UEG and EAES Rapid Guideline: Systematic review, meta-analysis, GRADE assessment and evidence-informed European recommendations on TaTME for rectal cancer by European Association for Endoscopic Surgery and other Interventional Techniques
This rapid guideline addresses questions on the use of TaTME in patients with rectal cancer.

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Disclaimer
This clinical practice guideline has been developed under the auspice of the European Association for Endoscopic Surgery (EAES). It is intended to be used primarily by health professionals (e.g. surgeons, anaesthetists, physicians) and to assist in making informed clinical decisions on diagnostic measures and therapeutic management. It is also intended to inform individual practice of allied health professionals (e.g. surgical nurses, dieticians, physical rehabilitation therapists, psychologists); to inform strategic planning and resource management by health care authorities (e.g. regional and national authorities, health care institutions, hospital administration authorities); and to inform patients wishing to obtain an overview of the condition of interest and its management.

The use of recommendations contained herein must be informed by supporting evidence accompanying each recommendation and by research evidence that might not have been published by the time of writing the present document. Users must thus base their actions informed by newly published evidence at any given point in time.

The information in the guideline should not be relied upon as being complete or accurate, nor should it be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care. With the rapid development of scientific knowledge, new evidence may emerge between the time the guideline is developed and when it is published or read. The guideline is not continually updated and may not reflect the most recent evidence. The guideline addresses only the topics specifically identified therein and is not applicable to other interventions, diseases, or stages of diseases. This guideline does not mandate any particular course of medical care. Further, the guideline is not intended to substitute the independent professional judgment of the treating provider, as the guideline does not necessarily account for individual variation among patients.

Even if evidence on a topic suggests a specific diagnostic and/or treatment action, users and especially health professionals may need to decide against the suggested or recommended action in view of circumstances related to patient values, preferences, co-morbidities and disease characteristics; available human, monetary and material resources; and healthcare infrastructures.

EAES provides this guideline on an “as is” basis, and makes no warranty, express or implied, regarding the guideline.
1. Summary

This rapid guideline provides a weak recommendation for the use of TaTME over laparoscopic or robotic TME for rectal cancer when expertise is available. It provides a summary of best available evidence with critical appraisal and assessment of the certainty of the evidence. The recommendations were developed within a rigorous evidence-to-decision framework in accordance with GRADE and Guidelines International Network principles.

This rapid guideline was sponsored and funded by the European Association for Endoscopic Surgery; the Association was not directly involved in the development of the guideline. A multidisciplinary group of stakeholders comprised the guideline panel. Importantly, both direct and indirect conflicts of interest of the entire guideline development group were recorded and appropriately managed, in order for the end product to represent a reliable and trustworthy piece to inform clinical practice, patient decision and policy making.

The guideline will be published in Surgical Endoscopy & Other Interventional Techniques, official journal of the EAES.
2. Introduction

Colorectal cancer affects a substantial proportion of the general population, with a lifetime risk of 4.3% for men and 4% for women [1]. Rectal cancer accounts for 23-32% of colorectal malignancies [2]. The anatomy of the rectum makes surgical treatment of low rectal cancer challenging. Laparoscopic surgery has been found to likely result in similar 5-year oncological outcomes and reduced minor morbidity compared to open surgery [3], whereas it facilitates improved visualization for dissection deep in the pelvis. Robotic surgery has been suggested to provide further technical advantages [4].

Rectal dissection is however challenging in low-lying tumors and in patients with unfavorable anatomy, such as male and obese individuals. Transanal total mesorectal excision (TaTME) has been developed as an alternative technique, that allows down-to-up dissection of the rectum and perineal dissection of the mesorectum without the need for deep abdominal dissection. It has been hypothesized that this approach may improve the quality of the specimen [5].

TaTME has attracted much attention over the past few years and it has stimulated a debate around its safety and efficacy [6][7][8][9][10]. Moreover, consensus panels and practice statements have provided conflicting recommendations [11][12][13][14]. Under consideration of dissenting views and opinions, and taking into account EAES members’ preferences who have prioritized colorectal cancer as a guideline topic in an online survey [15], UEG and EAES have sponsored the development of this project.

