Research Priority Setting in Barrett's Oesophagus and Gastroesophageal Reflux Disease

Authors

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Abstract

The incidence of Gastroesophageal Reflux Disease (GORD) and Barrett's Oesophagus (BO) is increasing. BO is the main precursor to oesophageal adenocarcinoma, which carries a poor prognosis. Considering the vast potential burden on patients and healthcare resources, there is a real need to define and focus research efforts. This priority setting exercise aimed to produce the "Top 10" uncertainties which truly matter to patients and healthcare providers. To achieve this, we adopted the robust and transparent methodologies previously outlined by the James Lind Alliance (JLA). This qualitative approach firstly involves an ideas-gathering survey which, once distilled, generates a long list of research uncertainties. These uncertainties are then prioritised via an interim ranking survey and a final workshop to achieve consensus agreement. The initial 629 uncertainties, generated from a survey of 170 individual respondents (47% professional, 53% non-professional) and 1 workshop, were narrowed down to the final top 10 priorities. These priorities covered a range of issues including: a need for improved patient risk stratification, alternative diagnostic and surveillance tests, efficacy of a dedicated BO service, cost effectiveness and appropriateness of current surveillance, advances in non-drug treatments for GORD, safety of long term drug treatment and questions regarding the durability and role of different endoscopic therapies in dysplastic BO. This is the first patient-centred assessment of priorities for researchers in this chronic disease setting. We hope that recognition and dissemination of these results influences the future direction of research and translates into meaningful gains for patients.

Key Words

Barrett's Oesophagus, Gastroesophageal Reflux Disease, Research Priority Setting, Endoscopic Surveillance, Endoscopic Therapies.

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Introduction

Research could be considered a well-established concept which aims to address important and relevant uncertainties. The question of who determines key research priorities is somewhat less clear. Why do some areas of research receive focus and funding, leaving others perhaps overlooked? Typically, research is funded by the government (public), industry (pharmaceutical and medical device companies) and charities. Past financial constraints on public research spending has produced strong links between academic researchers and industry (1), conceivably impacting the selection of research areas. Priorities of researchers that do not marry up with those of patients and healthcare staff (research users) have potentially significant deleterious consequences (2,3). Tallon et al first described this imbalance in the setting of the chronic disease osteoarthritis, clearly demonstrating an inappropriate focus of ongoing clinical trials on drug treatments. In stark contrast, the results of surveys and focus groups showed that patients, rheumatologists, physiotherapists and general practitioners all sought greater emphasis on non-drug treatments (4). Historically researchers have not routinely engaged with the agendas of the research user. Those that did used varying methods and levels of research user involvement demonstrating a lack of consensus as to the best approaches (5).

In an attempt to narrow the gap between the researcher and the research user there has been an increasing trend to seek patient and public involvement when setting research agendas (appendix p4, supplementary table 1). The publication of "Top 10 Research Priorities" has become a potentially powerful influence on the direction of future research (6,10). The James Lind Alliance (JLA) is a non-profit initiative dedicated to bringing together clinicians, patients and carers to discuss research priorities in a variety of disease and health care settings (11) Their methodologies have been recognised by the National Institute for Health Research (UK) (12) and should act as a guideline for those seeking to define research uncertainties in their own field of interest (13).

To date there remains no patient-centred assessment of priorities for research in the field of Barrett's Oesophagus (BO) and Gastroesophageal Reflux Disease (GORD). Considering the growing incidence of these diseases, their future burden on healthcare resources, and the poor advances in oesophageal adenocarcinoma (OAC) survivorship, there is a need to define and focus future research efforts (14,15). The aim of this project was to facilitate balanced input in the priority setting process for Barrett's oesophagus and GORD, resulting

in a consensus on the top 10 uncertainties in the field, with the hope of influencing the direction of future research agendas.

