartburn. He regularly suffered with heartburn and self-medicated, taking antacids "like smarties". Michael later went to his usual GP, who referred him to a gastroenterologist, as well as sending him for x-rays as his breathing was becoming laboured. He was told they expected he had a case of pneumonia. The gastroenterologist arranged for an immediate endoscopy, giving three possible reasons for food sticking the least likely of which was cancer, as he was too young at the age of 47.

Michael was informed bluntly of his diagnosis in three words. "It is cancer". Mimi emphasised the shock and dread that accompanied the unexpected diagnosis, as well as the looming fear of the unknown.

During the endoscopy biopsies were taken which returned inconclusive results, necessitating him to undergo the invasive procedure twice. Scans showed that the disease had spread throughout his body. By this point he was in excruciating pain, which was challenging to manage both in a hospital and home setting.

On treatment, Michael was administered chemotherapy for two weeks, before needing to have this stopped due to the severity of its side effects on his quality of life, such as irrevocable damage to his blood cell count, which forced him to undergo repeated blood transfusions. Michael experienced terrible side effects and co-morbidities, resulting from both the disease and the treatment. These included developing thrush, causing further eating problems, and blood clots, which ultimately caused a stroke five days before his death. The impact of treatment and the disease on Michael reached such depths, that he asked Mimi to end his life.

The burden of Michael's illness did not just fall on his shoulders, but also on those of his wife who, by necessity, became responsible for much of his care with little training, limited disease awareness and lacking adequate support.

Exactly nine weeks after his diagnosis, Michael died. He left behind a wife and two children, all of whom had their lives irrevocably changed by his diagnosis, treatment and death. Mimi firmly believes that if disease awareness had been better, the journey and experience for Michael and his family would have been very different and his death prevented.

CASE STUDY TWO

John was a fit, healthy man who had run over 50 marathons, ate a healthy diet, never smoked and rarely drank. All of which meant that when he was diagnosed with oesophageal cancer in late 2015 via an uncomfortable endoscopy following initial misdiagnosis as an ulcer, it came as a terrifying shock.

Following diagnosis, John searched the internet for his condition, and was immediately struck by its low survival rates. This didn't correlate to his outward physical health; he felt fine and continued to run and exercise regularly. The uncertainty was the worst immediate problem for John, and the lack of clarity on what his future would hold.

After beginning chemotherapy, John was struck by the severity of the side effects, which he found more extreme than the effects of the disease. The side effects were different each time, but included lethargy, cold extremities and nausea. The most striking side effect for John was his difficulty with eating. John then had an oesophagectomy and his cancer spread to his mouth, preventing him from opening it properly. This combination made John keeping himself fed challenging, causing weight loss and impacting other aspects of his physical and mental health.

John's treatment journey was difficult, with numerous types of treatments tried at different stages. The repeated renewal of hope followed by subsequent disappointment was damaging to John's mental health as was the constant anxiety of not knowing what course of treatment would be around the corner.

John sadly passed away in 2018. Before he passed away, John listed the three things he found most challenging in his experience of oesophageal cancer:

1. The continual uncertainty of being presented with hope, only for it to then fade away which is incredibly mentally draining.
2. The physical impact of treatments, which accumulate over time and put pressure on mental wellbeing as well as creating physical barriers.
3. The impact of the disease on personal relationships, the physical and mental symptoms damaging communication.

to reduce this impact, as this can provide patients with a familiar contact who can offer them reliable, accurate advice as well as humanising their experience of health services across the whole of the patient pathway.³⁴

What could be improved?

Dr Ruth Corbally (GP Lead and Facilitator for Powys for the MacMillan Primary Care Cancer Framework) advocated the need for a broader holistic evaluation of patients upon diagnosis, which was agreed by attendees. It was suggested that a thorough evaluation including psychological, economic and other social and medical considerations could be undertaken in order to ensure patients received all of the support they required to maintain a reasonable quality of life, although the additional time constraints that this would place on

healthcare professionals (HCPs) were noted, particularly in the context of workforce shortages, which as of 2018 totalled over 100,000 staff across the NHS.³⁵

Amongst patients diagnosed with oesophageal cancer, Alan Moss, Chairman of Action Against Heartburn, noted the frustration that patients experience at the point of diagnosis from being informed about the lack of curative treatment options available. This is exacerbated especially among cancer patients who have misunderstandings around the intentions of treatment and their overall progress.³⁶ This frustration is by no means exclusive to patients, and affects healthcare professionals as well, potentially affecting the treatment plans patients are given. Mr Moss noted that just 39% of patients are given curative treatment plans, meaning that the majority of patients end up in palliative care.³⁷

He suggested that this can also raise the issue of patients then being moved down a care pathway, either curative or palliative, which can leave a section of patients in 'a grey area' who cannot be appropriately transferred down either pathway and therefore do not receive the correct treatment. This is exacerbated by the lack of clearcut boundaries between curative and palliative care.³⁸ He noted the different impacts that treatment can have on patients, with some experiencing incredibly severe side effects and others less so, meaning that patients may not be being triaged effectively into a treatment programme that could benefit them.

Mr Moss clarified that in order to improve the average experience of patients, diagnosis techniques need to be improved. If patients are able to be identified earlier, prior to their cancer becoming too large or spreading, then their chances of successful treatment also improve,³⁹ helping to reduce anxiety and the mental strain on patients as well as generally improving patient's chances of survival.

“He was in excruciating pain, and there was nobody there.”

Mimi McCord, Founder Trustee, Heartburn Cancer UK

As a consequent of late stage diagnosis, Ms McCord made clear how quickly a patient's quality of life can reduce. In her initial case study, her late husband Michael, Ms McCord highlighted that in the short period of time (nine weeks) between his diagnosis and death, the metastatic disease in his lungs, liver and spine had a significant impact on his quality of life. In this period, he had a stroke, blood clots and thrush in his mouth. Consequently, this resulted in a number of extended hospital stays, with Mike's return home only sanctioned when his pain had stabilised and he no longer needed intravenous therapy.

Pain management was presented as a key aspect of both patient case studies, as was the dramatic impact of chemotherapy on patient experience. A consensus emerged that targeted treatments, such as immunotherapies, could potentially reduce these adverse side effects and improve patients' quality of life. However, patients are not always eligible for these treatments, for example patients who suffer from an autoimmune disease are typically disqualified from immunotherapy clinical trials.⁴⁰

The issue of proton pump inhibitors (PPIs) was a recurrent theme throughout the discussion. Ms McCord strongly advocated the risk presented by PPIs and felt that if she was aware that recurrent heartburn can be a symptom of cancer, she would have urged her husband to get a medical assessment more quickly. Other attendees agreed, with Mr Moss and Professor Russell Petty (Professor of Medical Oncology) concluding that the lack of awareness around heartburn constituted a public health issue, one which Professor Petty felt the state needed to take action on.