Objective

The objective of this rapid guideline was to develop reliable, trustworthy, pertinent, evidence-informed recommendations based on state-of-the art guideline development methodology on the use of TaTME versus laparoscopic or robotic surgery in patients with rectal cancer.
3. Methods

The protocol of this rapid guideline is available online [16]. It was reported in accordance with AGREE II and it was developed following GRADE, IOM and G-I-N standards [17][18][19]. Furthermore, we adhered to GRADE guidance published in the Journal of Clinical Epidemiology as part of a series of articles detailing and updating the GRADE methodology. This guideline was facilitated with the online authoring and publication platform MAGICapp.

This is an outline of the methodology; more detailed information is provided in MAGICapp (https://app.magicapp.org/#/guideline/4767) and in the Appendix; complete datasets are available online [20].

Steering group

The guideline steering group consisted of a general surgeon performing laparoscopic, robotic and transanal TME (coordinator, MM), a guideline methodologist with vast experience in evidence outreach, synthesis, assessment and guideline development, (supervisor, SAA); biostatisticians (KMK, DM); and a GRADE external auditor (POV). All members of the steering group disclosed no conflicts, direct or indirect [20].

Guideline panel

The guideline panel consisted of four general surgeons, a radiation oncologist, a radiologist, a pathologist, and a patient advocate (AA, NB, NB, ED, KF, NKF, JM, GT). The patient advocate resides in the USA and was nominated by the European Patients’ Forum, a non-profit umbrella organization of patient organizations across Europe. Panel members watched a short video tutorial outlining the guideline development methodology. The composition of panel members aimed to be representative of different parts of Europe, both genders, different age groups, and academic/non-academic surgical practice. Panel members disclosed no direct nor indirect conflicts [20]. External advisors were surgeons with clinical experience and/or research focus on TaTME (MA, LB, FBdL, MP). They were consulted throughout the guideline development process, but they did not vote on the direction, the strength and the wording of the recommendations.

Guideline questions

1. Should TaTME versus laparoscopic TME be preferred for the treatment of rectal cancer?
2. Should TaTME versus robotic TME be preferred for the treatment of rectal cancer?

Protocol

A protocol was developed a priori by the steering group [16]. The protocol draft was made publicly available through the EAES website and EAES members were invited through various channels to comment on the content. The guideline questions and outcomes were refined in collaboration with the guideline panel members, whereas EAES members’ comments were considered and several were addressed (see Appendix). Amendments to the protocol with justifications are provided in the Appendix.

Rating the importance of outcomes

The importance of outcomes was rated by the panel members using the GRADE scale [21]. The classification of outcomes into each of the three categories (not important, important, critical) was made by the steering group under consideration of panel members’ ratings available online [20]. We considered the importance of outcomes as follows:

1. 30-day or in-hospital mortality: critical
2. 30-day complications Clavien-Dindo ≥3 (major morbidity): critical
3. 30-day complications Clavien-Dindo ≤2 (minor morbidity): important
4. Anastomotic leakage: critical
5. Completeness of TME: critical
6. Disease recurrence at 2 years: critical
7. 5-year overall survival: critical
8. 5-year disease-free survival: critical
9. Low anterior resection syndrome: critical
10. Quality of life: critical

Setting minimal important differences

The evidence-to-decision framework was set within a fully contextualized approach [24]. An anonymous web-based survey of panel members was performed to define minimal important differences. The results of the survey are available online [20].

Under consideration of panel’s responses, the following minimal important differences were considered:

1. 30-day or in-hospital mortality: 10 per 1000
2. 30-day complications Clavien-Dindo ≥3 (major morbidity): 10-50 per 1000
3. 30-day complications Clavien-Dindo ≤2 (minor morbidity): 50-100 per 1000
4. Anastomotic leakage: 25 per 1000
5. Completeness of TME: 25-50 per 1000
6. Disease recurrence at 2 years: 25-50 per 1000
7. 5-year overall survival: 10-50 per 1000
8. 5-year disease-free survival: 10-25 per 1000
9. Low anterior resection syndrome: 50 per 1000
10. Quality of life: 5-10 out of 100

Search strategy

One strategy was developed for both guideline questions because of their affinity. The databases of Medline, EMBASE and OpenGrey were searched. The search syntaxes are available online [20].