Methodology

The project was launched at the 10th National Barrett's Symposium in April 2016, where attendees, including professionals, patients and charity representatives (panel 1), were invited to participate in an interactive workshop on research priority setting. Volunteers from this workshop formed a steering committee that included representatives from each group. The project was facilitated by, the research charity of the British Society of Gastroenterology (CORE), within the setting of a publicly funded National Health Service. The University of Manchester acting as an academic advisor throughout.

The process of identifying research priorities is outlined in Figure 1. The first step involved an initial data collection survey, distributed by charities and organisations, to generate a long list of research uncertainties (panel 2 lists the charities and organisations invited to help distribute the survey). These uncertainties were then subjected to rigorous review against the current evidence base to ensure that they are true unknowns (see appendix p4, supplementary table 2), after which we conducted an interim prioritisation survey with the aim of ranking uncertainties to generate a more concise short list. The short-listed uncertainties were then deliberated over in a final group workshop, in which a modified Nominal Group Technique (16) was used to identify and rank the final top 10 list. (for a detailed description of the methodology, see appendix p1-3)**.**

Findings

The initial survey generated 629 uncertainties from 171 survey respondents, including 301 from non-professionals (n=90), 320 from professionals (n=80) and 8 from the initial workshop. Of the initial 629 uncertainties, 107 met the criteria for immediate exclusion (48 from professionals and 59 from non-professional) (appendix p5, supplementary table 3). The remaining 522 uncertainties were assigned to a broad category to facilitate distillation of the content; repeated and similar uncertainties were then combined to form a single research question. This process was then repeated for each category ultimately producing a provisional long list of 50 research questions. This distillation process was conducted by a single analyst and overseen by the University of Manchester academic advisor. These 50 questions were reviewed by a professional subgroup of the steering committee, resulting in the exclusion of 13 questions as not true unknowns. One uncertainty was deemed to ask two separate questions and was therefore split, and a further five had significant crossover and

were combined. This verification process produced a final long list of 33 unique questions ready for the interim prioritisation survey.

The professional and non-professional rankings from the interim prioritisation survey were combined to produce a ranked list. The list was once again reviewed by the sub group of the steering committee and the top 22 ranking uncertainties were taken forward to the final workshop (Table 1). This cut off was chosen because beyond the top 22 there was clear agreement between both groups on their low priority status. We also did not want to over load participants in the final workshop with an unmanageable number of questions to process and rank.

The final workshop included 13 participants, of which five were healthcare professionals (3 consultant gastroenterologists and 2 specialist nurses) and 8 patient representatives, who were divided into three groups. Amongst the groups, there was unanimous agreement on 5 uncertainties that should be included in the top 10, including those that should rank in the top 3 positions. Following deliberation among all workshop participants, five uncertainties were deemed to overlap with others and were therefore combined, facilitating agreement on the remaining uncertainties to be included in the final top 10 (table 2). This discussion also allowed some important elements from lower ranked uncertainties to be pulled into the final top 10. Such priorities may not have made the final selection on their own merit. For example, elements of priority G from the short list ("How does current surveillance practice across the UK compare to the current national guideline and would a national Barrett's Oesophagus Audit or Registry improve standards or care?") were combined with the more popular priority M relating to the efficacy of a dedicated BO clinic. Secondary review of the excluded 7 uncertainties gave participants an opportunity to voice any final concerns or opinions. The final top 10 research priorities are listed in table 2.

Discussion

This exercise in research priority setting outlines 10 key areas in which research efforts and resources should be focused. We think these priorities highlight crucial areas that can facilitate significant long-term benefits to patients whilst equipping medical staff with greater knowledge, improved treatments and enhanced services.

