European Society of Gastrointestinal Endoscopy – Establishing the key unanswered research questions within gastrointestinal endoscopy

Background and study aim: Gastrointestinal endoscopy is a rapidly evolving research field. The European Society of Gastrointestinal Endoscopy (ESGE) plays a key role in shaping opinion and endoscopy activity throughout Europe and further afield. Establishing key unanswered questions within the field of endoscopy and prioritizing those that are important enables researchers and funders to appropriately allocate resources.

Methods: Over 2 years, the ESGE Research Committee gathered information on research priorities and refined them through a modified Delphi approach. Consultations were held with the ESGE Governing Board and Quality Improvement Committee to identify important unanswered questions. Research workshops were held at the 21st United European Gastroenterology Week. Research questions were refined by the ESGE Research Committee and Governing Board, compiled into an online survey, and distributed to all ESGE members, who were invited to rank each question by priority.

Results: The final questionnaire yielded 291 responses from over 60 countries. The three countries with the highest response rates were Spain, Italy, and United Kingdom. Most respondents were from teaching hospitals (62%) and were specialist endoscopists (51%). Responses were analyzed with weighted rankings, resulting in prioritization of 26 key unanswered questions. The top ranked generic questions were: 1) How do we define the correct surveillance interval following endoscopic diagnosis? 2) How do we correctly utilize advanced endoscopic imaging? 3) What are the best markers of endoscopy quality?

Conclusion: Following this comprehensive process, the ESGE has identified and ranked the key unanswered questions within the field of gastrointestinal endoscopy. Researchers, funders, and journals should prioritize studies that seek to answer these important questions.

Introduction

Gastrointestinal endoscopy is a diverse and rapidly evolving field. Modern advances in technology have revolutionized patient care through techniques such as endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy, endoscopic polypectomy, endoscopic ultrasonography (EUS), and endoscopic variceal ligation. Advancement in technology has unearthed gaps in existing knowledge that can only be answered with robust research. In this era of evidence-based medicine, quality research is important as it helps to inform policies and guidelines. Governing bodies such as the National Institute for Health and Care Excellence in the United Kingdom (UK) rely on research to benchmark standards and guidelines [1]. In Europe, approximately €40 per person per year is spent in the field of biomedical and health research [2]. In the UK, the Medical Research Council spent £771.8 million on government-funded medical research in 2014/15 [3]. In 2015, over 3500 published articles were identified (using PubMed search) that included the term “gastrointestinal endoscopy” in their titles or abstracts. In previous years, pharmaceutical and medical device industries have been accused of monopolizing the research agenda and not addressing questions about treatments that are held in high regard by patients and clinicians [4–6]. This has led to the creation of organizations such as The James Lind Alliance, which was set up with Priority Setting Partnerships to identify unanswered research questions that patients, carers, and clinicians feel are important [7].

Establishing research priorities is important to allow resources to be channeled into the most important research that will benefit patients. Studies that have the ability to answer important clin-
clical questions impacting practice and influencing policy often require multicenter collaborative research to optimize validity [8]. The European Society of Gastrointestinal Endoscopy (ESGE) was established in 1964 and among its aims is the promotion of interest, teaching, and research in the field of gastrointestinal endoscopy. It promotes international exchange of endoscopy data and technical advances, and supports large-scale international studies. The Research Committee of the ESGE has the mandate for establishing, discussing, and promoting clinical research in digestive endoscopy at a broad European level.

Over a 2-year period, the ESGE has sought to define the key unanswered questions within the field of gastrointestinal endoscopy. The ESGE believes that these should become priority areas for future endoscopy research and would encourage researchers within the field of gastrointestinal endoscopy to make these areas a priority. The ESGE would also encourage funding organizations to prioritize funding towards research that seeks to answer these questions.

**Methods**

The modified Delphi approach is a well-established methodological process for obtaining expert opinion and is used widely in health research [9]. Over a 2-year period, a three-step process was utilized to establish the key unanswered questions within gastrointestinal endoscopy. In Round 1, preparatory work was performed by creating a list of key unanswered research questions generated from the ESGE Research Committee, Governing Board, Quality Improvement Committee, and Quality Improvement working groups. In addition, research workshops were held during the 21st United European Gastroenterology Week to obtain feedback from individual ESGE members regarding research priorities.

In Round 2, the ESGE Research Committee and Governing Board refined the questions. Research questions were then divided into seven sections according to endoscopy procedure type – upper gastrointestinal, lower gastrointestinal, small bowel, and hepatopancreatobiliary endoscopy, which was further divided into EUS and ERCP; generic priorities and other cross-cutting themes or questions were also identified. Specific research questions were generated for each section and the wording of questions was revised over several iterations. The final number of questions in each section differed according to the size of the clinical field. Questions that overlapped were consolidated. Through these processes, a total of 58 key unanswered questions were identified (Table 1).