Raising awareness

Attendees discussed whether it would be an effective awareness raising programme to legislate in order to ensure PPI's packaging hosted advertising which made consumers aware of the potential link to oesophageal cancer, similar to the advertising linking cigarettes to lung cancer. A broad consensus emerged that this would be a positive development. This could be enacted under Public Health England's (PHE) 'Making Every Contact Count' campaign, in which PHE attempt to encourage behavioural change by affecting the day-to-day interactions that organisations and people have, with the aim of encouraging positive effects on the health and wellbeing of people and communities.⁴¹

It was noted that the challenge with raising awareness of oesophageal cancer is reaching the patient population, which can be unresponsive to awareness campaigns. The typical patient profile would be white, over-50 and male.⁴² Professor Crosby noted the problem that arises from the symptomatic response of oesophageal cancer patients to heartburn medication; repeated treatment of reflux symptoms with PPI's can mask the initial symptoms of oesophago-gastric cancers,⁴³ discouraging patients from further investigation and delaying diagnosis. He noted that as most cases of heartburn are suggestive of more benign conditions, such as gastro-oesophageal reflux disease,⁴⁴ encouraging patients to seek medical assistance prior to trying PPIs would put primary care services under unnecessary pressure, and could prove unmanageable for doctors, hence why PPIs are available to purchase over-the-counter. The problem arises when patients' self-medication continues beyond a short period of time, at which point it becomes increasingly likely that patients are treating a more severe condition. NHS advice suggests seeing a GP if heartburn persists on most days for three weeks or more.⁴⁵

Ms McCord acknowledged that minimising this strain on primary care services was necessary but stated that the public needed to be made aware of the risks of repeatedly taking PPI's and informed that they could be masking the symptoms of a far more serious condition. Attendees broadly concurred, though there is limited evidence that awareness-raising campaigns are always effective. For example, PHE's 'Be Clear on Cancer' Bowel Cancer Awareness campaign, did not ultimately result in a significant increase in the number of bowel cancers diagnosed associated with the campaign.⁴⁶

“If I had known that heartburn could kill him, I would have done something about it.”

Mimi McCord, Founder Trustee, Heartburn Cancer UK

CHALLENGES IN EARLIER OESOPHAGEAL CANCER INTERVENTION: HOW CAN NEW TECHNOLOGIES AND TREATMENTS BE USED TO IMPROVE PATIENT OUTCOMES?

This section of the discussion was due to be introduced and led by Professor Rebecca Fitzgerald, Professor of Cancer Prevention at the University of Cambridge, however due to illness she was unable to attend. Instead it was led by Chair Professor Crosby with Professor Fitzgerald's notes used to guide the discussion.

What technology and techniques are we using at the moment?

Professor Crosby initiated the discussion by noting the issues with existing diagnosis techniques, particularly highlighting the relative invasiveness caused to patients by endoscopies,⁴⁷ as well as the high costs associated with them.⁴⁸ Attendees noted the lack of a clear correlating factor associated with occurrence of oesophageal cancer and while lifestyle factors such as drinking alcohol, smoking and eating unhealthy diets do seem to aggravate the risk of contracting oesophageal cancer, it does not have a direct causal link like other cancers do,⁴⁹ for example the correlation between smoking and lung cancer.⁵⁰

Building on this discussion, Professor Crosby noted that current endoscopy referral patterns can vary greatly, which can affect patient outcomes from oesophageal cancer, particularly considering the rapid increase in capacity pressure regarding endoscopies.⁵¹ The establishment of clearer guidelines for endoscopy referral could help to resolve this concern, though Professor Crosby acknowledged both the cost implication and the high return of negative endoscopy results that would be associated with higher referral rates. Current NICE Quality Standards⁵² do not advocate the routine use of endoscopies for patients with Barrett's oesophagus and Ms McCord queried whether this was appropriate. Consensus was that there is relatively low correlation between Barrett's oesophagus and oesophageal cancer⁵³ and changing this advice could substantially increase the pressure on endoscopic service teams.

Implementing new diagnostic practice and technology

This discussion prompted conversation on the need for more effective triaging of patients in oesophageal cancer, based on the costs and discomfort of additional testing. Professor Fitzgerald's notes promoted the need to implement more targeted checks on a less widespread basis, for example by implementing specialised diagnostic tests such as Transnasal endoscopies, breath or blood tests, or the Cytosponge,⁵⁴ though she noted that some of these technologies were still developmental and not ready to be taken up across the NHS. Professor Mukherjee explained the recent Best3 study⁵⁴ for Cytosponge, which was primary care specific and tested over 3000 patients who were over 50 years old and had been prescribed PPI's for over 6 months. The test revealed that Cytosponge had a relatively high sensitivity, potentially demonstrating its potential as a screening tool at the primary care stage for patients. The ability to triage patients effectively at primary care could dramatically improve the rates of patients diagnosed at earlier stages of the disease, as well as reducing the need for invasive, painful endoscopies.

Due to the short time-scales involved in oesophageal cancer, the discussion centred around uptake of more effective diagnostic technologies at primary care facilities, though Dr Corbally noted the time constraints that GPs are under given rises in demand,⁵⁵ as well as the high diagnostic thresholds that must be achieved for medical devices to be used to investigate possible cancer diagnoses. However, considering the increase in staff and equipment that an increase in diagnostic activity would necessitate,⁵¹ new technologies may be a necessary step to improve early diagnosis rates.

Dr Corbally also noted the variation in standards and expectations on whether primary care health professionals should refer patients frequently or not. Current NICE Quality Standards do not advocate the referral for endoscopy of patients with Barrett's Oesophagus for example,⁵² though following the introduction of the Bowel Screening Programme in 2005, GPs were encouraged to refer a greater proportion of patients, leading to a marked increase in the number of colonoscopies and flexible sigmoidoscopies.⁵¹ She queried whether changing advice from NICE could discourage GPs from knowing whether to refer patients or not. Other attendees concurred and agreed that the existing NICE referral summaries are not clear enough, and that they could benefit from being more explicit and useable. Mr Moss noted the importance of heartburn as a symptom of oesophageal cancer and suggested that primary care professionals could benefit from further training on this connection. However, he acknowledged that GPs already absorbed a large burden of the work on diagnosing patients as part of their 'gatekeeper' role and recognised that it may not be appropriate for GPs to refer all patients suffering from heartburn on to a specialist due to the strain on secondary services.

Ms Wynter-Blyth moved the discussion towards the patients right to be involved in the decision-making process following referral. She noted anecdotally that many patients who are referred under the two-week wait system are not aware that they are on this referral pathway and are being assessed for cancer, leading to patients not being aware of their cancer risk prior to diagnosis. Professor Petty agreed, concurring that patients would benefit from increased assistance navigating the complex patient pathway, and more knowledge to assist them in this. Dr Corbally noted the advice of MacMillan Cancer Support, in the MacMillan Rapid Referral Guidelines which recommend urgent referral for endoscopy within 2 weeks for suspected oesophageal cancer for patients presenting with dysphagia (at any age) or if aged 55 or over with weight loss and upper abdominal pain, reflux, or dyspepsia. The MacMillan Cancer Quality Toolkit for General Practice encourages discussion and communication with patients and their families when they are referred on suspected cancer pathways. MacMillan's research later found that 71% of patients were very satisfied with the opportunity to discuss their cancer and the state of their health.⁵⁸ Rather than just acting as a warning, discussing with patients that they are being referred through an urgent suspected cancer pathway can prepare them for further discussions and additional investigations that may be required, as well as emphasising the importance of attending the appointments.

