

Revising the European Society of Gastrointestinal Endoscopy (ESGE) research priorities: a research progress update



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published online 1.4.2021

Bibliography

Endoscopy 2021; 53: 535–554

DOI 10.1055/a-1397-3005

ISSN 0013-726X

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This article is published by Thieme.

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

Appendix 1s

Supplementary material is available under

<https://doi.org/10.1055/a-1397-3005>

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ABSTRACT

Background One of the aims of the European Society of Gastrointestinal Endoscopy (ESGE) is to encourage high quality endoscopic research at a European level. In 2016, the ESGE research committee published a set of research priorities. As endoscopic research is flourishing, we aimed to review the literature and determine whether endoscopic research over the last 4 years had managed to address any of our previously published priorities.

Methods As the previously published priorities were grouped under seven different domains, a working party with at least two European experts was created for each do-

main to review all the priorities under that domain. A structured review form was developed to standardize the review process. The group conducted an extensive literature search relevant to each of the priorities and then graded the priorities into three categories: (1) no longer a priority (well-designed trial, incorporated in national/international guidelines or adopted in routine clinical practice); (2) remains a priority (i.e. the above criterion was not met); (3) redefine the existing priority (i.e. the priority was too vague with the research question not clearly defined).

Results The previous ESGE research priorities document published in 2016 had 26 research priorities under seven domains. Our review of these priorities has resulted in sev-

en priorities being removed from the list, one priority being partially removed, another seven being redefined to make them more precise, with eleven priorities remaining unchanged. This is a reflection of a rapid surge in endoscopic research, resulting in 27% of research questions having already been answered and another 27% requiring redefinition.

Conclusions Our extensive review process has led to the removal of seven research priorities from the previous (2016) list, leaving 19 research priorities that have been redefined to make them more precise and relevant for researchers and funding bodies to target.

SOURCE AND SCOPE

This progress report is an official statement from the European Society of Gastrointestinal Endoscopy (ESGE). It updates the 2016 ESGE document on the key unanswered research questions within gastrointestinal endoscopy.

Introduction

The practice of digestive endoscopy is evolving at a very rapid pace. This is driven by the development of new devices led by industry and the development of new techniques led by endoscopists. Whilst innovations are welcome, a robust system of testing and trialing these innovations would help to ensure that the benefits to patients outweigh any potential harms from such innovation. This requires a robust culture of good quality research.

There are distinct differences between traditional drug development and research compared with endoscopy device development and research. A drug cannot be licensed without large regulatory multicenter phase III randomized controlled trials (RCTs), whereas an endoscopy device can be licensed after a device safety study without robust efficacy data. One of the aims of the European Society of Gastrointestinal Endoscopy (ESGE) is to encourage, facilitate, and support high quality endoscopic research at a European level.

In 2014, the ESGE research committee set out to produce a list of key research priorities in the field of digestive endoscopy. These were developed over a 2-year period in a three-step process. This started with various ESGE committees generating a list of research questions, followed by the research committee refining and consolidating these questions under specific endoscopic domains, and finally prioritization voting by ESGE members to establish 26 research priorities under seven endoscopic domains. ESGE finally published a list of top research priorities in 2016 [1]. A published list is particularly useful for young researchers, industry looking for innovations, and funding bodies

ABBREVIATIONS

ADR	adenoma detection rate
AEI	advanced endoscopic imaging
AI	artificial intelligence
AUC	area under the curve
BLI	blue-light imaging
BSG	British Society of Gastroenterology
CD	Crohn's disease
CNN	convolutional neural network
CT	computed tomography
DBE	double-balloon enteroscopy
DOR	diagnostic odds ratio
EMR	endoscopic mucosal resection
ERCP	endoscopic retrograde cholangiopancreatography
ESD	endoscopic submucosal dissection
ESGE	European Society of Gastrointestinal Endoscopy
EUS	endoscopic ultrasound
GERD	gastroesophageal reflux disease
GI	gastrointestinal
GRADE	Grading of Recommendations Assessment, Development and Evaluation
IM	intestinal metaplasia
KQI	key quality indicator
MRCP	magnetic resonance cholangiopancreatography
MRI	magnetic resonance imaging
NBI	narrow-band imaging
NET	neuroendocrine tumor
POEM	peroral endoscopic myotomy
RCT	randomized controlled trial
SBI	Suspected Blood Indicator
SICUS	small-intestinal contrast ultrasound
SRI	somatostatin receptor imaging
SSP	sessile serrated polyp
VCE	video capsule endoscopy
WLE	white-light endoscopy

trying to decide on funding priorities. It is also important to note that endoscopic research is also being performed at a rapid pace and a topic that is considered to be a top priority today might not remain a priority in a years' time.

A PubMed search revealed that in the last 5 years, 96379 articles were published on endoscopy. This gives an idea of the speed at which research in the field of endoscopy is progressing. It may also bring into question the relevance of the ESGE published research priorities as of today. Therefore, we decided to conduct a thorough review of the literature to assess the current relevance of the ESGE set of research priorities. The aim of this review was to scrutinize the published literature related to each of the 26 priorities and decide whether or not the topic should continue to be a priority. If the topic remained a priority, we aimed to redefine the priority where necessary.

Methods

A preliminary meeting of the research committee was held at the ESGE Days meeting held in Prague in April 2019 to share methods, aims, timelines, and the entire position paper process. As the previously published priorities were grouped under seven different domains, a working party for each domain was created, with each group having at least two European experts, to review all the priorities under that domain. A structured review form was developed to standardize the review process (**Appendix 1 s**, see online-only Supplementary material).

The working parties independently carried out a systematic search for, and analysis of, the literature relevant to their domains, using the major electronic databases (PubMed, Scopus, Cochrane, and Embase), limiting the search period to 1 January 2015 to 31 May 2020. Relevant evidence was graded according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system [2]. Once these data had been collected, a web-based meeting of the entire group was held in July 2020 to review all the evidence and make a decision as to relevance of each previously published priority. The consensus group included 18 participants and was led by a chairman (P. B.).

Overall, 27 research priorities were submitted to the global consensus group for an open discussion driven by the chairman. This higher number of research priorities was the result of one research priority from the upper gastrointestinal (GI) domain in the 2016 paper ("What is the role of advanced imaging in dysplasia detection in Barrett's esophagus and squamous esophagus in high risk patients or intestinal metaplasia in the stomach") being split into two, because different priorities were provided for dysplasia in the esophagus vs. intestinal metaplasia (IM) in the stomach. Each revised research priority was discussed and a final decision was taken unanimously, placing it into one of three different categories: (1) no longer a priority (well-designed trial, incorporated in national/international guidelines or adopted in routine clinical practice); (2) remains a priority (i.e. the above criterion was not met); (3) redefine the existing priority (i.e. the priority was too vague with the research question not clearly defined).