In Round 3, all questions were incorporated into a simple online questionnaire with a ranking system, allowing participants to rank each question by order of priority using SurveyMonkey (www.surveymonkey.com) (see Appendix e1, available online). An online link was sent out via email to all ESGE members, including board members. Members were asked to rank the priority of each research question using a scale of 1 for highest priority to 5 for lowest priority. A weighting was applied to the questionnaire results to generate a final priority list. Higher weighting was given to scores with the highest priority (e.g. a rating of 1 received a weighted score of 5, a rating of 5 received a weighted score of 1), and the weightings were summed to give a score, which was used to rank the research questions. In addition, respondents were also asked to provide demographic information, namely their country of origin, type of hospital, and job title.

Completion of the survey was voluntary, with an iPad prize offered via a random draw as an incentive to participate.

**Results**

A total of 291 responses to the online survey were received, with participants working in over 60 countries. The three countries with the most respondents were Spain, Italy, and the UK. The majority of respondents were from teaching hospitals (62%), followed by community hospitals (23%), and private clinics (15%). Most respondents were specialist endoscopists (51%), followed by general gastroenterologists who performed endoscopy (43%), and trainees (6%). A weighted ranking matrix was used to analyze the results of the survey and to determine the priority of all of the key unanswered questions. As a result, 58 key unanswered questions were narrowed down to a total of 26 (Table 2).

Endoscopists from different countries or with different levels of practice did not rank the priorities significantly differently. The leading generic priority and priorities for upper and lower gastrointestinal endoscopy, respectively, all related to optimizing surveillance: How do we define the correct surveillance interval following initial endoscopic diagnosis? What is the correct surveillance strategy for atrophic gastritis and metaplastic gastritis?

What is the optimal surveillance of patients following coloscopic polypectomy? For small-bowel endoscopy, the question “How should we investigate occult or acute gastrointestinal bleeding following normal upper and lower gastrointestinal endoscopy?” was the number one priority. For EUS “How do we optimally diagnose and manage cystic pancreatic tumors?” and for ERCP “What are the roles for magnetic resonance cholangiopancreatography, ERCP, and EUS?” were ranked as most important. Additionally “How do we define the interface between endotherapy and gastrointestinal surgery?” was defined as the most important cross-cutting theme.

**Discussion**

This is the first large international collaborative effort to identify and prioritize key unanswered questions within the field of gastrointestinal endoscopy. These results provide a clear framework for ESGE researchers to determine important research questions and studies, and will help funders to identify key future research priorities that have the greatest relevance to improving patient care.

**Generic priorities**

Surveillance intervals for endoscopy remain a contentious issue, with some disease processes having been researched more than others. Colorectal cancer, inflammatory bowel disease, and post-polypectomy surveillance are examples of conditions where some evidence has allowed for guidelines to be developed [10, 11]. However, there is still a lack of high evidence level studies, and this applies to a myriad of other disease processes including gastric polyps, gastritis, and Barrett’s esophagus. Advanced endoscopic imaging modalities, such as narrow-band imaging, I-Scan (Pentax Endoscopy, Tokyo, Japan), Fuji Intelligent Color Enhancement (Fujinon, Tokyo, Japan), autofluorescence imaging, and confocal laser endomicroscopy, have yet to establish their role in gastrointestinal endoscopy [12–14]. Adenoma detection rate is currently regarded as the most important surrogate indicator of
## Table 1  Completed list of perceived key unanswered research questions in gastrointestinal endoscopy.

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<td>3. How do we correctly utilize advanced endoscopic imaging?</td>
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<td>4. What are the best markers of endoscopy quality?</td>
<td>9. What is the role of advanced imaging in dysplasia detection in Barrett’s esophagus, squamous cancer detection in high risk patients or intestinal metaplasia in the stomach?</td>
<td>22. Can we develop automatic reading analysis algorithms?</td>
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## Original article

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quality in colonoscopy and a low adenoma detection rate has been shown to correlate with higher interval colorectal cancers [15–18]. However, other markers that may reflect improvements in endoscopy quality have not, to date, been researched in detail.