The need for a multi-specialism approach to address variation

Regarding the relatively poor diagnosis rates of oesophageal cancer, Professor Rob Goldin (Professor of Liver & GI Pathology) highlighted the major role that pathology plays in the diagnosis and treatment of cancer,⁵⁹ as well as the increasing demand on the services, in terms of volume and complexity.⁶⁰ He suggested that the establishment of a centralised review process by histopathologists, where a centralised group of specialists were sent samples of high-risk patients' biopsies, could improve diagnosis rates. He also proposed that the establishment of such a process could reduce the time taken to diagnose oesophageal cancer by streamlining the complex patient pathway, and accordingly improve patient outcomes. Attendees agreed that patients should be given a CT scan while awaiting histopathology or biopsy results, again to expediate the process and streamline the process of diagnosis. Clarity on diagnosis would also help the patient navigate the pathway as well as allowing healthcare professionals to provide more accurate advice.

Ms Wynter-Blyth also raised the disparity in availability of Clinical Nurse Specialists (CNSs) at hospitals, which can result in patients being unsupported through the pathway. She built on comments made during Ms McCords case studies regarding patients sourcing information online as evidence of the need for a CNS to be present at the time of diagnosis. This would enable patients to be provided with credible information at the time of diagnosis and pointed towards further information from accredited sources. Attendees agreed that frontloading this support resulted in a proactive rather than a reactive role for CNS', which can be beneficial for patients who may be disoriented and frightened following diagnosis.⁶¹ It was felt that the role for CNS' was extremely important and should not be deprioritised as the NHS faces continuing funding challenges.

Dr Corbally noted that an important part of the success of the development of the National Optimal Pathway would be the role of key workers, particularly CNSs. A patient having access to a keyworker provides them with a single focal point for their interactions with the health care systems, which is reassuring. CNSs can also provide patients with consistent access to holistic needs assessments, key workers (such as oesophago-gastric dieticians), and ensure patients have access to recovery plans that provide them with support throughout their journey.

Ms Wynter-Blyth described her personal experience with patients, wherein patients who came to her centre had not been provided with an appropriate support network or information base. This meant that initial consultation with their CNSs necessitated a 20-minute debrief to discuss the patient pathway with them and ensure that they were on the correct pathway.

Krishna Moorthy (Upper GI Consultant Surgeon) highlighted the variance in quality of care, and attendees agreed that a consistent format needed to emerge which could standardise care pathways, though this needed to be balanced against the rapid uptake of new innovations as they emerged. Attendees also agreed that patient access and treatment from a specialist oesopho-gastric dietitian was very important to outcomes, and that diet was frequently cited as one of the factors oesophageal cancer patients struggled most with.

Professor Mukherjee noted the variance in the patient pathway. This variability exists across the pathway, from where diagnosis occurs; to how patients are referred; to how staging investigations take place and how long it takes for these to be undertaken. Professor Crosby concurred, and highlighted his work on the 'Single Cancer Pathway',⁶² which attempts to standardise the pathway for all patients from the point of diagnosis in Wales. Attendees acknowledged the importance of ensuring innovation and some tailored variation is still incorporated in this, to enable patients' holistic needs to be addressed, but attendees did not feel that a standardised pathway would interfere with delivering this type of care. Professor Crosby highlighted the National Optimal Pathways that have been created for other types of cancers, including colorectal⁶³ and prostate cancers,⁶⁴ and stated that an Optimal Pathway is being developed for oesophageal cancer, which could help to remove clinical variation for patients. He called on stakeholders to ensure that they participated in the development of the pathway and to provide constructive feedback, to ensure patients are properly supported and treated throughout the patient pathway.

TREATING OESOPHAGEAL CANCER

This section of the discussion was introduced by Professor Russell Petty, Professor of Medical Oncology at Dundee University, who began by providing an overview of the treatment landscape and existing challenges in the treatment of oesophageal cancer.

What treatments are being used currently? Are they effective?

On treating oesophageal cancer, the importance of histology and correct identification of the location and sub-type of cancer (squamous cell carcinoma or adenocarcinoma) was identified, with attendees highlighting that treatment options can be significantly held back by lack of information on the biological makeup of cancers. Different types of cancers have diverse histological types and clinicopathological features,⁶⁵ which can impact the efficacy of treatments. Attendees, particularly histopathologist Professor Rob Goldin, concurred, agreeing that the current methods of analysis of oesophageal cancer undertaken prior to treatment are unsatisfactory and could be damaging to patient outcomes. A consensus emerged on the unsatisfactory efficacy of standard biopsies, which take individual point samples and can therefore fail to capture heterogeneity which could impact on the effectiveness of treatment.⁶⁶

Accordingly, it was agreed that molecular biology is still an area in which considerable progress is required in order for effective treatments to be developed for oesophageal cancer, particularly considering the differing biologies of the cancer types.⁶⁵ To highlight this, the differing etiologies of adenocarcinomas and squamous cell cancers were noted, as well as the differing factors associated with their development. The fact that the different types of oesophageal cancer are essentially separate diseases inflicting the same organ has not been properly reflected in treatment regimes in the UK.⁶⁷

Professor Petty went on to explain that if it can be diagnosed early enough, effective treatment options do exist for oesophageal cancer, however some treatment options have not advanced at equal rates to others. He added that the most common form of modern chemotherapy used for treating oesophageal cancer is very similar to that used in 2002. This was not an issue that was replicated across other cancer indications,

and instead was a result of the relative complexity of classification of carcinomas involving the gastro-oesophageal junction.⁶⁸ Attendees agreed that the treatment standard, where curative options are so limited, needed to be improved more broadly across the UK.

Building on this discussion, the toxicity of current treatments was raised as the crucial factor that makes the treatment of oesophageal cancer patients so difficult. Professor Petty highlighted the small proportion of patients that are eligible for second-line or third-line treatments due to their deteriorating health condition and explained that this made it very difficult to treat patients. As evidence for potential second- or third- line treatments is hard to come by and inadequately summarised, it can be difficult to inform decision-making in clinical practice. Highlighting this, the 2018 National Oesophago-Gastric Cancer Audit found that 39% of oesophago-gastric patients were given curative treatment plans, but only 21% submitted a curative surgery record,³⁷ suggesting a large proportion of patients originally scheduled for surgery had 'dropped off', due to complicating factors such as the implications of treatment regimens on patient health.

“Toxicity is a major concern with these types of treatments [chemotherapy and radiotherapy]... and significantly limits the options available and outcomes for many of our ‘real world’ patients across the UK.”

Professor Russell Petty, Professor of Medical Oncology, Dundee University

What problems exist with treating oesophageal cancer patients?