Generic priorities

1 How do we define the correct surveillance interval following initial endoscopic diagnosis?

RECOMMENDATION

Redefine.

What is the impact of endoscopic surveillance on incidence and disease-specific survival?

Since the publication of the previous Research Priorities document [1], many guidelines specifically addressing the topic of surveillance following the endoscopic diagnosis of precancerous or cancerous conditions have been published by the ESGE, including surveillance of Barrett's esophagus [3], for gastric atrophy and IM [4], post-polypectomy [5], and after (endoscopic and surgical) resection of colorectal cancer [6]. Multiple observational studies have been published addressing the stratification of patients undergoing surveillance for precancerous or cancerous conditions [7–10]. These studies propose clinically useful stratification of such populations into high and low risk groups. Therefore, the question "who is at risk and what should the surveillance interval be?" has been successfully addressed. However, these studies have not yet assessed whether the surveillance intervention is able to reduce incidence or mortality and this deserves to be addressed in long-term randomized trials with clinically relevant end points (i.e. European Polyp Surveillance [EPoS], NCT02319928 [11]).

The surveillance interval-related question is no longer a priority but should be redefined to address the impact of endoscopic surveillance on incidence and disease-specific survival.

2 How do we correctly utilize advanced endoscopic imaging?

RECOMMENDATION

Redefine.

How can advanced endoscopic imaging be implemented to change clinical practice?

In lower GI endoscopy, several studies have evaluated the accuracy of advanced endoscopic imaging (AEI) for polyp detection and characterization [12, 13], so this aspect no longer represents a priority question. Similarly, how to implement a training program for AEI and how to maintain expertise has recently been addressed using objective methodology by a dedicated ESGE curriculum for optical diagnosis [14]. On the other hand, the clinical impact of this curriculum and ways to analyze its implementation are topics for future research. Similarly, the role of AEI in the upper GI tract has also been extensively explored [15]. There are ESGE standards that have already been set around the use of AEI [16].

However, AEI-assisted optical biopsy has still not replaced histological biopsy in clinical practice. Similarly, AEI has the potential to influence clinical decisions such as resect and discard

for diminutive adenomas, diagnose and leave for diminutive hyperplastic polyps in the rectosigmoid region, and direct referral to surgery for deep invasive GI cancers or endoscopic resection for superficial cancers. However, this kind of implementation of AEI in our routine endoscopic practice has still not happened, although the advent of artificial intelligence (AI) has raised high hopes of making this a reality.

For this reason, the question should be redefined to look at how AEI can be implemented to change clinical practice.

3 What are the best markers of endoscopy quality?

RECOMMENDATION

Redefine.

How can we implement and monitor adherence to the key quality indicators (KQIs) and quantify the long-term benefits of such implementation, as well as developing and validating the patient experience-related KQIs?

ESGE has produced position statements [12, 13, 17–19] on the most appropriate performance and key quality indicators (KQIs) for a whole range of endoscopic procedures and techniques. In addition, specific domains and subdomains have been generated for each technique. The best markers of quality in endoscopy are well defined and there is substantial evidence supporting the use of the main KQIs in relation to the efficacy and safety of the procedures. Defining the KQIs is no longer a priority, but a number of proposed quality indicators related to patient experience are in their infancy, without any supporting evidence, so further work in this area is required.

Further research needs to be performed to develop strategies related to the implementation and monitoring of KQIs. The priority related to quality in endoscopy should therefore be redefined to consider how we can implement and monitor adherence to the KQIs and quantify the long-term benefits of such implementation, while developing and validating the patient experience-related KQIs.

4 What are the best ways to train endoscopists?

RECOMMENDATION

No longer a priority.

Training for endoscopists has been the subject of research since the last research priorities document was published. The ESGE has been developing a series of curricula for training in various advanced endoscopic procedures [20]. Curricula for training in endoscopic submucosal dissection (ESD) [21], optical diagnosis [14], and small-bowel assessment [22] in Europe have already been published by the ESGE. The critical role of such publications has been in defining the key competencies for each technique and then developing training modules to achieve these competencies. As for training modalities, the most researched modalities are simulation-based training and training in AEI. Simulation-based training is the most researched

topic and this has been summarized in a published Cochrane review and meta-analysis [23]. Therefore, the question “how to train” has to a large extent been addressed. The remaining question is related to post-training suboptimal performance and ways of tackling it.

Upper gastrointestinal endoscopy

1 What is the correct surveillance strategy for atrophic gastritis and metaplastic gastritis?

RECOMMENDATION

Remains a priority.

Since 2015, no study has compared different surveillance strategies for gastric premalignant conditions. In fact, even before 2015, only one RCT had evaluated different surveillance strategies for patients with these conditions, but even this study only considered patients with autoimmune gastritis [24]. In the last 5 years, several studies have confirmed the importance of surveillance in patients with these conditions and this is reflected in two recent guidelines that recommend new surveillance intervals, according to different risk factors [4, 25]. However, both guidelines recognize that the timing for surveillance, even though similar in both, is based on expert opinion and is not evidence-based.

In this context, there is a need for well-designed randomized studies comparing different surveillance intervals for these patients. Moreover, these studies should also evaluate the influence of factors, such as the stage of gastritis (endoscopically and histologically), the presence of (in)complete IM, and a family history of gastric cancer, on the surveillance strategy. The impact of surveillance in these studies should be quantified, not only in terms of the prevention of gastric cancer, but also in terms of the detection of dysplasia or adenocarcinoma, the detection of neuroendocrine tumors (NETs), and also the progression to high risk stages for patients with low risk at baseline.

2 What is the correct surveillance strategy for Barrett's esophagus?

RECOMMENDATION

Remains a priority.

Several guidelines have recommended endoscopic surveillance at regular intervals for Barrett's esophagus. The supporting evidence is weak and such strategies vary between different settings, often being guided more by expert opinions than robust evidence [3, 26, 27]. Since the publication of the previous ESGE priorities, two systematic reviews have shown a survival advantage and lower risk of progression in patients undergoing endoscopic surveillance [28, 29]. No randomized trials on surveillance intervals have been published, but ESGE has pub-

lished new guidelines suggesting the surveillance interval should be based on the length of Barrett's esophagus [3].