Study selection

Titles and/or abstracts were screened (first level) and full text articles were scrutinized (second level) to identify eligible studies in duplicate (MM, SAA). Inclusion criteria were adult patients with adenocarcinoma of the rectum, TaTME compared with...
laparoscopic/robotic TME. Exclusion criteria were single incision and open surgery.

Risk of bias assessment

RoB-2 and ROBINS-I were used for risk of bias assessment in RCTs and cohort studies with a comparative arm, respectively [22][23]. Relevant considerations are provided in the Appendix.

Statistical analysis

We conducted random effects meta-analyses to synthesize quantitatively the evidence for the guideline questions since we expected much variation in the PICO criteria across studies [25]. We explored heterogeneity via the $I^2$ statistic that describes the percentage of the variability of effect estimates that is due to heterogeneity rather than sampling error. We further explored heterogeneity by computing the Q-statistic and the 95% predictive intervals that show the plausible range of effect size values for a future trial. All the analyses were performed in R statistical package version 4.0.3 using the meta package. All statistical analyses were performed independently by the statisticians’ group with no involvement of the steering group or panel members.

Evidence tables

We constructed GRADE evidence profiles of certainty for each outcome separately using MAGICapp. The certainty of evidence is determined by the risk of bias across studies, incoherence, indirectness, imprecision, publication bias and other parameters [26]. We used the most recent GRADE methodology to decide on the certainty of a body of evidence from RCTs and observational studies using RoB-2 and ROBINS-I, which recommends using the judgement of high certainty of evidence at baseline and downgrading due to risk of bias of RCTs and observational studies [27]. Minimal important differences determined in advance through a survey of panel members were used to inform judgements about precision and coherence. If very low certainty evidence on an outcome was found, we used a ’systematic observation form to retrieve expert-based evidence’ as previously described [28]. Evidence tables for Q1 were informed by the systematic observation form (relevant data are available online [20]), whereas experience with robotic TME was limited to provide substantial expert-based observation evidence.

Evidence-to-decision framework

The panel discussed the evidence within a GRADE evidence-to-decision framework coordinated by the guideline methodologist using MAGICapp. A formal anonymous Delphi process was carried out to finalize the judgements. A total of two online meetings were required.

Developing recommendations

Based on the evidence-to-decision framework, the panel anonymously voted on the strength and the direction of the recommendations through MAGICapp. There was unanimous consensus on the strength and the direction of the recommendations, whereas minor dissenting opinions were noted and reported accordingly in this manuscript.
4. Results

Some 822 records and 46 full text articles were screened, out of which 17 met the eligibility criteria. Sixteen studies addressed Q1 [29][30][31][32][33][34][35][36][37][38][39][40][41][42][43][44] and one study addressed Q2 [45]. The study selection flowchart and considerations on record selection, and risk of bias summaries are provided in the Appendix; detailed files including discarded records with reason and risk of bias judgements with detailed justifications are available online [20].

Data on disease-free and overall survival were provided by one study only [44]; local recurrence at 2 years was provided by two studies [40][44], however one study was at critical risk of bias with regard to this outcome and did therefore not enter the analysis as per ROBINS-I methodology [23]. Low anterior resection syndrome and quality of life were reported by only a few studies [35][43].

Several articles addressed parameters pertinent to the evidence-to-decision framework [46][47][48][49][50][51][52][53].

**Weak recommendation**

We suggest TaTME over laparoscopic TME if expertise is available.

**Evidence To Decision**

**Benefits and harms**

The panel considered moderate benefits with regard to 30-day mortality, TME completeness and 2-year locoregional recurrence. It was further suggested that the benefit may be greater when very low dissection is needed. Furthermore, there was no evidence of increased harm. The panel raised some concerns about the risk of urethral injuries, a serious complication unique to TaTME, which however is captured in major and minor complications reported in the literature.

**Certainty of the Evidence**

The certainty of evidence across outcomes is generally considered to be the lowest among judgements of the certainty on critical outcomes. The certainty of evidence on several critical outcomes was very low.

**Preference and values**

No relevant published evidence was identified. The panel, with specific input from the patient representative, suggested that substantial variability in patient values and preferences is anticipated, which may be determined by the invasiveness (patients would typically select the least invasive intervention), the expected quality of life (notably, limited evidence on disease-free survival, quality of life and low anterior resection syndrome is available), and cultural understanding of the interventions, which may vary across European countries.