**Upper gastrointestinal endoscopy**
Atrophic gastritis and metaplastic gastritis are precursor lesions for gastric cancer but endoscopy surveillance for this group of patients is poorly studied. Studies from Korea, UK, and elsewhere in Europe have advocated screening intervals of 1–3 years for high-risk subjects but randomized controlled trials (RCTs) are still required [19–21]. Barrett’s esophagus is a precursor for esophageal adenocarcinoma but there are currently no completed RCTs that support the practice of screening in these patients. The management of patients on anticoagulants with acute gastrointestinal bleeding can be challenging, as several factors such as type of anticoagulant, bleeding severity, and thrombotic risk have to be considered. There are no RCTs available to guide clinical practice. However, a retrospective cohort study of 1329 patients found that restarting warfarin after 7 days decreased the mortality and thromboembolism risk without increasing the risks exceed the benefits? 335
5. Can surveillance interval be adjusted depending upon both patient factors and the quality of the endoscopy? 310

**OTHER CROSS-CUTTING THEMES / QUESTIONS**
1. How do we define the interface between endotherapy and gastrointestinal surgery? 318
2. Can we better understand the prevalence and natural history of diseases diagnosed and treated by gastrointestinal endoscopy – in particular neoplasia? 314
3. How do we validate and establish the clinical application of scoring and diagnostic tools for gastrointestinal endoscopy? 304

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**Table 1**

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<td>367</td>
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**UPPER GASTROINTESTINAL ENDOSCOPY**
1. What is the correct surveillance strategy for atrophic gastritis and metaplastic gastritis? 500
2. What is the correct surveillance strategy for Barrett’s esophagus? 469
3. When can anticoagulant medication be restarted following gastrointestinal bleeding? 440
4. What is the role of advanced imaging in dysplasia detection in Barrett’s esophagus, squamous cancer detection in high risk patients or intestinal metaplasia in the stomach? 387
5. Can training modules improve image interpretation and lesion recognition for endoscopists? 366

**LOWER GASTROINTESTINAL ENDOSCOPY**
1. What is the optimal surveillance of patients following colonoscopic polypectomy? 566
2. What is the importance of sessile serrated polyps? 556
3. Can further polyp characterization (sessile serrated lesions, number of polyps, and size of polyps) be a better predictor of interval cancer rates than adenoma detection rate? 370
4. What are the risks and benefits of leaving smaller polyps in place in older persons? Is it possible to define an age cutoff where the risks exceed the benefits? 335
5. Can surveillance interval be adjusted depending upon both patient factors and the quality of the endoscopy? 310

**SMALL-BOWEL ENDOSCOPY**
1. How should we investigate occult or acute gastrointestinal bleeding following normal upper and lower gastrointestinal endoscopy? 626
2. What is the optimal imaging modality for the small bowel? 424
3. How can capsule endoscopy be used therapeutically? 361
4. Should we perform capsule endoscopy or deep enteroscopy? 307
5. Can we develop automatic reading analysis algorithms? 298

**HEPATOPANCREATICOBILIARY ENDOSCOPY – EUS**
1. How do we optimally diagnose and manage cystic pancreatic tumors? 311
2. How do we improve noninvasive diagnostic methods (e.g. contrast-enhanced endoscopic ultrasonography, 3D-reconstruction) for differential diagnosis of pancreatic cancer and inflammatory diseases? 286

**HEPATOPANCREATICOBILIARY ENDOSCOPY – ERCP**
1. What are the roles for magnetic resonance cholangiopancreatography, endoscopic retrograde cholangiopancreatography, and endoscopic ultrasonography? 355
2. What is the optimal approach to access the biliary tree in patients with altered anatomy? 310
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**Table 2**

List of top key unanswered questions within the field of gastrointestinal endoscopy.

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more RCTs are required [23–25]. Training modules including simulators have been shown to accelerate the learning of practical skills in gastrointestinal endoscopy [26]. However, no large RCTs have examined the role of training modules in improving image interpretation and lesion recognition among endoscopists.

**Lower gastrointestinal endoscopy**

To date, no large randomized trials have assessed the benefit of surveillance in post-polypectomy patients. Current guidelines that are available focus on epidemiological data, screening studies, and expert opinion [10]. Sessile serrated polyps represent 15%–20% of all serrated polyps [27]. In recent years, the pathway from serrated polyp to colorectal cancer has been described but clinical data are still lacking, with many unanswered questions concerning the transition of serrated polyps to cancer [28]. Adenoma detection rate has been shown to be an independent predictor of interval cancer rates [16–18]. However, further polyp characterization and its relationship with interval cancer rate have yet to be studied. The relationship between the benefits and risks of leaving small polyps in older patients has not been studied. Colonoscopy surveillance that takes into account individual patient factors and quality of endoscopy is also under-reported.