One randomized trial showed the advantage of wide-area transepithelial sampling (WATS) on random biopsies for the detection of high grade dysplasia and esophageal adenocarcinoma [30]. One feasibility randomized tandem endoscopy trial of the Seattle protocol vs. acetic acid chromoendoscopy showed that acetic acid-guided biopsies can dramatically reduce the number of biopsies taken per neoplasia detected, but a fully powered non-inferiority study would require 2828 patients [31]. Several prospective studies have shown the importance of a dedicated list and advanced imaging technologies, including narrow-band imaging (NBI) and confocal laser endomicroscopy. An evidence-based model for Barrett's surveillance following radiofrequency ablation suggests the possibility of reducing the number of surveillance endoscopies and increasing the surveillance interval based on the grade of dysplasia [32].

In conclusion, although guidelines are suggesting the prolongation of the surveillance interval in certain subgroups, this is not based on any good quality data, or on the availability of techniques/modalities to perform this. Barrett's surveillance is a rapidly evolving field, but defining and standardizing our strategies to show a meaningful impact on the outcome of Barrett's patients should remain a priority.

3 When can anticoagulant medication be restarted following gastrointestinal bleeding?

RECOMMENDATION

Remains a priority.

The right timing for anticoagulant and antiplatelet resumption following GI bleeding remains uncertain. Recently a new class of drugs, direct oral anticoagulants (DOACs), has been introduced. There is a lack of good evidence on their management following GI bleeding. High quality prospective studies should be prioritized to get direct data from patients. Two systematic reviews showed survival advantage after anticoagulant resumption, no RCT or prospective study has been published, but six retrospective studies were found [33–38]. Anticoagulant resumption increased the rate of GI bleeding and decreased the rate of thromboembolism, with a net benefit on mortality [38].

In conclusion, results on the timing of resuming anticoagulation are often inconclusive. There is a need for randomized studies evaluating the net patient benefit of different timings for the re-introduction of anticoagulants with risk stratification to individualize treatment.

4 What is the role of advanced imaging in the detection of dysplasia in Barrett's esophagus and squamous esophagus in high risk patients and for the detection of intestinal metaplasia in the stomach?

RECOMMENDATION FOR BARRETT'S ESOPHAGUS AND SQUAMOUS NEOPLASIA

Remains a priority.

RECOMMENDATION FOR INTESTINAL METAPLASIA IN THE STOMACH

No longer a priority.

The role of AEI in dysplasia detection in Barrett's esophagus and squamous cancer detection in high risk patients remains a research priority. Guidelines have different positions on the use of AEI. Since the publication of the previous ESGE priorities, 17 studies examining NBI, blue-light imaging (BLI), i-scan, and chromoendoscopy with acetic acid and Lugol's iodine have been published and were analyzed, of which nine were prospective and eight retrospective [39–55]. An additional 19 studies were found on less common techniques including endomicroscopy and the application of computer-assisted diagnosis. The level of evidence of these studies was moderate or low.

NBI showed a higher sensitivity for the diagnosis of esophageal cancer compared with white-light endoscopy (WLE), at 91%–92% vs. 51%–69% [41, 42], with higher rates of accurate lesion delineation [41]. A retrospective study showed that NBI and iodine staining were both superior to WLE for the diagnosis of esophageal cancer and precancerous lesions ($P < 0.05$), with the diagnostic accuracy of NBI, iodine staining, and WLE being 92.6%, 93.3%, and 67.8%, respectively [45].

In conclusion, these new technologies need to be standardized and validated. Further randomized studies and a cost-analysis study need to be conducted to evaluate their benefit. Scientific societies will have a pivotal role in implementing these technologies once their role is established by high quality research trials.

Regarding the role of AEI in gastric precancerous conditions, three systematic reviews were performed prior to 2015 that found a high accuracy for NBI for the diagnosis of IM and dysplasia, although there was less evidence for other technologies [56–58]. Since 2015, 21 studies have focused on this research question (3 RCTs and 13 cross-sectional studies with prospective recruitment, with 13 evaluating NBI and 6 BLI).

Two RCTs (1 with NBI and 1 with BLI) showed an advantage of these technologies over WLE in the diagnosis of IM and in the detection of early gastric cancer in patients under surveillance [59, 60]. NBI and BLI have been shown to have a high diagnostic accuracy and are useful for the detection and staging of gastric premalignant conditions and in patient surveillance, at least in expert hands. A scale for endoscopic staging of gastric IM (Endoscopic Grading of Gastric Intestinal Metaplasia [EGGIM])

has also been developed and validated, showing high accuracy for IM endoscopic diagnosis [61–63].

There is a need for standardization of patterns and evaluation of the diagnostic yield of AEI in less experienced hands, but it is clear that NBI and BLI increase the accuracy of endoscopic diagnosis and should be used by trained endoscopists using validated classifications, as suggested in the ESGE guidelines [4, 15].

5 Can training modules improve image interpretation and lesion recognition for endoscopists?

RECOMMENDATION

Remains a priority.

Even if AEI shows an advantage in expert hands, it is not clear how to become an expert in endoscopic diagnosis. Since 2015, only four studies have evaluated the impact of training on image interpretation. An RCT evaluated the effect of an e-learning training program with video lectures and self-exercises with immediate feedback, and showed an increase in accuracy of 7.4% in the e-learning group (for differentiating cancerous and non-cancerous lesions) [64]. A post-hoc analysis of this RCT showed a greater benefit for depressed and small lesions [65]. A retrospective study also showed that even non-structured training improved the early gastric cancer detection rate [66]. Therefore, only one RCT showed the benefit of a particular e-learning program for the characterization of dysplastic/neoplastic lesions, but there are no studies evaluating training programs for gastric precancerous conditions.

Data related to training in the use of image-enhanced endoscopy in the detection of Barrett's neoplasia are scanty. A single study evaluated the impact of a web-based platform in training endoscopists in the use of acetic acid-enhanced detection of Barrett's neoplasia [67]. They reported a significant improvement in the performance of endoscopists when trained with carefully selected endoscopic images and videos using a web-based platform. Similarly, another recent study using another web-based platform demonstrated a significant improvement in Barrett's neoplasia detection, as well as delineation [68].

Further work is needed to standardize the training structures and demonstrate the impact of these training interventions during real-time endoscopy and clinically meaningful impacts.

Lower gastrointestinal endoscopy

1 What is the optimal surveillance of patients following colonoscopic polypectomy?

RECOMMENDATION

No longer a priority.

Since the publication of the previous ESGE research priorities, multiple studies have addressed the question of the optimal surveillance of patients following colonoscopic polyp-

ectomy. The guidance for the optimal surveillance strategy following polypectomy has recently been radically updated by the British Society of Gastroenterology (BSG), with an emphasis toward reducing the number of patients entering into surveillance programs and prolonging the surveillance interval [69]. Most recently, the ESGE has introduced an update for post-polypectomy colonoscopy surveillance, which differs from the BSG guidelines, but again aims to reduce the need for surveillance [5]. Therefore, the question of the surveillance interval following polypectomy has been successfully addressed.