**Resources and other considerations**

No cost-benefit analyses were identified. A single cost analysis of TaTME v. laparoscopic TME was found [46].

"Cost data were automatically gathered from the hospital warehouse manager. The overall hospital direct costs were divided into two groups: operative costs and costs related to postoperative management. Operative resources included cost of required supplies (instruments, staplers, and other disposable devices). Costs for postoperative management included the use of hospital resources during the hospital stay: medications (antibiotics, anti-thrombotics, electrolytes solutions), postoperative laboratory tests, radiology exams and consultations."

"Standardized techniques for both lapTME and taTME were used. Briefly, in lapTME mesorectal dissection started at the level of the sacral promontory and was carried down to the levator muscle plane with preservation of the hypogastric, sacral, and pelvic autonomic nerves. The rectum was divided distally with a laparoscopic stapler (60 mm ± 45 mm cartridge), and extracted through a mini-incision (suprapubic or left iliac fossa). An end-to-end or side-to-end colorectal anastomosis was created with a circular stapler (28 or 31 mm). For taTME, a Lone Star retractor™ (Cooper Surgical, Trumbull, CT, USA) along with transanal..."
operative platform (GelPOINT Path™, Applied Medical, Rancho Santa Margarita, CA, USA). Continuous pneumorectum with a dedicated insufflation platform was created (Airseal™, ConMed, Inc., Utica, NY, USA). A purse-string was placed distally to the tumor and, after rectotomy, dissection of the mesorectum was performed with bottom-up technique as already described. The additional surgical team was present in the OR for the rendez-vous step of the procedure in majority of cases to facilitate the identification of the mesorectal plane and to safely enter the peritoneal cavity from below. After completion of the mesorectal dissection, the specimen was extracted either transabdominally or transanally through a double-ringed wound protector–retractor. A second purse-string was placed on the rectal cuff and an end-to-end colorectal anastomosis was created with a circular stapler (28 or 31 mm)."

The study was not matched for important confounders, including age, sex, ASA class, tumor height, tumor stage, node status and tumor size.

"Operative surgical supplies had an overcost of 754,54€ in the taTME procedure with respect to lapTME. There was no significant difference in mean operative time across groups (lapTME 266 ± 92.85 min Vs taTME 271 ± 83.63, p = 0.50)."

| Table 2 Specific surgical supplies for laparoscopic and transanal TME |
|---------------------------------|-----------------|-----------------|---------|
| Alexis™ 5–9 cm                  | lapTME (number of devices) | taTME (number of devices) | Δ |
| Endopath Xcel™ TROCARS         | 4                | 4                |        |
| Endopath Trocar Hasson         | 1                | 1                |        |
| Harmonic ACE + 7™ Laparoscopic Shears | 1            | 1                |        |
| Endo GIA Ultra™ Universal stapler | 1              | –                |        |
| Premium Plus CLEA™ Circular stapler | 1            | 1                |        |
| Endo GIA™ 60 mm                | 1                | –                |        |
| Endo GIA™ 45 mm                | 1                | –                |        |
| Airseal™ smoke evacuation kit  | –                | 1                |        |
| Anoscope kit                   | –                | 1                |        |
| Gelpoint Path™ transanal access platform | –        | 1                |        |
| Lone Star Retractor™ ring      | –                | 1                |        |
| Lone Star Retractor™ self-retaining retractors | –        | 2                |        |
| Total cost of procedure (€)    | 1049.22          | 1803.76          | 754.54€ |

TME total mesorectal excision

"The cost of hospital resources for the management of postoperative course including diagnostics (blood tests, radiology exams and consultations) and medications was comparable between the two groups."

| Table 5 Hospital resources to manage postoperative course |
|---------------------------------|-----------------|-----------------|---------|
| LapTME cost (€)                 | TaTME cost (€)  | p value         |
| Blood work                      | 46.00 (35.40–93.50) | 50.80 (39.20–112.50) | 0.55" |
| Radiology exams and consultations | 39.70 (19.50–82.51) | 39.50 (19.50–70.37) | 0.85" |
| Medications                     | 29.40 (23.40–79.40) | 39.40 (25.10–88.20) | 0.33" |

Value are express in median (IQR). "Mann–Whitney test

The panel suggested that relevant evidence is limited and we cannot estimate the cost-effectiveness of TaTME at this stage. It
was highlighted, however, that TaTME can be performed with either disposable or reusable ano-rectoscopes and with either standard or specifically designed insufflators, with substantial effect on the use of resources.