**Small-bowel endoscopy**

Patients with occult or overt gastrointestinal bleeding with negative upper gastrointestinal endoscopy and colonoscopy can present a diagnostic challenge. Capsule endoscopy, push or single-/double-balloon enteroscopy, computed tomography (CT) angiography, radionuclide imaging, and small-bowel follow through have all been described as modalities to investigate this group of patients [29]. However, there are a lack of large randomized trials to advocate the use of one modality over the other. Furthermore, the optimal imaging modality for the small bowel is unclear. Successful imaging of the small bowel depends on the use of available and appropriate radiology to answer a particular clinical question. A range of imaging techniques including small-bowel barium study, abdominal ultrasound, CT enteroclysis, and magnetic resonance imaging (MRI) enteroclysis are available, but more studies are required to determine the role of each modality in different disease processes. Capsule endoscopy is becoming increasingly recognized as a diagnostic tool for the small bowel [30,31]. However its role in therapeutics is unclear and more research will be required to determine this. As the role of capsule endoscopy becomes more established, studies comparing the benefits and risks of deep enteroscopy against capsule endoscopy also need to be performed. Automatic reading analysis algorithms have begun to be developed for capsule endoscopy, but will require more progress before being adopted for general use [32,33].

**Hepatopancreaticobiliary endoscopy – EUS**

Increased use of abdominal cross-sectional imaging has allowed for increased detection of pancreatic cystic tumors. However, these lesions remain difficult to classify without surgical resection, and a lack of evidence into the management of these lesions makes them difficult to treat [34]. EUS and MRI are accepted techniques for pancreatic imaging [35], but more research needs to be done to investigate ways of improving these methods for diagnosing and staging patients with pancreatic cancer. Research is currently under way to improve EUS imaging capabilities, including elastography and contrast enhancement, and also to increase the accuracy of sampling procedures based on EUS-guided fine-needle aspiration [36,37].

**Hepatopancreaticobiliary endoscopy – ERCP**

Magnetic resonance cholangiopancreatography (MRCP), ERCP, and EUS are imaging modalities that are used to investigate pancreaticobiliary disease. The role of each modality has not been clearly established. A review found EUS to be more sensitive than ERCP in diagnosing chronic pancreatitis, and superior to MRCP in the detection of microcalculi and in evaluating pancreatic divisum [38]. However, there are a lack of large randomized trials comparing each modality. Cap-assisted ERCP and double-balloon enteroscopic ERCP have been shown in small series to show promising results in patients with altered anatomy [39,40]. Large scale RCTs are still required to investigate this in further detail. Precut sphincterotomy is an alternative used when standard methods of biliary access have failed. Most studies have reported high cannulation rates of more than 90%, but complication rates of 13.9% have been reported with common bile duct diameters of ≤4mm [41,42].

**Cross-cutting themes / questions**

The emergence of endotherapy has added to the arsenal of minimally invasive techniques available to manage patients with perforations, leaks, and fistulae that may have required surgical intervention in the past [43]. Although these may only be applicable to a select group of patients, more studies are required to compare the outcomes of endotherapy techniques with conventional gastrointestinal surgery. There are large gaps in the understanding of the prevalence and natural progression of other types of gastrointestinal neoplasia, which should be studied. Scoring and diagnostic tools are being used increasingly in gastrointestinal endoscopy. The Glasgow–Blatchford Bleeding Score and Rockall Score are examples of scoring tools established to assess the need for treatment in patients with acute upper gastrointestinal bleeding. In particular, the Glasgow–Blatchford Bleeding Score was developed 15 years ago, but only a handful of studies have looked at its validity in discriminating between patients at risk of bleeding [44–46].

**The next step**

The current study provides insight into the research priorities of ESGE members. However, translation of these priorities into more specific research questions will require discussion and planning. It is hoped that this study will provide a stimulus for researchers to address these questions and develop collaborative research. Moreover, it is hoped that research themes that have been identified as priorities by the ESGE will receive prioritization from funding organizations. Finally, a gastrointestinal endoscopy research question that has been identified as a priority based on a gap in current evidence is more likely to lead to publication of the research in a high quality journal. Although no list can incorporate all important research questions, this study aims to identify the most important areas through a wide ranging of consultation of all ESGE members. This is the first international piece of work established to set the priorities for research within the field of gastrointestinal endoscopy. Similar approaches have been adopted in other areas of medicine, including public mental health care [47,48], palliative cancer care [49], colorectal surgery [50], and breast cancer care [51]. Similarly, the American Society of Colon and Rectal Surgeons utilized a modified Delphi approach to highlight key re-

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search priorities for colorectal surgery [52]. Other specialties that have prioritized key research questions within their field include pediatric palliative care in America [53], elderly care physicians in Canada [54], and gynecologists in Australia [55]. The World Health Organization recently published the key research priorities that were identified to improve global newborn health and prevent stillbirths by 2025 [56]. There is a lack of evidence to illustrate the impact or outcomes of setting research priorities, partly as these processes do not normally cover impact measurement or analysis of outcomes [57].