Attendees noted that the limited number of patients eligible for second or third-line treatments coupled with the rapid progression and poor prognosis of the disease makes developing new treatment options difficult.⁷⁰ Professor Petty stated that while patient responses to new treatments, such as immunotherapies, were often more robust than reactions to traditional chemotherapies, it was difficult to measure this response meaningfully, as patients are frequently unable to continue the treatment for the amount of time (around two months) which it takes to record a meaningful response, due to the rapid progression of the disease – especially in second line and beyond setting. However, Professor Petty clarified that technological developments, including improvements to the genomic landscape and biomarkers,⁷¹ the advent of new tools such as liquid biopsies⁷² and the development of sophisticated studies, as well as the increasing incidence, are all helping to build a better biological understanding of the disease.⁶⁷ This could lead to an increased role for new treatment types including immunotherapies, and predictive biomarkers to make treatment selection more precise as it aims to create a better data set from which efficacy can be more accurately assessed.

Attendees, particularly Professor Mukherjee, explained that the toxicity of treatments combined with poor patient outcomes and the quick progression of oesophageal cancer also plagues the advancement of clinical research, as proving the effectiveness of new treatments can be time-consuming and expensive,⁷³ and patients under review in trials' survival rates are often too poor to demonstrate clinical responsiveness to testing. This lack of documented outcomes meant that no consensus had emerged on the optimal treatments or treatment pathway for oesophageal cancer patients, leading to a regional disparity in treatment options, carrying over to clinical outcomes. Participants agreed that ad-hoc decision-making on patients next steps based on a quick clinical assessment is a result of sub-standard pre-operative treatment or assessment. Mr Moorthy suggested that a more effective way of creating a consensus on treatment

options would be a risk-stratification system of patients based on their response to pre-operative treatment.

The approach to how treatments are offered to patients can be reliant on local expertise, or on guidance from regional multi-disciplinary teams (MDTs), removing the element of patient choice from the treatment regime. This variance is amplified by clinicians' lack of consensus on what treatment options are the most effective, as well as which are the most suitable in which cases. This is reflected in the variation in treatments employed around the UK, as well as in the resultant patient outcomes, and is demonstrated in the 2018 Oesophago-Gastric Clinical Audit,³⁷ which showed variation in care for oesophageal cancer across England and Wales, for example through the choice of palliative modality. Local variance can have a drastic impact on which treatments patients receive, and how they respond to them, but lack of clinical consensus can equally drive divergence in standards. The lack of consensus on treatment in the UK could be explained by a workforce which is not aware of the benefits of alternative practices, or properly equipped to offer or deliver it.

Mr Moorthy highlighted that surgical outcomes have improved quite dramatically in recent years, particularly due to initiatives like the World Health Organisation's Surgical Safety Checklist,⁷⁴ which Mr Moorthy assisted in underpinning the research for. While Mr Moorthy acknowledged that there was still scope for improvement, he felt that the field of surgery deserved more credit than it got in the treatment of oesophageal cancer. This feeling was shared across the group, and it was felt that the imagery of surgery needed improving, which could potentially result in more patients being operated on when appropriate for them.

Another treatment issue that was highlighted by the group was the high local recurrence rates associated with oesophageal cancer⁷⁵ which is often associated with unpleasant and hard to control symptoms. This problem is universal following surgical, chemotherapy and radiotherapy treatments, and is exacerbated by the lack of targeted treatments that exist in oesophageal cancer. This local recurrence is most pronounced in patients who have been treated with chemoradiotherapy,⁸⁰ which Professor Petty estimated had around a 60-70% local recurrence rate. The lack of targeted treatment options for recurrent cancers was a particular concern for the

attendees, due to the toxicity of treatments, which is amplified by the inability to target these treatments at particular areas of concern and the high recurrence rates, particularly among patients whose cancers are HER2 negative.⁷⁶ Accordingly, attendees felt that there was a great demand for more effective adjuvant treatments to complement other treatments and reduce the currently unmanageable recurrence rates.

Another factor that was raised for consideration was the potential separation of patients based on age. On average in the UK between 2013 and 2015, over 40% of new cases of oesophageal cancer occurred in people aged 75 and over.⁴² Elderly patients require different types of treatments to younger patients, and attendees felt that developing separate treatment standards accordingly would improve patient outcomes. Professor Petty reflected that this type of stratification could also be welcomed in research, where there is a lack of diversity in trial subjects, particularly regarding age, leading to a deficiency in knowledge of how treatment options will affect sub-sections of patients. Professor Crosby highlighted the Oelixir project,⁷⁶ an ongoing effort to establish a genetic catalogue of patients in order to assess the most effective methods of treatment for individual patients, creating a form of personalised medicine.

“Co-morbidities are massive with this disease, and the ability to be able to tolerate the treatments.”

**Professor Tom Crosby, (Chair),
National Cancer Clinical Director for Wales**

How can we improve the way we treat patients?

On moving forward with patient stratification, Mr Moorthy suggested that the development of an increased role for neoadjuvant chemotherapy could be used to assess patient's suitability for surgery and more strenuous treatments. Attendees felt that patients were being misclassified according to their perceived ability to tolerate aggressive treatments such as 3 drug chemotherapies, based on subjective ad hoc decision making by health care professionals. This is mirrored in other cancers, such as colon cancer where a study showed that around 40% of patients in their 70s did not receive adjuvant therapy after therapy⁷⁸ Increasing the role of neoadjuvant treatment could more accurately stratify patients for prospective treatments, as well as building an evidence base for how patients should be treated, eventually leading to a consensus and minimising variation in treatment options provided.

The provision of palliative care was a factor which attendees felt limited patients access to the most effective treatment regimes for them. This resulted from the same issue as above; misclassification of patients based on individual decision-making by HCPs rather than a coherent unified system existing for patient stratification. Within palliative care, Professor Petty anecdotally noted that around one third of patients receive chemotherapy, around a third receive supportive care only, and the remaining third were split fairly evenly between radiotherapy and endoscopic treatment. However, as with other aspects of treatment, this was largely variable. Professor Petty estimated that across the country, the number of patients in palliative care receiving only supportive treatment, as opposed to anything more robust, differed by as much as twofold. Attendees concurred that for patients being treated in palliative care, survival rates were generally fairly poor, with most patients with advanced cancer surviving between 3 to 12 months following diagnosis¹⁶ and only around 15-20% of patients considered 'exceptional responders', surviving over 2 years. However, patients would only achieve this standard of progress if treated effectively, leading to questions being raised over why so much variance existed in the way patients were being treated and whether this damaged patient outcomes.

Regardless of what stage in the patient pathway patients were at, Dr Corbally emphasised the value of improving communication between healthcare professionals working in different sectors. This included those working in secondary and tertiary care ensuring that GPs were kept informed on patients' treatment regimens so that they could manage patients appropriately. The lack of communication between HCPs working in different sectors is exacerbated by the level of cross-discipline work involved in the management of oesophageal

cancer.¹³ Encouraging HCPs to communicate effectively with each other and primary care specialists could prove an important way of improving patient's standard of care and outcomes.