### Equity

The panel suggested that TaTME may reduce equity in terms of resource utilization and particularly operating room time, which is typically longer with TaTME, especially during the initial stage of implementation at an institution.

### Acceptability

The panel did not identify any barriers with regard to acceptability of TaTME by key stakeholders.

### Feasibility

Observational studies addressing the learning curve of TaTME suggest 40-70 cases with major morbidity as indicator \[47\][48]; 45 cases with quality of TME as indicator \[49\][50], and 20-70 cases with operation time as indicator \[48\][51].

A survey of Canadian surgeons performing TaTME suggests a minimum of 12 cases annually to maintain proficiency \[52\]. As many as 95% of surgeons having participated in cadaveric hands-on courses and practicing TaTME believe that training should be required before performing TaTME \[53\].

The panel suggested that TaTME be performed in high volume centers, which allow centralization of care and accumulation of expertise. They recognized that feasibility of the intervention, in these terms, varies across settings.

### Rationale

The panel identified some evidence of benefit in critical outcomes with TaTME and no evidence of harm, nevertheless the overall certainty of the evidence was very low, primarily due to confounding bias and imprecision of effect estimates, whereas evidence on some critical outcomes, primarily survival outcomes, was very low. Substantial variability in patient values and preferences is anticipated and patient aids might be useful in this context. There is uncertainty around the use of resources, whereas equity might be reduced, due to lack of widespread expertise and longer use of operating room resources, at least during the early stages of implementation. The panel considered the intervention to be acceptable to key stakeholders, whereas feasibility was considered to vary and depend on annual volume of cases and centralization of care. An important parameter which determines the direction of the recommendation is (surgical and operating room staff) expertise. External validity of relevant research evidence is determined by the degree of expertise of surgeons and operating room staff. Consensus documents detailing training and considerations on expertise can be found here \[11\].

### Clinical Question/ PICO

|   | Population: | Interventions: | Comparator: |
|---|-------------|----------------|-------------|
|   | Patients with mid/low rectal cancer | TaTME | Lap TME |