2 Can surveillance interval be adjusted depending on both patient factors and the quality of the endoscopy?

RECOMMENDATION

Remains a priority.

The surveillance intervals for patients with family history of colorectal cancer, those with sessile serrated polyps (SSPs), and those with (previous) colitis or colectomy following colon cancer have not been defined in recent years.

It has been questioned whether surveillance intervals could be adjusted dependent on both patient factors and the quality of the colonoscopy. Attempts have been made to identify patient factors which could affect surveillance intervals, with some success [70]. It has been established that the risk of post-colonoscopy cancer is not the same for all endoscopists, and those with the highest adenoma detection rates (ADRs) have the lowest rates of post-colonoscopy cancer [71].

Bowel cleansing is a procedure-related issue, with poorer cleansing negatively affecting ADR and the occurrence of post-colonoscopy cancer [72]. The standard of care is to re-scope patients with inadequate preparation, although this is not always adhered to [73]. It is unclear whether differentiation of surveillance intervals based on excellent, good, and adequate preparation is of benefit, with a published suggestion that there is no difference in adenoma detection between patients with intermediate and high quality preparation [74].

Currently there is insufficient evidence to recommend personalizing surveillance intervals based on either patient factors or the quality of endoscopy and therefore this remains a priority.

3 What is the importance of sessile serrated lesions?

RECOMMENDATION

Redefine.

What is the best technique for detection, resection, and surveillance of sessile serrated polyps?

The BSG provided a position statement on serrated lesions in the colon and rectum discussing: the premalignant potential of serrated lesions; the detection and resection of serrated

lesions; surveillance strategies after detection of serrated lesions; serrated polyposis syndrome (including surgery); and serrated lesions in colitis [75]. The previous question relating to the importance of SSPs has been addressed and, although guidance relating to the detection, resection, and surveillance of SSPs has been issued, this statement is based more on expert opinions rather than good evidence. We have therefore re-defined the priority to focus on identifying the best technique for detection, resection, and surveillance of SSPs.

4 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?

RECOMMENDATION

Remains a priority.

The best predictors of post-colonoscopy cancer rate (sessile serrated lesions, number of polyps, etc.) are still not well understood and research into the question of the best predictors of post-colonoscopy cancer is of the utmost importance. Most studies have only focused on the ADR and factors influencing the ADR. Therefore, the question of post-colonoscopy cancer rate in respect to the ADR has been satisfactorily addressed, but the impact of other polyp factors, such as the SSP detection rate, polyp detection rate, size of polyps, and type of polyps, among others, has not been sufficiently addressed, and therefore this remains a priority.

5 What are the risks and benefits of leaving smaller polyps in place in older patients? Is it possible to define an age cutoff where the risks exceed the benefits?

RECOMMENDATION

Remains a priority.

The risks and benefits of leaving smaller polyps in place in older patients is unclear, and the question has been asked as to whether it is possible to define an age cutoff where the risks exceed the benefits. Polyps do recur in older patients, possibly at a more rapid rate than in younger patients (35% vs. 19% within 3 years) [76]. However, the adverse impact of polypectomy-related complications in older patients is likely to be more serious than in younger patients [77].

Whilst it is established that large polyps > 1 cm in size carry a significant risk of harboring cancer, the absolute risk from diminutive polyps is less clear, with a very large prospective study suggesting that, among 36 000 polyps < 5 mm and 6000 polyps 6–9 mm in size, no cancers were found [78]. Therefore, the risk of cancer in small polyps is extremely low and the benefits of resection are almost entirely based on preventing later transformation into cancer. In older patients with a limited life expectancy the risk of removal may outweigh any benefits.

Unfortunately, the rate of cancerous transformation is unclear. The only available information comes from a very old study from 1987, which examined non-resected polyps of 10 mm or more in size over time. It suggested that, over a 6-year period, the cumulative risks of malignant transformation at 5, 10, and 20 years were 2.5%, 8%, and 24%, respectively [79].

Whilst it is established that polypectomy during colonoscopy reduces the risk of cancer [80], the benefit may come largely from the resection of larger, high risk polyps regardless of a patient's age. However, this has to be balanced against the individual patient's risk. Older patient populations are more heterogeneous, with increasing co-morbidities, and the risk/benefit of polypectomy cannot be assessed on age only.

This is an area where research is needed. With an aging population, guidance on how to manage diminutive polyps in older patients is urgently required.

Small-bowel endoscopy

1 What is the optimal imaging modality for the small bowel?

RECOMMENDATION

Redefine.

How can we better stratify small-bowel investigations for patients with small-bowel inflammation and tumors?

Small-bowel investigations for occult and overt bleeding have been addressed elsewhere, hence the focus of this research priority statement should be on non-bleeding indications for small-bowel investigations. These include Crohn's disease (CD), small-bowel tumors, familial polyposis syndromes, and celiac disease.

Crohn's disease

Since 2016, a number of systematic reviews and meta-analyses aiming to establish the best imaging modality to investigate the small bowel for the evaluation of CD have been published.

Kopylov et al. published a meta-analysis with the aim of comparing the diagnostic yields of video capsule endoscopy (VCE), magnetic resonance enteroclysis, and small-intestinal contrast ultrasound (SICUS) in the detection of active small-bowel inflammation in patients with suspected and/or established CD, and in the monitoring of the disease [81]. VCE showed a similar diagnostic yield to that of magnetic resonance enteroclysis (odds ratio [OR] 1.17, 95% confidence interval [CI] 0.83–1.67) and SICUS (OR 0.88; 95%CI 0.51–1.53) in the detection of active small-bowel CD.

A systematic review and meta-analysis by Yung et al. compared the accuracy of diagnostic yield for VCE, magnetic resonance enteroclysis, and ultrasound in order to evaluate the correct diagnostic approach to detect postoperative recurrence in CD. The sensitivity, specificity, diagnostic odds ratio (DOR), and area under the curve (AUC) for VCE were 100% (95%CI 91%–100%), 69% (95%CI 52%–83%), 30.8 (95%CI 6.9–138), and 0.94, respectively. The sensitivity, specificity, DOR, and AUC

for magnetic resonance enteroclysis were 97% (95%CI 89%–100%), 84% (95%CI 62%–96%), 129.5 (95%CI 16.4–1024.7), and 0.98, respectively. Ultrasound showed a sensitivity, specificity, DOR, and AUC of 89% (95%CI 85%–92%), 86% (95%CI 78%–93%), 42.3 (95%CI 18.6–96.0), and 0.93, respectively [82].

The role of endoscopic imaging modalities in the diagnosis, monitoring, and evaluation of treatment response (i. e. mucosal healing) in CD needs to be further explored.