The incidence of GORD and subsequent diagnoses of BO are increasing. Considering that the majority of people with reflux do not have BO, this poses a huge problem for future healthcare resources, an issue that is reflected strongly in our top 10. A better understanding of who to screen (priority 1) coupled with an accurate and cost-effective primary care

screening test (priority 3) would obviate the need for invasive endoscopy in many patients. This might not only be more acceptable to patients but would dramatically reduce some of the pressures experienced by many endoscopy departments. Interestingly priorities 1 and 3 were ranked much lower in the interim priority setting survey (combined ranks of 14 and 18, respectively), particularly by non-professionals. It is not uncommon for discrepancies to exists between the final workshop results and those of the interim survey. One of the roles of the final workshop is to highlight imbalances between professionals and non-professionals, identify areas which may be important to a minority group or indeed areas that may have been under represented during the process. For example, the discrepancy seen here may reflect differences in the composition of the non-professional group who took part in the initial survey and those involved in the interim survey. The latter group might have more experience with BO and relatively less vested interest in the wider GORD population, the area to which these priorities relate to. During the final workshop, all non-professional participants agreed on the importance of these issues after considering the wider population implications and initial survey responses.

Currently there is insufficient data to accurately stratify risk in patients diagnosed with BO (priorities 2 and 7) (17). Hence the majority of patients are faced with long term surveillance, for which the evidence of efficacy is limited (18). Current data suggest that the majority of patients with BO have low malignant potential and are perhaps more likely to die from other diseases than OAC (19,20). This suggests that blanket surveillance may not be cost effective nor beneficial to most patients (priority 9) (21). Without improved risk stratification, this chronic disease may impose an unnecessary burden on endoscopy provisions and patients. This is clearly frustrating for both clinicians and patients and is echoed by several items in the top 10 list. P53 immunohistochemistry remains the only biomarker recommended for clinical use to aid histopathological diagnosis (22), but the efficacy of this biomarker has met with some doubt in a recent consensus statement (23). To date it has been very challenging to predict the progression of non-dysplastic BO using biomarkers, especially translating research advances into routine clinical use (24). The mutational profile of BO appears highly heterogenous with mutations already occurring in non-dysplastic tissue. More recent developments in genomic sequencing are promising, and further research is clearly warranted (priority 7) (25). We expect that improved individual risk stratification would influence surveillance practices and perhaps allow for greater focus or treatment of high risk patients while safely relaxing follow-up intervals or even discontinuing surveillance for others.

Advances in screening and risk stratification will take years to fully develop before they influence standard care. Therefore, some uncertainties focused on an immediate need to improve service delivery and quality (priority 4). Assessing the impact of a dedicated BO service (endoscopy surveillance and Barrett's clinic) should provide some insight into the efficacy and acceptability of current treatment delivery pathways. Some historical evidence suggests that BO patients have often received haphazard and inconsistent follow up care (26), but the true impact of BO and its follow up care on patients remains unknown. The design and implementation of a dedicated service must consider the patient's perspective, and its success measured using both clinical outcomes as well as patient-centred outcomes. A randomised intervention study assessing the suitability and efficacy of a dedicated service against current practice would provide valuable insight and could help to shape future healthcare delivery for patients with BO. We envisage the establishment of dedicated surveillance endoscopy services and new patient clinics that could be run by trained nurse endoscopists alongside a consultant gastroenterologist with an interest in BO and OAC.

Some uncertainties might be considered more patient or professionally orientated. One particular area that received consistent patient interest was safe effective treatment of acid reflux (priorities 6 and 8). Many patients with GORD and the majority of those with BO face long term treatment with proton pump inhibitors (PPI), sometimes for decades. Patients are rightly concerned about long-term drug safety, which a number of observational studies have questioned (27). Although no causality can be proven in these studies, this remains an important area that needs further clarity, particularly when one considers the vast, unmonitored, usage of these drugs. This uncertainty appears to have been overlooked or possibly dismissed by professionals based on the limitations of epidemiological and observational studies. In order to address this crucially important patient question, future studies should be more specific and definitive in focus and prospective in design (28). For example, Jo et al. prospectively examined the impact of PPI usage on parameters of bone health (29). This small RCT demonstrated that eight weeks of PPI therapy may directly alter bone metabolism particularly in those aged over sixty. Substantial proportions of patients are intolerant, poorly responsive or unwilling to take PPIs; this issue was also deemed crucially important to the non-professionals involved in this process. Such patients can be difficult to treat, as there are few adequately developed or widely available alternatives to PPIs. This issue was echoed in the top 10 list by an interest in newer, minimally invasive or surgical non-drug treatments (priority 8). This perhaps reflects a need for a low-risk, long-term treatment strategy alongside concerns over lifelong oral medication. Some minimally