Having completed this work, the ESGE will seek to disseminate these results widely to stakeholders in order to encourage prioritization of these areas. Researchers themselves should be encouraged to develop research that addresses these unanswered questions. The ESGE will disseminate these priorities within member societies. Where large-scale collaboration is required, this should be supported and facilitated by the ESGE. Secondly, it is important that funders should be encouraged to prioritize research that addresses these areas. It is also important to note that research priorities often can only be answered by long-term studies, which in turn require longitudinal funding, and funders should thus be encouraged to consider this. The ESGE will seek to engage with international funders such as the European Union and then with funding bodies within member countries. Some countries have horizon scanning organizations, which aim to collate priority areas across the whole field of biomedical research. It is important that where these organizations exist they are advised about the priorities in endoscopy research. Finally, the ESGE will engage with industry to encourage commercial partners to align their priorities with these unanswered questions.

Conclusion

This list of leading research priorities was generated using a systematic, transparent, and inclusive approach across multiple countries. The research priorities cover a wide range of important topics, and it is hoped that these findings will be used to encourage researchers, funders, and journals to prioritize research that addresses these areas within the field of gastrointestinal endoscopy.

Appendix e1

European Society of Gastrointestinal Endoscopy research priorities questionnaire.

Competing interests: R. Bisschops has received consultancy fees from Boston Scientific (2015); speaker’s fees from Covidien (2009–2016) and Norgine (2015); speaker’s fee and hands-on training sponsorship from Olympus Europe (2013–2014); consultancy fees, speaker’s fee, and research support from Pentax Europe (2008–2016) and Fujifilm (2013–2016); support from FWO Flanders; research support from Cook Medical (2015–2016); hands-on training sponsorship from Erbe (2013–2015); and an editorial fee from Thieme Verlag as coeditor of Endoscopy. E. Dekker receives a research grant and equipment on loan from Olympus, equipment on loan from Fujifilm and medical advice from Tillotts. M. Dinis-Ribeiro receives funding from Thieme Verlag for editorial work for the journal Endoscopy. His department has also received support from Olympus in relation to a teaching protocol (from August 2014 to July 2015). P. Fockens has a consulting role during 2016 with Fujifilm, Olympus, Medtronic and Cook. R. Jover’s department has received research grants from MSD and he has an advisory role with Norgine. M. F. Kaminski has a lecturing and teaching role for Olympus, Poland. S. Meisner has a consultancy role with Olympus Europa and SE & CO. KG. T. Ponchon receives advisory board member’s fee from Olympus, Ipsen Pharma, Boston Scientific in 2014 and 2015; speaker’s fee from Fujifilm, Ipsen Pharma in 2014 and 2015 and from Covidien in 2014; advisory board member’s fee from Cook medical in 2014; training support from Ferring in 2014; speaker’s fee from Olympus in 2014 and 2015; research support from Boston Scientific, Olympus in 2014 and 2015. C. Rees receives research funding from Olympus, Aquilard and arc Medical. M. Rutter’s department receives research funding from Olympus for a colitis surveillance trial (2014 to present). A. Salfouli had a consulting role with Mediglobe Corporation f in 2015 and 2016 and own stock with Medinsys from 2012 til 2016; receives an editorial fee for Ultrasound International Open (UIO) from Thieme Verlag. P. D. Siersema’s department has received research grants from Endo-Stim, Cook Medical, Dr. Falk Pharma Benelux, Motus GI, Yakult, Pentax, World Cancer Research Fund. He is a consultant for Endo-Choice USA, Endostim USA, Motus GI Israel and Medi-Globe Germany. He also conducts paid editorial work for the journal Endoscopy. C. Spada has received training support from Covidien, Alfa Wasserman and Norgine. R. Valori is a director of Quality Solutions for Healthcare LLP, a company providing consultancy for improving quality in healthcare, and of AnderVal Ltd., a company providing endoscopy skills training. L. Aabakken, M. Bretthauer, M. Ciocirlan, D. Domagk, I. Galnek, T. Hucl, O. Le Moine, W. S. Ngu and J. Regula have no competing interests.

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Appendix e1

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