Small-bowel tumors

The role of imaging modalities for investigating small-bowel tumors is poorly evaluated, particularly in relation to tumor subgroups. Manguso et al. reviewed a database of 85 patients with primary small-bowel NET [83]. The sensitivities for NET detection were 59.7%, 54%, 56%, and 88.1% for computed tomography (CT), magnetic resonance imaging (MRI), somatostatin receptor imaging (SRI), and double-balloon enteroscopy (DBE), respectively. DBE was significantly more accurate for primary NET diagnosis than CT, MRI, or SRI ($P=0.004$, $P=0.007$, and $P=0.01$, respectively). When comparing DBE to radiological tests, DBE was recently demonstrated to have a higher overall accuracy for the detection of small-intestinal tumors when compared with multidetector CT: 92.0% ($n=81/88$) vs. 75% ($n=66/88$); $P<0.01$ [84].

In conclusion, small-bowel tumors represent a rare condition. Their low incidence makes it difficult to perform large studies. There is a requirement for multicenter trials to improve the current knowledge. Other small-bowel conditions requiring imaging include polyposis syndromes and celiac disease, but no new trials have been published in the last 5 years.

The choice of small-bowel imaging modality depends on the indications, skills, and availability. In many circumstances, different imaging modalities play a complementary rather than an alternative role. New endoscopic techniques are emerging (i. e. pan-enteric capsule endoscopy, steerable capsule endoscopy, motorized spiral enteroscopy) [85–88]. The roles of such new technologies are unknown and studies evaluating their roles are a priority in the field of small-bowel disease. The new priority should be redefined to consider how we can better stratify small-bowel investigations for patients with small-bowel inflammation and tumors.

2 Should we perform capsule endoscopy or deep enteroscopy?

RECOMMENDATION

No longer a priority.

Several recent investigators have compared VCE and DBE as modalities to investigate the small bowel [89–93]. Zhang et al. prospectively compared VCE and DBE demonstrating comparable diagnostic yields [89]. Brito et al. performed a recent meta-analysis comparing the two modalities for small-bowel bleeding [93]; 17 studies were included (1477 lesions), with VCE detecting 58.5% of lesions and DBE 41.5%. The sensitivity

of DBE was 84% and specificity was 92%. Performing DBE after VCE increased the diagnostic yield of vascular lesions by 7%, from 83% to 90%. Performing VCE before DBE helps direct the insertion route at DBE and improves diagnostic yields [94]. This has been included in both the ESGE technical review and, more recently, in the ESGE quality improvement initiative [12,95]. Based on this information, this is no longer a research priority.

3 How can capsule endoscopy be used therapeutically?

RECOMMENDATION

Remains a priority.

Several VCE subtypes have been developed to obtain biopsies and for clip placement, along with therapeutic VCE for the treatment of GI bleeding [96–100]. Despite these technical innovations, no prototypes exist for clinical use. The labor intensity and weight of the external magnet has limited the use of externally controlled steerable capsules [101,102]. Whilst the Ankon capsule (motorized VCE), which uses a magnetic field generated by an external industrial robot, has allowed steerability, this has not yet extended beyond the stomach [103,104]. Further innovation is required to see these developments transform into clinical use before this can be prioritized as clinical research.

4 How should we investigate occult or acute gastrointestinal bleeding following normal upper and lower gastrointestinal endoscopy?

RECOMMENDATION

No longer a priority.

For occult bleeding, two systematic reviews, three prospective studies, and 12 retrospective studies have demonstrated a high yield for VCE in patients with iron deficiency anemia [105,106], with a pooled diagnostic yield of 47%. The yield is increased in older patients [107,108] and those with a low hemoglobin [109], although significant pathology can also be found in young patients [110]. Comparisons of VCE and DBE have shown similar yields of pathology [89]. Comparisons of VCE with CT enteroclysis have suggested that VCE is superior to CT enteroclysis when patients with iron deficiency anemia are included [111,112].

For overt bleeding, recent studies have suggested that early VCE, within 48 hours, had a high diagnostic yield, leading to a higher therapeutic intervention rate and shorter hospital stay than when it was delayed to over 48 hours [113–115]. Recent evidence has reinforced the importance of performing VCE before DBE, with a higher diagnostic yield [116,117]. Enteroscopy was found to be superior to CT angiography in patients with overt bleeding [118]. In mixed overt and occult bleeding, the combined sensitivity of VCE and CT enteroclysis is greater than either technique alone [112].

This supports the notion that there is no single optimal diagnostic modality to explore the small bowel. Despite the heterogeneity of the data, there are enough studies suggesting the use of VCE in the context of iron deficiency anemia when bidirectional endoscopies have been negative. Furthermore, VCE has been adopted across Europe and is the accepted modality to be used for investigation of the small bowel after negative bidirectional endoscopies. For this reason, this should no longer be a priority.

5 Can we develop automatic reading analysis algorithms?

RECOMMENDATION

Redefine.

Can automated reading algorithms be safely introduced into clinical practice?

A recent meta-analysis evaluated the sensitivity, specificity, and DOR of the Suspected Blood Indicator (SBI; a tool available in RAPID Reader software, Medtronic, USA) for the detection of potentially bleeding lesions and/or active GI bleeding [119]. Overall, the sensitivity, specificity, and DOR were 0.553, 0.578, 12.354, respectively; however, the sensitivity, specificity, and DOR for active bleeding were 0.988, 0.646, and 229.89, respectively. This confirmed the limited sensitivity of SBI overall, but the very high sensitivity in cases with active GI bleeding.

In the latest version of one of the VCE systems, the RAPID Reader software has been incorporated, and it was found to be able to automatically select the 100 images that mostly likely contained abnormalities. The concordance of findings between the “TOP 100” selection and the standard reading was evaluated, in a retrospective study published by Arieira et al., in 97 consecutive patients presenting with suspected small-bowel bleeding [120]. The TOP 100 identified all sites of active bleeding ($n=9$), as well as the vast majority of significant lesions ($n=81/97$; 83.5%). This sensitivity for the TOP 100 suggests that it cannot entirely replace standard video reading; however, it might be used for preview reading.

Similarly, a novel EndoCapsule software algorithm (Omni Mode; Olympus) was recently developed with the aim of removing duplicate images without losing accuracy in lesion detection. The software was tested in a prospective multicenter study of 315 patients with an indication for VCE. The sensitivity of Omni Mode was 0.89 for clinically significant lesions. On comparing the miss rate of the standard mode and the Omni Mode, the standard mode reading was associated with an accuracy of 0.70, whereas the accuracy of the Omni Mode reading was 0.75, without significant differences between either reading mode. The use of the Omni Mode was significantly faster ($P<0.001$) than standard mode (42.5 minutes), with an average saving time of 24.6 minutes (95%CI 22.8–26.9), equivalent to a 40% reduction in reading time [121].