invasive surgical and endoscopic anti-reflux techniques have shown promise. However, these trials are often small and uncontrolled, with no clear standardised methods of assessing subjective or objective endpoints. Stretta, radiofrequency energy delivered to the lower oesophageal muscle via endoscopy, has been used for 15 years, yet there are still conflicting reports regarding its efficacy (30-33). Perhaps greater focus should now be given to newer, promising techniques including magnetic sphincter augmentation (34), EndoStim (35-37) and transoral incisionless fundoplication (38, 39). Assessment of the efficacy and durability of these approaches will require larger, multicentre, randomised studies (priorities 5 and 10). Researchers in this field must consider a standardised approach of assessing primary and secondary outcomes in order to draw clearer between-study comparisons and more definitive conclusions.

Advances in radiofrequency ablation (RFA) technologies and regimens have led to significant improvements in the safety and efficacy of dysplastic BO treatment. This is reflected by recent durability data from the Halo registry (40). However, there is a significant minority of patients with disease recurrence (41). Long term surveillance after endoscopic therapy is therefore imperative. In order to develop optimal surveillance strategies, we need longer-term durability studies coupled with a better appreciation of disease recurrence at a cellular level (Priorities 5 and 7).

Although RFA, particularly circumferential treatments, have become the mainstay of flat dysplastic BO therapy, there remains some controversy around the most effective methods for treating focal disease (42) and the potential roles of adjunctive treatments (e.g. Argon Plasma Coagulation and Cryotherapy) in these care pathways (43,44).

Within the excluded uncertainties, 3 were perhaps surprising. Firstly, the use of RFA to treat non-dysplastic BO is common in other healthcare settings, particularly the private US system (45). Although this ranked highly during interim prioritisation, the final workshop thought further research to investigate this was impractical and expensive within a publicly funded NHS. There is also sufficient evidence arguing against this practice when one considers non-dysplastic cancer conversion rates, procedural complications and cost effectiveness. Secondly, the role of chemoprophylaxis was highly rated in previous rounds, and its ultimate exclusion might be due to the imminent conclusion of the AspECT Trial. This phase III randomised trial assessing the role of aspirin and esomeprazole chemoprevention in BO will provide some answers to this unknown (46,47). Thirdly the effect of lifestyle on symptoms and BO disease progression was popular amongst patient participants during earlier rounds but fell out of favour in the final workshop. One explanation for this could be

the difficulty this research question poses in terms of trial design, outcome measures and the long term follow up needed to generate reliable results.

Throughout this process, we tried to engage a diverse, representative group to ensure the democratic legitimacy of the results. Final workshop participants were chosen based on a high level of previous expertise and experience to provide a more contributory role. Some may argue that this group is therefore exclusive and not truly representative of the broader interested parties. However, participants, particularly non-professionals, were empowered to speak on behalf of all patients by supplying them with a wider selection of population data from the previous rounds of voting. It also allowed them to reflect not only on their individual experiences but also the views of the wider patient population (6,9).

Previous priority setting partnerships that used the same methodologies have been criticised for generating loosely defined questions which are difficult to transform into actual research proposals. Therefore, we have attempted to formulate detailed, well-defined uncertainties that still reflect the original scope of responses.

The methodologies used are somewhat selective by nature. Firstly, the survey was conducted solely in the English language, and was primarily internet based with no means of calculating response rates (48). Secondly many respondents, particularly those associated with charities, are likely to be white, middle class, and with a higher background education. In comparison, those hardest to reach, such as lower socio-economic groups and vulnerable patients, may have the most to benefit and the greatest unmet needs (49). However, engaging the disengaged is extremely challenging especially with finite financial resources and man power. Thirdly, in order to distil the original verbatim responses into a representative short list, a degree of interpretation must occur. It is conceivable that ideas or information might be lost or misunderstood during this process.