| Outcome | Timeframe | Study results and measurements | Comparator | Intervention | Certainty of the Evidence (Quality of evidence) | Plain language summary |
|--------|-----------|--------------------------------|------------|-------------|---------------------------------------------|------------------------|
| Major morbidity | 1 | 30 days | Odds Ratio 0.81 (CI 95% 0.47 – 1.39) Based on data from 550 participants in 7 studies. | Lap TME | TaTME | Moderate Due to serious risk of bias \(^3\) | TaTME may have little or no effect on major morbidity |
| Outcome | Timeframe | Study results and measurements | Comparator Lap TME | Intervention TaTME | Certainty of the Evidence (Quality of evidence) | Plain language summary |
|---------|-----------|--------------------------------|--------------------|-------------------|-----------------------------------------------|------------------------|
| Minor morbidity | 4 30 days | Odds Ratio 0.87 (CI 95% 0.52 – 1.44) Based on data from 486 participants in 6 studies. | Difference: 21 fewer per 1000 (CI 95% 60 fewer – 39 more) | Moderate Due to serious risk of bias | TaTME may have little or no effect on minor morbidity |
| Mortality | 7 30 days | Odds Ratio 0.27 (CI 95% 0.08 – 0.88) Based on data from 1,859 participants in 11 studies. | Difference: 167 per 1000 | Low Due to few events, due to serious risk of confounding bias | TaTME may decrease 30-day or in-hospital mortality |
| Anastomotic leakage | 10 7 Critical | Odds Ratio 1.16 (CI 95% 0.82 – 1.63) Based on data from 1,657 participants in 8 studies. | Difference: 79 per 1000 | Low Due to serious risk of bias and due to serious imprecision | TaTME may have little or no effect on anastomotic leakage |
| Stoma construction | 13 | Odds Ratio 1.21 (CI 95% 0.56 – 2.63) Based on data from 1,407 participants in 7 studies. | Difference: 596 per 1000 | Very low Due to serious inconsistency and due to very serious imprecision | We are uncertain whether TaTME increases or decreases odds of stoma construction |
| TME completeness | 16 | Odds Ratio 1.9 (CI 95% 0.81 – 4.44) Based on data from 1,415 participants in 7 studies. | Difference: 724 per 1000 | Low Due to serious risk of bias and due to serious imprecision/inconsistency | TaTME may have little or no effect on TME completeness |
| Clear CRM | 19 | Odds Ratio 1.36 (CI 95% 0.88 – 2.08) Based on data from 1,909 participants in 12 studies. | Difference: 945 per 1000 | Moderate Due to serious risk of bias | TaTME probably has little or no effect on clear CRM |
| Clear DRM | 22 | Odds Ratio 1.51 (CI 95% 0.7 – 3.24) | Difference: 981 per 1000 | Moderate Due to serious risk | TaTME probably has little or no effect on clear |
| Outcome Timeframe | Study results and measurements | Comparator Lap TME | Intervention TaTME | Certainty of the Evidence (Quality of evidence) | Plain language summary |
|-------------------|-------------------------------|-------------------|-------------------|-----------------------------------------------|------------------------|
| Low anterior resection syndrome | Based on data from 1,521 participants in 8 studies. 23 (Observational (non-randomized)) | 6 more per 1000 (CI 95% 8 fewer — 13 more) | 913 per 1000 | Very low Due to very serious imprecision and due to serious inconsistency 24 | We are uncertain whether TaTME increases or decreases odds of low anterior resection syndrome. There was inconsistency in reported effect by panel members. |
| Local recurrence | Odds Ratio 0.63 (CI 95% 0.1 — 4.21) Based on data from 46 participants in 1 studies. 25 (Observational (non-randomized)) Follow up: 6 months. | 44 fewer per 1000 (CI 95% 401 fewer — 65 more) | 869 per 1000 | Low Due to serious risk of bias, due to serious imprecision 26 | TaTME may decrease local recurrence |
| Overall survival | Hazard Ratio 0.4 (CI 95% 0.23 — 0.69) Based on data from 710 participants in 1 studies. 27 (Observational (non-randomized)) Follow up: 3 years. | 56 fewer per 1000 (CI 95% 73 fewer — 29 fewer) | 96 per 1000 | Very low Due to serious risk of bias, due to serious indirectness, due to serious imprecision 28 | We are uncertain whether TaTME increases or decreases overall survival |
| Disease-free survival | Hazard Ratio 0.81 (CI 95% 0.65 — 1.02) Based on data from 710 participants in 1 studies. 29 (Observational (non-randomized)) Follow up: 3 years. | 43 fewer per 1000 (CI 95% 79 fewer — 5 more) | 178 per 1000 | Very low Due to serious risk of bias, due to serious indirectness, due to serious imprecision 30 | We are uncertain whether TaTME increases or decreases disease-free survival |
| Quality of life | Based on data from: 54 participants in 1 studies. 31 (Observational (non-randomized)) Follow up: 6.6 months. | Only one study at critical risk of bias reports on quality of life | | Very low Due to very serious risk of bias and due to very serious imprecision 32 | We are uncertain whether TaTME improves or worsens quality of life. There was inconsistency in reported effect by panel members. |

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We suggest TaTME over robotic TME if expertise is available.

The panel recognized the scarcity of evidence. Potential benefits and harms are expected to be similar to the comparison of TaTME v. lap. TME. Most panel members supported that there is little difference between the interventions, whereas some supported trivial benefits. TaTME may facilitate low transection of the rectum, whereas difficulties may be encountered with placing the stapler at an appropriate level in robotic surgery. TaTME may be particularly helpful in low, bulky tumors. The same concerns about the risk of urethral injuries with TaTME apply.
Evidence was scarce, with only one study appropriately adjusting for confounders being available and no studies addressing several critical outcomes.

The same considerations as for the comparison TaTME v. lap. TME apply. Substantial variability in patient values and preferences is anticipated, which may be determined by the invasiveness (patients would typically select the least invasive intervention), the expected quality of life (notably, limited evidence on disease-free survival, quality of life and low anterior resection syndrome is available), and cultural understanding of the interventions, which may vary across European countries.

No relevant evidence was found. The use of resources depends on whether a laparoscopic-assisted or a robotic-assisted TaTME is applied.