In parallel to the development of these software programs, AI is entering into the field of digestive endoscopy. Tsuboi et al. tested a convolutional neural network (CNN) AI system to automatically detect small-bowel angioectasia in VCE images [122]. The AUC for the detection of angioectasia was 0.998. The sensitivity, specificity, positive and negative predictive values of the CNN-based system were 98.8%, 98.4%, 75.4%, and 99.9%, respectively. Similarly, Leenhardt et al. developed a CNN-based algorithm that showed a 100% sensitivity, a 96% specificity, a 96% positive predictive value, and a 100% negative predictive value for the detection of angioectasia, with an optimal reproducibility and a reading process time for an entire small-bowel VCE of 39 minutes [123]. The “Deep CNN” system was also trained to recognize blood and was compared to the SBI (RAPID Reader Software) [124]. The AUC for the detection of blood content was 0.9998. The sensitivity, specificity, and accuracy of the CNN-based algorithm were 96.63%, 99.96%, and 99.89%, respectively, which were significantly higher than those of the SBI (76.92%, 99.82%, and 99.35%, respectively). The CNN system was proven to be extremely fast, allowing 10 208 test images to be evaluated in 250 seconds.

Most of the systems are still in a development phase that does not yet allow the use of the technology in clinical practice. Ankon Technologies (Shanghai, China) recently developed a CNN-based algorithm that is currently in the process of being embedded in the NaviCam Engine reading support platform, which will work together with their already available NaviCam small-bowel capsule system. To our knowledge, this will be the first VCE system to use a deep learning algorithm for routine clinical use. This CNN-based algorithm was evaluated by Ding et al. and showed a per-patient and per-lesion sensitivity for the detection of small-bowel abnormalities of 99.88% (95%CI 99.67–99.96) and 99.90% (95%CI 99.74–99.97), respectively [125]. The sensitivities of conventional reading were 74.57% (95%CI 73.05–76.03) and 76.89% (95%CI 75.58–78.15) in the per-patient and per-lesion analyses, respectively. The mean (standard deviation) reading time was 96.6 (22.53) minutes by conventional reading and 5.9 (2.23) minutes by CNN-based auxiliary reading ($P<0.001$).

The CNN architectures have been developed and trained in order to recognize ulcers and/or erosions, also with a 92%–95% accuracy, a 91%–96% sensitivity, and a 92%–96% specificity [126–128]. Excellent results were also reported by Klang et al. who described a CNN algorithm trained for patients with CD [129]. The system showed an AUC of 0.99, with an accuracy ranging from 95.4% to 96.7% in detecting ulcers in randomly split images.

CNN-based methods have been evaluated in other less frequent small-bowel disorders investigated by VCE. When trained to distinguish celiac disease patients from controls, the CNN achieved a 100% sensitivity and specificity, also being able to furnish quantitative measurement of the pathology and its degree of severity [130]. Polyp recognition was also evaluated with an accuracy of 98%, 99.5%, 99%, and 95.5%, for the detection of polyps, bubbles, turbid images, and clear images, respectively; the average overall recognition accuracy was 98% [131]. Similarly, another novel deep CNN system, able to detect

protruding lesions, showed an AUC of 0.911 (95%CI 0.9069–0.9155), with a sensitivity and specificity of 90.7% (95%CI 90.0%–91.4%) and 79.8% (95%CI 79.0%–80.6%), respectively [132]. The system was shown to properly classify polyps, nodules, epithelial tumors, submucosal tumors, and venous structures, with sensitivities of 86.5%, 92.0%, 95.8%, 77.0%, and 94.4%, respectively. In individual patient analysis (n = 73), the detection rate of protruding lesions was 98.6%.

In conclusion, during the next decade, computerized medicine including AI will rapidly expand. Most of the current data come from prototype systems and from images and videos from stock library. It seems that the concept of automated reading algorithms has been proven, so the question should be redefined to assess whether automated reading algorithms can be safely introduced into clinical practice.

Hepatopancreatobiliary endoscopy – ERCP

1 What is the optimal approach to access the biliary tree in patients with altered anatomy?

RECOMMENDATION

Remains a priority.

The different approaches to accessing the biliary tree in patients with altered anatomy have been included in ESGE guidelines, based on low quality evidence and weak recommendations [133–135]. Most of the studies have assessed different techniques, rather than comparing them in prospective studies or meta-analyses/systematic reviews.

Endoscopic retrograde cholangiopancreatography (ERCP) after Billroth II gastrectomy is challenging, with a reported incidence of perforation of 2.7%. Biliopancreatic cannulation and sphincterotomy has been reported to be successful with side- and forward-viewing endoscopes in 80% and 83% of patients, respectively. Cannulation using the side-viewing duodenoscope offers better visualization of the papilla and the elevator assists in the correct orientation of the catheters. For these reasons, a side-viewing duodenoscope should be the approach of choice for ERCP in Billroth II patients and forward-viewing endoscopes should only be used after a failed attempt with a duodenoscope. Prospective data comparing these two approaches are still lacking. Balloon-assisted enteroscopy can increase the success rate of duodenal stump intubation in Billroth II patients. However, the therapeutic role of balloon enteroscopy-assisted ERCP is limited because of the forward view, small operative channel, lack of elevator, and the absence of ERCP-dedicated catheters [136–138]. This question therefore remains a priority.

2 Where is precut indicated and safe?

RECOMMENDATION

No longer a priority.

Precut is indicated when biliary cannulation fails, as an alternative to repeated multiple attempts and the double-guidewire cannulation technique. Precut can be performed using two different techniques: conventional precut and fistulotomy. The first technique is usually defined as the use of a needle-knife to perform a stepwise incision of the mucosa starting at the upper margin of the papillary orifice and cutting in the direction of the bile duct until the underlying biliary sphincter is visualized. The second technique is usually defined as the use of a needle-knife to perform a stepwise incision of the mucosa starting directly over the roof of the papilla and followed by an upward or downward cut until the underlying biliary sphincter is visualized. The goal of the latter technique is to avoid thermal injury to the pancreatic orifice and therefore, theoretically, reduce the risk of post-ERCP pancreatitis.

Several meta-analyses and systematic reviews have been published (the last two in 2018) addressing the indications, safety, and efficacy of precut papillotomy [133, 139–143]. On pooled analyses, fistulotomy and early precut significantly decrease the risks of post-ERCP pancreatitis compared with conventional precut and precut performed after multiple cannulation attempts. This issue is no longer a research priority.

3 What are the roles for MRCP, ERCP, and EUS?

RECOMMENDATION

No longer a priority.