Professor Crosby also highlighted the level of cross-discipline work that is involved in the treatment of oesophageal cancer, including primary care professionals, surgeons, oncologists, histopathologists, clinical nurse specialists and others, and observed that there was limited dialogue through medical professionals involved in oesophageal cancer, both between different clinical specialists and geographic areas, which hindered the spread of best practice. Accordingly, Professor Crosby suggested the potential usefulness of establishing an oesophageal cancer mixed clinician service group, where best practice would be shared in the treatment of oesophageal cancer patients. Mr Moorthy highlighted that such a group existed among surgeons, wherein fourteen centres of upper GI surgical specialists meet, usually annually, to discuss how to improve patient outcomes. The attendees agreed that the formation of a multi-disciplinary clinical service group would be an effective way to share learnings in the treatment of oesophageal cancer, and accordingly to develop an effective best-practice pathway.

The attendees also agreed that one of the major issues in improving treatment options and patient outcomes in oesophageal cancer is the association of the indication with a non-vocal patient population, the predominant patient population being aged over-50, white, and male.⁴²

“What I’ve realised is, everyone does something well, but nobody does everything well”

**Krishna Moorthy, Upper GI Consultant Surgeon,
Imperial College Healthcare**

RECOMMENDATIONS

Professor Crosby brought the discussion to an end by running through some of the key themes and recommendations that had emerged:

1. Public health interventions are necessary to improve prevention of oesophageal cancer

— Public health campaigns targeting weight loss, smoking, alcohol and improving exercise are necessary to prevent oesophageal cancer and to ensure patients are fit for treatment.

2. Dyspepsia and heartburn should be classified as a public health issue

— An investigation into the sale and advertising of PPIs should be initiated, to raise awareness of the link to oesophageal cancer and to encourage referral in high-risk cases.

3. Diagnostic facilities must be preserved and encouraged, including pathology, radiology and endoscopy facilities, which are crucial in early disease detection.

4. The patient pathway needs to be standardised nationally

— Variation in treatment standards is preventing patients from accessing forms of treatment that may be the most effective for them.

— A standardised care pathway would create an opportunity for consistent holistic

needs support, as well as the development of care plans and improved access to key workers including specialised gastroenterologist nutritionists.

5. More research is required to assess the complex biological makeups of oesophageal cancers

— There is a tendency to group cancers together, such as those in the oesophagus with gastro-intestinal, squamous cell carcinoma and adenocarcinoma and others.

— More targeted research that acknowledges these differences and focuses on specialisation could yield more promising results and technological developments in the diagnosis and treatment of oesophageal cancer.

6. Regional variation in standards of care needs to be addressed to improve patient access and outcomes

— Regional treatment modalities interpret evidence around oesophageal cancer differently, resulting in different approaches to treatment and different standards of care developing.

— There is a need to ensure that all regional systems afford

patients the same access to high quality treatment options, and the same level of patient choice in their treatment.

— Treatment options can be dependent on regional specialties or regional multi-disciplinary team decisions. These factors must not interfere with patient access to their preferred or the most effective treatment option for them.

7. Patients need to be afforded access to new, innovative treatments as they become available

— Clinical trial selection criteria in oesophageal cancer is outdated and does not reflect the patient population. This criteria must be updated to ensure patients can access innovations as they become available.

— The development of a strategic, coordinated programme of clinical trials across the country would ensure more patients had access to relevant clinical trials to them, improving their access to treatments and building a larger data set for the treatment of oesophageal cancer.

ROUNDTABLE CONTRIBUTORS

- **Professor Tom Crosby, (Chair)**, National Cancer Clinical Director for Wales
- **Professor Russell Petty, (Speaker)**, Professor of Medical Oncology, Dundee University
- **Ms Mimi McCord, (Speaker)**, Founder Trustee, Heartburn Cancer UK
- **Professor Somnath Mukherjee**, Senior Clinical Researcher, University of Oxford
- **Dr Elizabeth Smyth, Consultant in Medical Oncology**, Cambridge University Hospitals NHS Foundation Trust
- **Professor Maria Hawkins**, MRC group leader, University of Oxford
- **Dr Ruth Corbally**, GP Lead and Facilitator for Powys for the MacMillan Primary Care Cancer Framework
- **Professor Rob Goldin**, Professor of Liver & GI Pathology, Imperial College Healthcare
- **Ms Venetia Wynter-Blyth**, Upper GI Cancer Nurse Specialist, Imperial College Healthcare
- **Mr Krishna Moorthy**, Upper GI Consultant Surgeon, Imperial College Healthcare
- **Mr Alan Moss**, Chair, Action Against Heartburn
- **Mr Stuart Barber**, Policy, Advocacy and Government Affairs Manager, Bristol-Myers Squibb
- **Mr Alex Holden**, Consultant, Hanover Communications
- **Mr Joe Pither**, Account Executive, Hanover Communications