Our study has a smaller sample size compared to some JLA publications, especially considering the prevalence of BO and GORD. This was counteracted by asking respondents to choose up to 5 initial uncertainties. The subsequent qualitative elements within the methodologies ensures that the success of the project does not rely purely on a majority vote. Clear thematic saturation of research uncertainties was achieved during the initial survey, allowing progression through the ranking stages. Considered deliberation in the final workshop also allowed for the inclusion of priorities originally generated by a minority group. Finally, BO and GORD is a global condition, and is particularly prevalent in the developed

world. This study is representative of patients and frontline staff in the UK NHS, and other countries with different healthcare provisions may produce different priorities.

Effective dissemination of these research priorities to the appropriate audience is essential for the success of this project. This paper is the first publication to tackle this important issue in BO and GORD, and we hope that it will be taken into consideration by researchers and potential funders (such as The National Institute for Health Research (NIHR), The Association for Medical Charities (AMRC) and the Medical Research Council (MRC)). Further dissemination via conference presentation and communication of the results via CORE will be essential.

It would be interesting to assess the more immediate effect of these results by assessing the number of research projects undertaken, developed or funded within 1-2 years of publication. Assessing the longer term and broader population benefits of this work will be much more difficult. Previous PSPs have been successful for a variety of reasons. Some have highlighted areas previously overlooked or not considered (48,50). Others have significantly influenced the immediate direction of research; most notably the PSP for urinary incontinence helped attract funding and research developments in 6/10 priorities within 12 months of publication (10).

Conclusions

The advent of patient and public involvement in both research and healthcare improvement is undoubtedly essential. The identification of research priorities is perhaps where their greatest impact can be had. This top 10 list of patient-centred research questions is the first of its kind in BO and GORD. It has been generated by a recognised, robust and transparent process. We hope these priorities will help focus researchers' efforts and influence future funding into areas where meaningful gains can be made for patients. Considering the prevalence of BO and GORD, this has the potential to impact a vast number of patients and healthcare providers. As the research landscape moves forward, this process should be repeated to maintain a relevant and up-to-date focus for researchers.