The panel suggested that relevant evidence is limited and we cannot estimate the cost-effectiveness of TaTME at this stage.

As for the comparison TaTME v. lap. TME, the panel suggested that TaTME may reduce equity, especially in terms of resource utilization and particularly operating room time, which is typically longer with TaTME during the initial stage of implementation at an institution.

The panel did not identify any barriers with regard to acceptability of TaTME by key stakeholders.

The same considerations as for the comparison TaTME v. lap. TME apply.

Observational studies addressing the learning curve of TaTME suggest 40-70 cases with major morbidity as indicator [47][48]; 45 cases with quality of TME as indicator [49][50], and 20-70 cases with operation time as indicator [48][51].

A survey of Canadian surgeons performing TaTME suggests a minimum of 12 cases annually to maintain proficiency [52]. As many as 95% of surgeons having participated in cadaveric hands-on courses and practicing TaTME believe that training should be required before performing TaTME [53].

The panel suggested that TaTME be performed in high volume centers, which allow centralization of care and accumulation of expertise. They recognized that feasibility of the intervention, in these terms, varies across settings.

The panel recognized that the evidence was very limited to allow assessment of the balance between benefits and harms with confidence. Several panel members suggested that surgeon’s expertise plays a vital role and probably affects outcomes, so that both options may be appropriate. Substantial variability in patient values and preferences is anticipated and shared decision making after discussion of surgeon’s preference and expertise, and perceived benefits and harms is encouraged. There is uncertainty around the use of resources, which depends on whether robotic-assisted or laparoscopic-assisted TaTME is performed, and on the selection between disposable or reusable instruments for laparoscopic-assisted TaTME. Equity might be reduced, due to lack of widespread expertise and longer use of operating room resources, at least during the early stages of implementation. The panel considered the intervention to be acceptable to key stakeholders, whereas feasibility was considered to vary and depend on annual volume of cases and centralization of care. Consensus documents detailing training and considerations on expertise can be found here [11].
### Clinical Question/ PICO