REFERENCES

1. Less Survivable Cancers Taskforce. Help Us Close the Gap. Available at: <http://less survivablecancers.org.uk/help-us-close-the-gap/member-of-public/> [Accessed May 2019]
2. Cancer Research UK. Tackle cancers with substantial unmet need: our research strategy. Available at: <https://www.cancerresearchuk.org/funding-for-researchers/our-research-strategy/tackle-cancers-with-substantial-unmet-need> [Accessed May 2019]
3. Cancer Research UK. Stomach cancer mortality statistics. Available at: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/oesophageal-cancer#heading-One> [Accessed May 2019]
4. Cancer Research UK. Oesophageal cancer survival statistics. Available at: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/oesophageal-cancer/survival#heading-Zero> [Accessed May 2019]
5. Cancer Research UK. Oesophageal Cancer Incidence by age. Available at: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/oesophageal-cancer/incidence> [Accessed May 2019]
6. NHS Choices. Oesophageal Cancer Causes. Available at: <https://www.nhs.uk/conditions/oesophageal-cancer/causes/> [Accessed May 2019]
7. Cancer Research UK. Oesophageal Cancer Deprivation Incidence. Available at: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/oesophageal-cancer/incidence#heading-Seven> [Accessed May 2019]
8. Cancer Research UK. Routes to Diagnosis. Available at: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/oesophageal-cancer/diagnosis-and-treatment#heading-Zero> [Accessed May 2019]
9. Cancer Research UK. Oesophageal Cancer Diagnosis Statistics. Available at: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/oesophageal-cancer/incidence#heading-Three> [Accessed May 2019]
10. NHS Choices. Oesophageal Cancer Treatment. Available at: <https://www.nhs.uk/conditions/oesophageal-cancer/treatment/> [Accessed May 2019]
11. Cancer Research UK. Oesophageal Cancer Mortality. Available at: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/oesophageal-cancer#heading-One> [Accessed May 2019]
12. NHS Choices. Oesophageal Cancer Symptoms. Available at: <https://www.nhs.uk/conditions/oesophageal-cancer/symptoms/> [Accessed May 2019]
13. NHS England. Oesophageal and gastric cancer commissioning guide. Available at: <https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2014/03/b11-cancer-oesop-gast.pdf> [Accessed May 2019]
14. Rashid, N. et al. Current management of oesophageal cancer. Available at: <http://www.bjnp.org/content/current-management-oesophageal-cancer> [Accessed May 2019]
15. Viklund, P. and Lagergren, J. A care pathway for patients with oesophageal cancer. Available at: <https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.1365-2354.2007.00790.x> [Accessed May 2019]
16. Cancer Research UK. Oesophageal cancer survival data. Available at: <https://www.cancerresearchuk.org/about-cancer/oesophageal-cancer/survival> [Accessed May 2019]
17. NHS. Living with Oesophageal Cancer. Available at: <https://www.nhs.uk/conditions/oesophageal-cancer/living-with/> [Accessed May 2019]
18. Anandavadevelan, P. and Lagergren, P. Cachexia in patients with oesophageal cancer. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/26573424> [Accessed May 2019]
19. Best, L.M.J. et al. Non-surgical treatment versus surgical treatment for oesophageal (gullet or food-pipe cancer). Available at: https://www.cochrane.org/CD011498/UPPERGI_non-surgical-treatment-versus-surgical-treatment-oesophageal-gullet-or-food-pipe-cancer [Accessed May 2019]
20. University of Aberdeen. Scientists establish a foot in the door in precision medicine for oesophageal cancer. Available at: <https://www.abdn.ac.uk/news/10881/> [Accessed May 2019]
21. Kogo, M. et al. 2011. Analysis of the risk factors for myelosuppression after chemoradiotherapy involving 5-fluorouracil and platinum for patients with esophageal cancer. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21830394> [Accessed May 2019]
22. Cancer Research UK. Infection during or after treatment. Available at: <https://www.cancerresearchuk.org/about-cancer/coping/physically/fever/causes/infection/during-or-after-treatment> [Accessed May 2019]
23. American Cancer Society. Treating Esophagus Cancer. Available at: <https://www.cancer.org/content/dam/CRC/PDF/Public/8617.00.pdf> [Accessed May 2019]
24. Cancer Research UK. Cancer in the UK 2019. Available at: https://www.cancerresearchuk.org/sites/default/files/state_of_the_nation_april_2019.pdf [Accessed May 2019]
25. NHS Inform. Oesophageal Cancer. Available at: <https://www.nhsinform.scot/illnesses-and-conditions/cancer/cancer-types-in-adults/oesophageal-cancer> [Accessed May 2019]
26. National Cancer Registration and Analysis Service. Routes to Diagnosis. Available at: http://www.ncin.org.uk/publications/routes_to_diagnosis [Accessed May 2019]
27. MacMillan Cancer Support. What you can do if a treatment is not available. Available at: <https://www.macmillan.org.uk/information-and-support/treating/treatment-decisions/coming-to-your-decision/when-treatment-not-available.html> [Accessed May 2019]
28. MacMillan Cancer Support. Types of Oesophageal Cancer. Available at: <https://www.macmillan.org.uk/information-and-support/oesophageal-gullet-cancer/understanding-cancer/types-oesophageal-cancer.html> [Accessed May 2019]
29. Cancer Research UK. Oesophageal Cancer Survival. Available at: <https://www.cancerresearchuk.org/about-cancer/oesophageal-cancer/survival> [Accessed May 2019]
30. The King's Fund. The quality of GP diagnosis and referral. Available at: <https://www.kingsfund.org.uk/sites/default/files/Diagnosis%20and%20referral.pdf> [Accessed May 2019]
31. MacMillan Cancer Support. Emma on treatable but not curable cancer. Available at: <https://www.macmillan.org.uk/information-and-support/resources-and-publications/stories/emma/emma-incurable-cancer.html> [Accessed May 2019]
32. Yajuan, LV. et al. Quality of life in patients with esophageal cancer receiving definitive chemoradiotherapy or esophagectomy. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4106730/> [Accessed May 2019]
33. Lewis, L. et al. Patient factors influencing symptom appraisal and subsequent adjustment to oesophageal cancer: A qualitative interview study. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28857296> [Accessed May 2019]
34. Health Service Journal. Workforce supplement: The benefits of specialist nurses. Available at: <https://www.hsj.co.uk/downloads/workforce-supplement-the-benefits-of-specialist-nurses/5082712.article> [Accessed May 2019]
35. The King's Fund. The health care workforce in England: Make or break? Available at: <https://www.kingsfund.org.uk/publications/health-care-workforce-england> [Accessed May 2019]
36. Wsam, G. A. Palliative care in cancer: managing patients' expectations. Available at: <https://onlinelibrary.wiley.com/doi/full/10.1002/jmrs.188> [Accessed May 2019]
37. National Oesophago-Gastric Cancer Audit 2018. Available at: <https://www.nogca.org.uk/content/uploads/2018/09/NOGCA-2018-Annual-Report-1.pdf#page=46> <https://www.nogca.org.uk/content/uploads/2018/09/NOGCA-2018-Annual-Report-1.pdf> [Accessed May 2019]
38. Kaur, J. and Mohanti, B. K. Transition from Curative to Palliative Care in Cancer. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3098537/> [Accessed May 2019]
39. Cancer Research UK. Why is early diagnosis important? Available at: <https://www.cancerresearchuk.org/about-cancer/cancer-symptoms/why-is-early-diagnosis-important> [Accessed May 2019]
40. Cancer Research Institute. Have an Autoimmune Disease? You Still May Be Able To Receive Cancer Immunotherapy. Available at: <https://www.cancerresearch.org/blog/july-2016/have-an-autoimmune-disease-immunotherapy> [Accessed May 2019]
41. Health Education England. Making Every Contact Count. Available at: <https://www.makingeverycontactcount.co.uk/> [Accessed May 2019]