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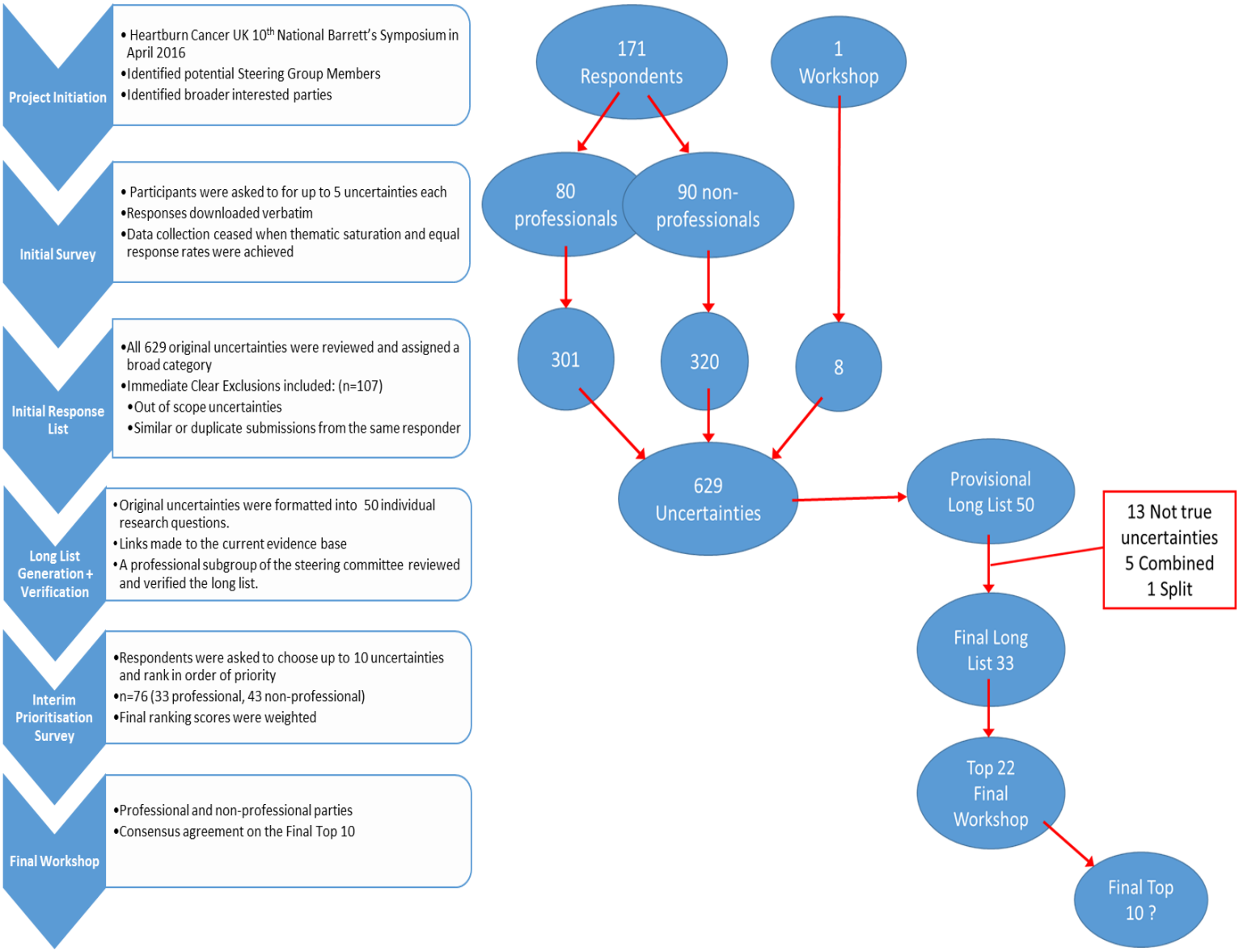
Figure 1: Summary of The Methodology



Panel 1 Interested Parties

Professional	• Gastroenterologists • Upper Gastro-Intestinal Surgeons • Registrar Trainees • Nurse Endosopists and Endoscopy Nurses • Histopathologists • Clinical Researchers/Clinician Scientists
Non-Professional	• Patients (Barrett's Oesophagus, Gastroesophageal Reflux Disease and Oesophageal Adenocarcinoma) • Family members or friends of patients • Charities
Excluded	• Non-Clinical Researchers • Associated Industry Employees (e.g. drug and medical device companies)

Panel 2 Charities and Organisations Invited to Distribute the Survey

Interested Parties	Organisation
Professional	BSG - British Society of Gastroenterology AUGIS – Association of Upper GI Surgeons PCSG – Primary Care Society for Gastroenterology.
Non-Professional	CORE – Fighting Gut and Liver Disease Action Against Heartburn Barrett's Oesophagus Campaign Barrett's Wessex Cancer Research UK CARD – Campaign Against Reflux Disease FORT – Fighting Oesophageal Reflux Together Gutsy Group – Patient Support Group Heartburn Cancer UK Humberside Oesophageal Support Group Michael Blake Foundation - Oesophageal Cancer Awareness and Prevention. Oesophagoose – Oesophageal and Gastric Cancer Awareness Campaign OOSO- Oxfordshire Oesophageal and Stomach Organisation OCHRE charity – Promoting awareness of Oesophageal Cancer. Scotland. OPA – Oesophageal Patients Association