There have been a significant number of studies including systematic reviews and meta-analyses published so far on the roles for magnetic resonance cholangiopancreatography (MRCP), ERCP, and endoscopic ultrasound (EUS) [16, 31, 144–160]. The role of these modalities has been extensively discussed in various guidelines, which have been routinely adopted in clinical practice. ESGE has also published performance measures for ERCP and EUS. This topic is therefore no longer a research priority.

Hepatopancreatobiliary endoscopy – EUS

1 How do we optimally diagnose and manage cystic pancreatic tumors?

RECOMMENDATION

No longer a priority.

Within the last 5 years, a large number of studies have been published addressing the topic of pancreatic cystic neoplasm, with most of these being retrospective large series and meta-analyses. The American Gastroenterological Association (AGA), International Association of Pancreatology (IAP), and European study group on Cystic Tumours of the Pancreas have each published guidelines on the management of different types of pancreatic cystic neoplasm [161–163]. Moreover, precise guidance

on the absolute and relative indications for surgery have been identified.

The role of EUS has been defined in the evaluation of mural nodules and pancreatic duct dilation, with both features being suggestive of high risk neoplasia. Contrast-enhanced EUS has been effective in enhancing nodules, with high positive predictive value [164]. The diagnosis and management of cystic pancreatic tumors is therefore no longer a research priority. However, in terms of the EUS-guided acquisition of cystic fluid or tissue, fine-needle biopsy or more recently through-the-needle biopsy forceps are promising new tools and need to be further evaluated in large prospective studies [165].

2 How do we improve non-invasive diagnostic methods (e. g. contrast-enhanced endoscopic ultrasonography, 3D reconstruction) for the differential diagnosis of pancreatic cancer and inflammatory diseases?

RECOMMENDATION

Remains a priority.

ESGE guidelines recommend performing EUS-guided sampling as the first-line procedure when a pathological diagnosis of pancreatic pathology is required [166]. There has been remarkable progress in the field of less invasive diagnostic methods like EUS elastography and contrast-enhanced imaging [167–170]. Although the evidence from prospective studies looks promising, it is still not enough to change practice. AI-based interpretation of EUS and elastography has shown promising results, but is still a research tool [171]. This area remains an active research priority.

Cross-cutting priorities

1 How do we define the interface between endotherapy and gastrointestinal surgery?

RECOMMENDATION

Redefine.

How can we explore the interface between endotherapy and surgery to identify the conditions and patients that are best treated by surgery, endotherapy, or a combination of both?

The rapid development of various endoscopic techniques in the last decade has resulted in a major paradigm shift. A large number of conditions, which were conventionally treated by radical surgery, are now being treated endoscopically. Early GI neoplasia, achalasia, obesity, GI leaks, and fistulas, among others are examples of conditions that previously fell under the surgical domain, but are now being treated endoscopically in tertiary centers by select experts. Data on the efficacy and safety of these new endoscopic techniques have rapidly

emerged, proving the feasibility and safety of these techniques in expert hands, but data are needed on the generalization of these techniques and also for direct comparisons of the endoscopic techniques with surgery. It remains an important research priority to compare those different approaches in prospective trials to assess which option offers the better benefit/risk ratio.

Peroral endoscopic myotomy (POEM) has been proven to be a valuable option in treating achalasia, but it has been shown to result in a high rate of gastroesophageal reflux disease (GERD) [172, 173]. It was recently compared with laparoscopic Heller's myotomy in a prospective multicenter RCT and was proven to be as effective as surgery but with an apparent higher rate of GERD [173]. Nevertheless, the long-term impact of this GERD should be evaluated to define whether POEM or Heller's myotomy should be proposed as the first-line treatment depending on the patient's age and co-morbidities.

Recently, the principles of POEM have led to the development of third-space endoscopy or submucosal endoscopy as a new interface between endoscopy and surgery. This approach has also been used to treat different motility disorders, such as gastroparesis [174] and non-achalasia esophageal motility disorders [175], Zenker's diverticulum [176], and submucosal tumors with techniques like submucosal tunneling endoscopic resection [177] and combined endoscopic and surgical approaches [178]. These techniques have been reported in non-comparative studies and it is now necessary to compare them to the corresponding surgery or other endoscopic treatment modalities.

The treatment of obesity is becoming increasingly important owing to the global increase in its incidence. Endoscopy has two roles in this pathology, as a primary treatment with an endoscopic gastroplasty procedure [179–181] and as a means of managing surgical complications [182–184]. The place of endoscopy and surgery in obesity treatment is still based on low levels of evidence, and prospective protocols with comparative design are needed to determine the most appropriate approaches, according to the severity of obesity, the type of complication it is causing, or the metabolic profile of the patient. Metabolic endoscopy, for example with duodenal mucosal resurfacing, should also be compared with the different surgical concepts [185]. This question should therefore be redefined to address how we can explore the interface between endotherapy and surgery and identify the conditions and patients that are best treated by surgery, endotherapy, or a combination of both.

► **Table 1** Decisions made on review of the previous research priorities.

Research priority	Remains	Redefined	Removed
Generic priorities			
How do we define the correct surveillance interval following initial endoscopic diagnosis		X	
How do we correctly utilize advanced endoscopic imaging?		X	
What are the best markers of endoscopy quality?		X	
Upper gastrointestinal endoscopy			
What is the correct surveillance strategy for atrophic gastritis and metaplastic gastritis?	X		
What is the correct surveillance strategy for Barrett's esophagus?	X		
When can anticoagulant medication be restarted following gastrointestinal bleeding?	X		
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?	X (Barrett's and squamous neoplasia)		X (Intestinal metaplasia in the stomach)
Can training modules improve image interpretation and lesion recognition for endoscopists	X		
Lower gastrointestinal endoscopy			
What is the optimal surveillance of patients following colonoscopic polypectomy?			X
What is the importance of sessile serrated polyps?		X	
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?	X		
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?	X		
Can surveillance interval be adjusted depending upon both patient factors and the quality of the endoscopy?	X		
Small-bowel endoscopy			
How should we investigate occult or acute gastrointestinal bleeding following normal upper and lower gastrointestinal endoscopy?			X
What is the optimal imaging modality for small bowel?		X	
How can capsule endoscopy be used therapeutically?	X		
Should we perform capsule endoscopy or deep enteroscopy?			X
Can we develop automatic reading analysis algorithms?		X	
Hepatopancreaticobiliary endoscopy – EUS			
How do we optimally diagnose and manage cystic pancreatic tumors?			X
How do we improve non-invasive diagnostic methods (e. g. contrast-enhanced endoscopic ultrasonography, 3D reconstruction) for differential diagnosis of pancreatic cancer and inflammatory diseases?	X		
Hepatopancreaticobiliary endoscopy – ERCP			
What are the roles for magnetic resonance cholangiopancreatography, endoscopic retrograde cholangiopancreatography, and endoscopic ultrasonography?			X
What is the optimal approach to access the biliary tree in patients with altered anatomy?	X		
Where is precut indicated and safe?			X
Other cross-cutting themes/questions			
How do we define the interface between endotherapy and gastrointestinal surgery?		X	
Can we better understand the prevalence and natural history of diseases diagnosed and treated by gastrointestinal endoscopy, in particular neoplasia?			X

► **Table 1** (Continuation)

Research priority	Remains	Redefined	Removed
How do we validate and establish the clinical application of scoring and diagnostic tools for gastrointestinal endoscopy?	X		
EUS, endoscopic ultrasound; ERCP endoscopic retrograde cholangiopancreatography.			