42. Cancer Research UK. Oesophageal cancer incidence statistics. Available at: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/oesophageal-cancer/incidence#heading-Eight> [Accessed May 2019]
43. Cancer Research UK. Oesophago-gastric cancer. Available at: <http://www.bopawebsite.org/sites/default/files/imce/course-resources/CancerResearchFactsheet.pdf> [Accessed May 2019]
44. NHS England. Heartburn and acid reflux. Available at: <https://www.nhs.uk/conditions/heartburn-and-acid-reflux/> [Accessed May 2019]
45. NHS England. Overview: Oesophageal Cancer. Available at: <https://www.nhs.uk/conditions/oesophageal-cancer/> [Accessed May 2019]
46. COI. Evaluation of the Bowel Cancer Awareness Pilot in the South West and East of England: 31 January to 18 March 2011. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/215106/dh_133125.pdf [Accessed May 2019]
47. NHS England. Endoscopy. Available at: <https://www.nhs.uk/conditions/endoscopy/> [Accessed May 2019]
48. NHS England. Pill-size camera may make cancer diagnosis easier. Available at: <https://www.nhs.uk/news/cancer/pill-size-camera-may-make-cancer-diagnosis-easier/> [Accessed May 2019]
49. Cancer Research UK. Oesophageal Cancer Risk. Available at: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/oesophageal-cancer/risk-factors> [Accessed May 2019]
50. Cancer Research UK. Lung Cancer: Risks and Causes. Available at: <https://www.cancerresearchuk.org/about-cancer/lung-cancer/risks-causes> [Accessed May 2019]
51. Cancer Research UK. Capacity to diagnose? An analysis of cancer diagnostic activity in England. Available at: https://www.cancerresearchuk.org/sites/default/files/mar18_capacity_to_diagnose.pdf [Accessed May 2019]
52. NICE. Dyspepsia and gastro-oesophageal reflux disease in adults. Available at: <https://www.nice.org.uk/guidance/qs96/chapter/quality-statement-4-discussion-about-referral-for-nonurgent-endoscopy> [Accessed May 2019]
53. Cancer Research UK. Barrett's Oesophagus. Available at: <https://www.cancerresearchuk.org/about-cancer/oesophageal-cancer/causes-risks/barretts-oesophagus> [Accessed May 2019]
54. Cancer Research UK. A trial looking at the Cytosponge test in GP surgeries for people with heartburn symptoms (BEST3). Available at: <https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-the-cytosponge-test-in-gp-surgeries-for-people-with-heartburn-symptoms-best3> [Accessed May 2019]
55. Royal College of General Practitioners. College reveals worrying decrease in number of GPs per patient - despite increasing demand for general practice services. Available at: <https://www.rcgp.org.uk/about-us/news/2019/january/new-data-analysis-by-the-royal-college-of-gps-has-found-a-concerning-decrease.aspx> [Accessed May 2019]
56. MacMillan Cancer Support. Rapid Referral Guidelines. Available at: https://www.macmillan.org.uk/documents/aboutus/health_professionals/pccr/rapidreferralguidelines.pdf [Accessed May 2019]
57. MacMillan Cancer Support. Improving the quality of cancer care in primary care. Available at: https://www.macmillan.org.uk/_images/revalidation-toolkit_tcm9-291970.pdf
58. MacMillan Cancer Support. Evaluation of MacMillan's Cancer Care Review Template. Available at: https://www.macmillan.org.uk/documents/aboutus/health_professionals/primarycare/macmillancancersupportrevisedreportfinal.pdf [Accessed May 2019]
59. Cancer Research UK. Our policy on pathology capacity. Available at: <https://www.cancerresearchuk.org/about-us/we-develop-policy/our-policy-on-early-diagnosis/our-policy-on-diagnostic-services/our-policy-on-pathology-capacity> [Accessed May 2019]
60. Royal College of Pathologists. Cancer Diagnostics. Available at: <https://www.rcpath.org/discover-pathology/public-affairs/cancer-diagnostics.html> [Accessed May 2019]
61. Journal of Oncology Practice. New Diagnosis Bundle: Improving Care Delivery for Patients With Newly Diagnosed Cancer. Available at: <https://ascopubs.org/doi/full/10.1200/jop.2016.011163> [Accessed May 2019]
62. NHS Wales. The Single Cancer Pathway - the new target within Wales for diagnosing cancer and getting treatment started. Available at: <http://www.wales.nhs.uk/news/50377> [Accessed May 2019]
63. NHS England. Implementing a timed colorectal cancer diagnostic pathway. Available at: <https://www.england.nhs.uk/wp-content/uploads/2018/04/implementing-timed-colorectal-cancer-diagnostic-pathway.pdf> [Accessed May 2019]
64. NHS England. Implementing a timed prostate cancer diagnostic pathway. Available at: <https://www.england.nhs.uk/wp-content/uploads/2018/04/implementing-timed-prostate-cancer-diagnostic-pathway.pdf> [Accessed May 2019]
65. Lam, A. K. Cellular and Molecular Biology of Esophageal Cancer. Available at: https://link.springer.com/chapter/10.1007/978-3-319-20068-2_2 [Accessed May 2019]
66. University of Cambridge. 'Pill on a string' could help spot early signs of cancer of the gullet. Available at: <https://www.cam.ac.uk/research/news/pill-on-a-string-could-help-spot-early-signs-of-cancer-of-the-gullet> [Accessed May 2017]
67. DeMeester, S.R. Epidemiology and Biology of Esophageal Cancer. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2684731/> [Accessed May 2019]
68. The Royal College of Pathologists. Dataset for the histopathological reporting of oesophageal carcinoma (2nd Edition)
69. Ter Veer, E. et al. Second- and third-line systemic therapy in patients with advanced esophagogastric cancer: a systematic review of the literature. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5035657/> [Accessed May 2019]
70. Liang, H. et al. Cancer Biology & Medicine. Epidemiology, etiology, and prevention of esophageal squamous cell carcinoma in China. Available at: <http://www.cancerbiomed.org/index.php/coocr/article/view/1005/1123> [Accessed May 2019]
71. Pusung, M. et al. Genomics of Esophageal Cancer and Biomarkers for Early Detection. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27573775> [Accessed May 2019]
72. Smith, R. and Lam, A.K. Liquid Biopsy for Investigation of Cancer DNA in Esophageal Adenocarcinoma: Cell-Free Plasma DNA and Exosome-Associated DNA. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29600371> [Accessed May 2019]
73. Torjesen, I. Drug development: the journey of a medicine from lab to shelf. Available at: <https://www.pharmaceutical-journal.com/publications/tomorrows-pharmacist/drug-development-the-journey-of-a-medicine-from-lab-to-shelf/20068196.article?firstPass=false> [Accessed May 2019]
74. Haynes, A. B. et al. A Surgical Safety Checklist to Reduce Morbidity and Mortality in a Global Population. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMsa0810119> [Accessed May 2019]
75. Lou, F. et al. Esophageal Cancer Recurrence Patterns and Implications for Surveillance. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4066875/> [Accessed May 2019]
76. Cancer.Net. Esophageal Cancer: Treatment Options. Available at: <https://www.cancer.net/cancer-types/esophageal-cancer/treatment-options> [Accessed May 2019]
77. National Cancer Research Institute. NCRI Upper Gastrointestinal Cancer Clinical Studies Group. Available at: <http://csg.ncri.org.uk/wp-content/uploads/2018/10/NCRI-Upper-Gastrointestinal-Cancer-CSG-2017-2018-Annual-Report.pdf> [Accessed May 2019]
78. Doyle, C. Caring for the Frail, Older Patient With Cancer: Four Practical Approaches. Available at: <https://www.ascopost.com/issues/december-10-2017/caring-for-the-frail-older-patient-with-cancer-four-practical-approaches/> [Accessed May 2019]

NOTES



Bristol-Myers Squibb

WHAT NEEDS TO BE DONE TO IMPROVE OUTCOMES FOR OESOPHAGEAL CANCER PATIENTS?

This document is a summary of an expert roundtable discussion on issues facing patients and healthcare professionals. A more detailed write up is available.

Oesophageal cancer is a type of cancer that develops within the oesophagus – the tube that carries food from the throat to the stomach.¹ In 2016, oesophageal cancer was the seventh most common cause of death in the UK² and has been designated by the Less Survivable Cancers Taskforce³ and Cancer Research UK as one of the four “cancers with substantial unmet need”.⁴

This roundtable, chaired by Professor Tom Crosby, National Clinical Director for Wales, offered a forum to discuss systemic issues around patient experience and quality of life for oesophageal cancer patients, with the aim of facilitating discussion between a range of experts from across the oesophago-gastric field to collate their perspectives on the solutions required to improve patient outcomes.

“If I had known that heartburn could kill him, I would have done something about it.”