Table 1 Interim Prioritisation Long List Ranking

ID	Uncertainty	Professional Rank	Non-professional Rank	Combined Rank
K	How can we identify which patients with Barrett's Oesophagus are at most risk of developing cancer in order to target surveillance more appropriately?	1	2	1
P	How does the patient's genetic makeup and family history relate to their risk of disease progression (from Reflux - Barrett's Oesophagus - Precancerous - Cancer) and potential response to treatments?	7	9	2
O	When should we intervene with Barrett's Oesophagus; Is there a role for endoscopic intervention (ablation) of Barrett's Oesophagus with no precancerous changes?	9	7	2
Y	What are the most appropriate intervals for surveillance? And when can it be discontinued?	10	8	4
V	Which endoscopic therapy and techniques (RFA) are most effective, safest and economical when treating Barrett's Oesophagus with pre-cancer? Is there a role for other methods? (for example, cryoablation or argon plasma coagulation)	2	18	5
E	How effective are lifestyle interventions (diet, exercise, weight loss, smoking cessation) in improving reflux symptoms and can they alter individuals risk of Barrett's Oesophagus or cancer?	16	5	6
M	Should Barrett's surveillance and new patient clinic be conducted by a dedicated service rather than all endoscopists? What impact would this have on patients, particularly pre-cancer diagnosis rates, patient education and satisfaction?	3	21	7
N	What key factors can be identified at a cellular level in the progression from a normal oesophagus - Barrett's Oesophagus - Precancerous - Cancer? Are these factors the same in younger patients or those post endoscopic treatment (ablation) for example?	22	3	8
S	Are there any long-term complications or risks with prolonged PPI use? Particularly their effects on bone density, salts in the blood (electrolytes), kidney function and cognitive impairment?	24	1	8
R	Are PPIs the only long term answer for treating reflux? What other treatment options are available for patients who are intolerant, unresponsive or unwilling to take PPIs? (for example, surgery, minimally invasive techniques and newer medications)	21	4	8
T	What is the long-term effectiveness of endoscopic treatment for precancerous Barrett's or early cancers? Are response rates sustained? How does this effect the need for future endoscopic surveillance in these patients?	12	13	8
U	Is there any role for the newer, less invasive, techniques in controlling reflux? For example, electrical stimulation of the lower oesophagus from a device implanted underneath abdominal skin (endostim) or radiofrequency energy to the lower oesophageal muscle via endoscopy (stretta).	8	19	12
D	How can we raise the public awareness and profile of Acid Reflux and its links to Barrett's Oesophagus and Cancer?	18	10	13
Z	How can we accurately identify the high-risk people from the general population to target Barrett's Oesophagus screening?	5	24	14
X	Can Barrett' Oesophagus be reversed or its progression to cancer be halted by drug therapy (chemoprophylaxis)?	19	10	14
W	Is there a role for anti-reflux surgery to prevent Barrett 's with no precancerous changes progressing or to prevent disease recurrence after endoscopic treatment for pre-cancer or early cancer?	13	16	14
C	What key factors contribute to Gastroesophageal reflux? How significant is the presence of a hiatus hernia with regards to reflux severity, symptoms and cancer risk?	26	6	17
B	Is there a more acceptable, cost effective and accurate test for surveillance and screening of Barrett's Oesophagus in a primary care setting (GP's surgeries)?	4	30	18
J	How do we cope with the increasing demand for diagnostic and surveillance services? Is "blanket" surveillance of all Barrett's beneficial to patients or cost effective in its current model?	13	22	19
F	Are we able to distinguish between bile reflux and stomach acid reflux? What implications does this have on Barrett's Oesophagus development, cancer risk and treatments?	26	12	20
G	How does current surveillance practice across the UK compare to the current national guideline (British Society of Gastroenterology)? Would a national Barrett's Oesophagus Audit or Registry improve standards or care?	11	27	20
L	Is there a role for acetic acid or endoscopic image enhancers in routine Barrett's surveillance? What impact would this have on pre-cancer diagnosis, patient outcome and patient satisfaction.	6	32	20
	CUT OFF AFTER INTERIM PRIORITISATION			
	How does primary care (GP's, nurse practitioners and pharmacists) perceive Gastroesophageal Reflux and Barrett's Oesophagus? Does this have an impact on patients health behaviour, endoscopy referrals or prescribing practices for example?	23	17	**23**
	Is Barrett's Oesophagus over or under diagnosed at endoscopy? What training resources are there to help and improve our accuracy to prevent inappropriate surveillance and burden to patients?	15	26	24
	What is the impact of Barrett's Oesophagus and its care pathways on patients day to day quality of life?	17	24	24
	Do patients with night time acid reflux have more severe disease and greater cancer risk. How can these symptoms be optimally treated?	30	15	26
	How common is Barrett's Oesophagus in the general population and is it increasing in people of younger age?	33	13	27
	How can we accurately identify and treat the less obvious, non-oesophageal, symptoms that can be caused by reflux? For example, a recurrent cough.	24	23	28
	Are there any identifiable patient risk factors or triggers which are associated with breakthrough and treatment resistant symptoms?	20	28	29
	How can the various associated charities and patient support groups work together more effectively?	29	20	30
	Do environmental factors influence the number of people, from one region to another, diagnosed with Gastroesophageal reflux, Barrett's Oesophagus or Oesophageal Cancer?	26	31	31
	Is there a role for using mobile phones and apps to create an interactive reflux or Barrett's Oesophagus network? Could these devices be used to support patients and also provide large amounts of research data more rapidly?	31	29	32
	What is the role of pH testing (measuring acid reflux via a probe in the oesophagus) in Barrett's Oesophagus? What other parameters are available to measure reflux severity and impact?	32	33	33