► **Table 2** The revised research priorities.

Generic priorities
What is the impact of endoscopic surveillance on incidence and disease-specific survival?
How can advanced endoscopic imaging be implemented to change clinical practice?
How can we implement and monitor adherence to the KQIs and quantify the long-term benefits of such implementation, as well as developing and validating the patient experience-related KQIs?
Upper gastrointestinal endoscopy
What is the correct surveillance strategy for atrophic gastritis and metaplastic gastritis?
What is the correct surveillance strategy for Barrett's esophagus?
When can anticoagulant medication be restarted following gastrointestinal bleeding?
What is the role of advanced imaging in the detection of dysplasia in Barrett's esophagus and squamous esophagus in high risk patients?
Can training modules improve image interpretation and lesion recognition for endoscopists?
Lower gastrointestinal endoscopy
Can surveillance interval be adjusted depending on both patient factors and the quality of the endoscopy?
What is the best technique for detection, resection, and surveillance of sessile serrated polyps?
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?
What are the risks and benefits of leaving smaller polyps in place in older patients? Is it possible to define an age cutoff where the risks exceed the benefits?
Small-bowel endoscopy
How can we better stratify small-bowel investigations for patients with small-bowel inflammation and tumors?
How can capsule endoscopy be used therapeutically?
Can automated reading algorithms be safely introduced into clinical practice?
Hepatopancreaticobiliary endoscopy – ERCP
What is the optimal approach to access the biliary tree in patients with altered anatomy?
Hepatopancreaticobiliary endoscopy – EUS
How do we improve non-invasive diagnostic methods (e. g. contrast-enhanced endoscopic ultrasonography, 3D reconstruction) for the differential diagnosis of pancreatic cancer and inflammatory diseases?
Other cross-cutting themes
How can we explore the interface between endotherapy and surgery to identify the conditions and patients that are best treated by surgery, endotherapy, or a combination of both?
How do we validate and establish the clinical application of scoring and diagnostic tools for gastrointestinal endoscopy?
KQI, key quality indicator; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound.

2 How do we validate and establish the clinical application of scoring and diagnostic tools for gastrointestinal endoscopy?

RECOMMENDATION

Remains a priority.

Currently, we have numerous scores for various pathologies, among which are the prognostic scores for GI bleeding and for endoscopic resection of GI neoplasia.

There are two scores that deal with technical difficulty or prediction of recurrence after endoscopic mucosal resection (EMR) of colorectal polyps [186–192]. The first score, called the SMSA score, is based on the variables size (S), morphology (M), site (S), and access (A), and has been studied by various groups, who have demonstrated the link between the SMSA score and the outcome of colonic EMR [187–190]. The second score, the Sydney EMR Recurrence Tool (SERT), has been shown to predict post-EMR recurrence [191]. This score has also recently been validated in another study [192]. There are two further scoring systems to predict delayed bleeding following colorectal EMR [193, 194], with another study recently validating and optimizing the previous scores [195]. There is also a publication that classifies deep mural injury and perforation risk [196]; however, there are no tools to predict this complication.

In reference to ESD, there are a few studies that have described scoring systems to predict difficulty in resection, obtaining an en bloc resection, perforation, and delayed bleeding [197–199]. None of these have external validation.

It seems that a series of scoring systems have been developed, but they have not become part of routine clinical practice. It therefore remains a priority to validate these existing scoring systems and integrate them into clinical practice.

3 Can we better understand the prevalence and natural history of diseases diagnosed and treated by gastrointestinal endoscopy, in particular neoplasia?

RECOMMENDATION

No longer a priority.

The natural history and prevalence of GI neoplasia and other conditions have been appropriately addressed under the relevant dedicated sections, so this no longer remains an independent priority.

Conclusions

The previous ESGE research priorities document published in 2016 had 26 research priorities under seven domains. Our review of these priorities has resulted in seven priorities being removed from the list, one priority being partially removed, another seven being redefined to make them more precise,

and 11 priorities remaining unchanged (► **Table 1**). This has led to the development of a new list of 19 research priorities under seven domains (► **Table 2**). This is a reflection of a rapid surge in endoscopic research resulting in 27% of research questions already having been answered and another 27% of research questions requiring redefinition.

Competing interests

A. Anderloni has provided consultancy for Boston Scientific (2016 to date), Olympus (2018 to present), and Medtronic (2018–2019). M. Barthet has received a research grant from Boston Scientific (2016 to present). P. Bhandari has received educational event support from Olympus, speaker's fees and grants from Pentax, Medtronic, Boston Scientific, and 3-D Matrix, and is on the advisory board and received a research grant from Fujifilm (all 2017 to present). M. Dinis-Ribeiro has provided consultancy for Medtronic (2020); he is co-Editor-in-Chief of *Endoscopy*. R. Haidry has received research funding from Medtronic (2013), Pentax (2013 to present), and Cook Endoscopy (2016 to present). H. Neumann has provided consultancy for Fujifilm, Sonoscope, Boston Scientific, and Medtronic (2019–2020). T. Ponchon has provided consultancy for Olympus, Boston Scientific, Norgine, and Ipsen (2020 to present); his department has received research funding from Olympus and Boston Scientific (2020 to present). A. Repici has received research grants and consultancy fees from Boston Scientific, Fujifilm, Medtronic, and Erbe. P.D. Siersema receives research support from Pentax, The eNose company, Norgine, Motus GI, and MicroTech; he is Editor-in-Chief of *Endoscopy*. C. Spada has provided consultancy for Medtronic, AlfaSigma, Norgine, Pentax, and Olympus (2016 to present). P.A. Testoni's department has received meeting sponsorship and trials support from Pentax (2000 to present). E. Albeniz, G. Antonelli, L. Diogo, L. Fuccio, C. Hassan, G. Longcroft-Wheaton, P. Pimentel-Nunes, M. Pioche, and R. Sidhu declare that they have no conflict of interest.

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