Mimi McCord, Founder Trustee, Heartburn Cancer UK

Improving the patient experience

A recurrent theme throughout the discussion was the issues caused by **the advancement of the disease by the point of definitive diagnosis**. The public are unaware of symptoms – such as heartburn and dyspepsia⁵ – and self-medicate to mask them, masking the seriousness of the disease. Accordingly, a public health campaign could be used to raise public awareness of these issues and restrictions could be placed on the sale of medication for heartburn and indigestion, including proton pump inhibitors (antacids).

Attendees noted that **existing treatments for oesophageal cancer have high toxicities**,⁶ limiting the number of patients that can tolerate second- or third- line treatments, as well as devastating patients' quality of life while they are undergoing treatment. They can also lead to severe associated illnesses, including thrush, blood clots and strokes.

A pervasive issue through the session was the **need for better communication and integration between primary and secondary care**. Lack of continuity can leave patients feeling isolated and like they have no one to talk to, underlining the importance of named clinical nurse specialists and ensuring there are enough for patients to have someone to turn to.

Beyond this, it was widely noted that **patients can have issues with their treatment journeys based on their location**. Variation in referral advice and management of patients across the country leads to variance in referral patterns and compromises the integrity of the referral process.¹⁰

How can new technologies and treatments be used to improve earlier diagnosis and patient outcomes?

Improving earlier diagnosis is unquestionably important in improving patient management and outcomes in oesophageal cancer.⁸ Diagnostic services in the UK are not currently up to this challenge, as evidenced by the number of patients who are diagnosed with oesophageal cancer through emergency services, which make up a fifth of all definitive diagnoses.⁹

A leading contributory factor to this poor performance in earlier diagnosis is the failure to effectively risk-stratify patients. Patients are not triaged effectively, leading to delays in referral, increasing the time to definitive diagnosis, and thereby increasing the time taken for patients to receive treatment. This means that by the time patients receive treatment, their disease is more advanced and patients may be less able to tolerate the toxicity of treatment or ineligible for curative treatment.

“We're saying about the precariousness and fragility of our diagnostic framework. Pathology and radiology is pretty dire, in terms of availability of specialists.”

Professor Tom Crosby, (Chair), National Cancer Clinical Director for Wales

The variation in standards and expectations on whether primary care professionals should frequently refer patients or not was also discussed as an issue. **Changing advice from NICE and NHS England on whether to frequently refer patients can affect GPs awareness on whether to refer patients onwards or not.**¹⁰

Research funding could also be allocated more effectively, to prioritise cancers with the highest mortality rates, rather than those with the highest prevalence.

Promising diagnostic technologies exist which could dramatically improve early diagnosis and patient outcomes, such as the Cytosponge,¹¹ but a lack of research funding and subsequent limited real world evidence (RWE) affects the development of new technologies to improve outcomes relating to the disease. This is a factor which is applicable to diagnostics, as well as treatments and patient management schemes.

Issues with treating oesophageal cancer

Attendees agreed that there is a level of nihilism around the treatment and management of patients with oesophageal cancer. Even when a cancer cannot be treated curatively, a culture must be instilled amongst HCPs that it can still be treated.

Patient pathways for treatment are disjointed and have a high level of regional variation, dictated by local specialties, prescribing habits and local health needs. **This variation affects patients' ability to access treatments which can lead to different patient outcomes in different localities.**

The toxicities and side-effects of current treatment options for oesophageal cancer are incredibly damaging to patients' quality of life.⁶ There is a great need for treatment options to become available which have less toxicity than current options, as well as options with greater potential for getting the disease under control.

"I think there is a bit of nihilism about oesophageal cancer... we see the progress, but we need to inform others that the progress is there."

Dr Elizabeth Smyth, Cambridge University Hospitals NHS Foundation Trust

Patients need to be afforded access to new, innovative treatments as they become available. **Selection data for clinical trials is outdated and is not reflective of the patient population, preventing some patients from being able to access treatment. An example of this would be patients with autoimmune diseases, who are typically disqualified from immunotherapy clinical trials.**¹² A more strategic programme of clinical trials would ensure that more patients have access to relevant clinical trials, building a better data set and affording more patients access to the treatments that could help to get their disease under control.

There is also a **need for greater recognition of the distinct subtypes of oesophageal cancer**,¹³ with the different risk factors and treatment sensitivities associated with adenocarcinomas and squamous cell carcinomas quite distinct. Developing new treatment options will necessitate a better understanding and appreciation of these complexities.

References

1. NHS: Overview – oesophageal cancer. Available at: <https://www.nhs.uk/conditions/oesophageal-cancer/> [Accessed: July]
2. Cancer Research UK. Oesophageal cancer mortality statistics. Available at: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/oesophageal-cancer#heading-One> [Accessed July 2019]
3. Less Survivable Cancers Taskforce. Help Us Close the Gap. Available at: <http://lessurvivablecancers.org.uk/help-us-close-the-gap/member-of-public/> [Accessed July 2019]
4. Cancer Research UK. Tackle cancers with substantial unmet need: our research strategy. Available: <https://www.cancerresearchuk.org/funding-for-researchers/our-research-strategy/tackle-cancers-with-substantial-unmet-need> [Accessed July 2019]
5. NHS Choices. Oesophageal Cancer Symptoms. Available at: <https://www.nhs.uk/conditions/oesophageal-cancer/symptoms/> [Accessed July 2019]
6. Best, LMJ. et al. Non-surgical treatment versus surgical treatment for oesophageal (gullet or food-pipe cancer). Available at: https://www.cochrane.org/CD011498/UPPERGI_non-surgical-treatment-versus-surgical-treatment-oesophageal-gullet-or-food-pipe-cancer [Accessed July 2019]
7. Macmillan Cancer Support. Types of Oesophageal Cancer. Available at: <https://www.macmillan.org.uk/information-and-support/oesophageal-gullet-cancer/understanding-cancer/types-oesophageal-cancer.html> [Accessed July 2019]
8. Cancer Research UK. Why is early diagnosis important? Available at: <https://www.cancerresearchuk.org/about-cancer/cancer-symptoms/why-is-early-diagnosis-important> [Accessed July 2019]
9. Cancer Research UK. Routes to Diagnosis of Oesophageal Cancer. Available at: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/oesophageal-cancer/diagnosis-and-treatment#heading-Zero> [Accessed July 2019]
10. The King's Fund. The quality of GP diagnosis and referral. Available at: <https://www.kingsfund.org.uk/sites/default/files/Diagnosis%20and%20referral.pdf> [Accessed July 2019]
11. Cancer Research UK. A trial looking at the Cytosponge test in GP surgeries for people with heartburn symptoms (BEST3). Available at: <https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-the-cytosponge-test-in-gp-surgeries-for-people-with-heartburn-symptoms-best3> [Accessed July 2019]
12. Cancer Research Institute. Have an Autoimmune Disease? You Still May Be Able To Receive Cancer Immunotherapy. Available at: <https://www.cancerresearch.org/blog/july-2016/have-an-autoimmune-disease-immunotherapy> [Accessed May 2019]
13. DeMeester, S.R. Epidemiology and Biology of Esophageal Cancer. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2684731/> [Accessed July 2019]