Table 2 Final "Top 10" Research Priorities for Barrett's Oesophagus and Gastroesophageal Reflux Disease

Research Priority	ID	Final Rank
How can we accurately identify the high-risk people from the general population to target Barrett's Oesophagus screening?	Z	1
How can we achieve individual risk stratification of patients with Barrett's Oesophagus in order to target surveillance more appropriately?	K	2
Is there a more acceptable, cost effective and accurate test for surveillance and screening of Barrett's Oesophagus in a primary care setting?	B	3
Should Barrett's surveillance and new patient clinics be conducted by a dedicated service? How would this compare to current standards of practice in the UK and what impact would this have on patients? (for example, pre-cancer diagnosis rates, patient education, quality of life and satisfaction)	M+G	4
What is the long-term effectiveness of endoscopic treatment (RFA) for precancerous Barrett's or early cancers? How does this effect the need for future endoscopic surveillance in these patients? Is there a role for other methods such as cryoablation or APC in these care pathways?	T + V	5
Are there any long-term complications or risks with prolonged PPI use? Particularly their effects on bone density, salts in the blood (electrolytes), kidney function and cognitive impairment?	S	6
How does a patients genetic makeup relate to their risk of disease progression at a cellular level (from Reflux - Barrett's Oesophagus - Precancerous - Cancer)? Particularly in younger patient groups, those with a strong family history or those with disease recurrence after endoscopic treatment (ablation)?	N+P	7
Are PPIs the only long term answer for treating reflux? What other treatment options are available for patients who are intolerant, unresponsive or unwilling to take PPIs? (for example, surgery, newer medications or minimally invasive techniques such as endostim and stretta)	R+U	8
Is "blanket" surveillance of all Barrett's Oesophagus beneficial to patients or cost effective in its current model? Are current surveillance intervals appropriate and when can surveillance be safely discontinued?	Y+J	9
Is there a role for anti-reflux surgery to prevent Barrett's with no precancerous changes progressing or to prevent disease recurrence after endoscopic treatment for pre-cancer?	W	10

Footnote

Endostim; Electrical stimulation of the lower oesophagus from a device implanted underneath abdominal skin.
Stretta; Radiofrequency energy to the lower oesophageal muscle via endoscopy.

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