**Population:** Patients with mid/low rectal cancer  
**Intervention:** TaTME  
**Comparator:** Robotic TME

| Outcome | Study results and measurements | Comparator | Intervention | Certainty of the Evidence (Quality of evidence) | Plain language summary |
|---------|--------------------------------|------------|--------------|------------------------------------------------|------------------------|
| **Mortality**<sup>1</sup>  
30 days  
9 Critical | Odds Ratio 0.33 (CI 95% 0.02 — 6.81) Based on data from 596 participants in 1 studies.<sup>2</sup> (Observational (non-randomized)) Follow up: 30 days. | 5 per 1000  
Difference: 3 fewer per 1000 (CI 95% 5 fewer — 28 more) | 2 per 1000 | Very low  
Due to very serious imprecision<sup>3</sup> | We are uncertain whether TaTME increases or decreases mortality |
| **Anastomotic leakage**<sup>4</sup>  
8 Critical | Odds Ratio 1.12 (CI 95% 0.65 — 1.91) Based on data from 596 participants in 1 studies.<sup>5</sup> (Observational (non-randomized)) | 100 per 1000  
Difference: 11 more per 1000 (CI 95% 33 fewer — 75 more) | 111 per 1000 | Very low  
Due to serious risk of bias and due to very serious imprecision<sup>6</sup> | We are uncertain whether TaTME increases or decreases odds of anastomotic leakage |
| **Stoma construction**<sup>7</sup> | Odds Ratio 3.6 (CI 95% 1.97 — 6.55) Based on data from 596 participants in 1 studies.<sup>8</sup> (Observational (non-randomized)) | 808 per 1000  
Difference: 130 more per 1000 (CI 95% 84 more — 157 more) | 938 per 1000 | Very low  
Due to very serious imprecision<sup>9</sup> | We are uncertain whether TaTME increases or decreases odds of stoma construction |
| **TME completeness**<sup>10</sup> | Odds Ratio 0.48 (CI 95% 0.23 — 1) Based on data from 596 participants in 1 studies.<sup>11</sup> (Observational (non-randomized)) | 962 per 1000  
Difference: 38 fewer per 1000 (CI 95% 109 fewer — 0 fewer) | 924 per 1000 | Very low  
Due to very serious imprecision<sup>12</sup> | We are uncertain whether TaTME increases or decreases odds of TME completeness |
| **Clear CRM**<sup>13</sup> | Odds Ratio 1.07 (CI 95% 0.52 — 2.23) Based on data from 596 participants in 1 studies.<sup>14</sup> (Observational (non-randomized)) | 943 per 1000  
Difference: 4 more per 1000 (CI 95% 47 fewer — 31 more) | 947 per 1000 | Very low  
Due to very serious imprecision<sup>15</sup> | We are uncertain whether TaTME increases or decreases odds of clear CRM |
| **Clear DRM**<sup>16</sup> | Odds Ratio 0.15 (CI 95% 0.02 — 1.35) Based on data from 596 participants in 1 studies.<sup>17</sup> (Observational (non-randomized)) | 997 per 1000  
Difference: 17 fewer per 1000 (CI 95% 128 fewer — 1 more) | 980 per 1000 | Very low  
Due to very serious imprecision<sup>18</sup> | We are uncertain whether TaTME increases or decreases odds of clear DRM |
| Outcome                     | Timeframe | Study results and measurements | Comparator | Intervention | Certainty of the Evidence (Quality of evidence) | Plain language summary |
|-----------------------------|-----------|--------------------------------|------------|--------------|------------------------------------------------|------------------------|
| Major morbidity             | 30 days   |                                 | Robotic TME | TaTME        | 8 Critical                                      | No studies were found that looked at major morbidity |
| Minor morbidity             | 30 days   |                                 | Robotic TME | TaTME        | 8 Critical                                      | No studies were found that looked at minor morbidity |
| Local recurrence            | 2 years   |                                 | Robotic TME | TaTME        | 8 Critical                                      | No studies were found that looked at local recurrence at 2 years |
| Overall survival            | 5 years   |                                 | Robotic TME | TaTME        | 8 Critical                                      | No studies were found that looked at 5-year overall survival |
| Disease-free survival       | 5 years   |                                 | Robotic TME | TaTME        | 8 Critical                                      | No studies were found that looked at 5-year disease-free survival |
| Low anterior resection syndrome |          |                                 | Robotic TME | TaTME        | 8 Critical                                      | No studies were found that looked at low anterior resection syndrome |
| Quality of life             |          |                                 | Robotic TME | TaTME        | 8 Critical                                      | No studies were found that looked at quality of life |

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5. Discussion

Implications for policy makers

TaTME represents an option for the treatment of low rectal cancer, next to laparoscopic and robotic rectal resection. Although evidence on economic considerations is limited, empirical evidence does not suggest increased overall cost. Centralization of rectal cancer management may be necessary to allow accumulation of experience, which may play a vital role in operative outcomes.

Implications for healthcare professionals

Surgeons with experience in TaTME are not advised against performing TaTME in patients with low rectal cancer, as evidence from comparative observational studies which have adjusted for confounders does not indicate increased harm, moreover there is evidence of moderate certainty suggesting lower 30-day mortality and lower rate of recurrence at 3-years.

Substantial new evidence is awaited within the next few years, so that surgeons who are not trained in TaTME may not change their practice for the present. Importantly, evidence considered in this rapid guideline derives primarily from centers and surgeons with experience in TaTME, guideline users are therefore advised to exercise caution in extrapolating the evidence summarized herein.

Implications for patients

Patients can be informed that available evidence suggests similar outcomes between TaTME and laparoscopic TME, whereas 30-day mortality and 3-year locoregional recurrence may be lower with TaTME, if the surgeon has experience in this technique. Furthermore, they may want to discuss expected benefits and potential harms, and their surgeon's experience and preference.

Implications for researchers

There are important gaps in evidence, which are expected to be addressed by future research:

TaTME v. laparoscopic TME: De novo RCTs may not be necessary, because several trials are currently underway and their results are expected to be published within the next years (see Validity period below). Matched cohort studies are needed to address the outcomes major morbidity, 30-day or in-hospital mortality, 2-year recurrence, 5-year disease-free and overall survival, low anterior resection syndrome and quality of life. Importantly, further reports of unmatched cohorts do not contribute reliable information to the body of evidence and may be redundant and potentially misleading. Researchers may want to consider performing analyses that have adjusted for sex, BMI, ASA classification, tumor stage and distance from anal verge, and neoadjuvant chemoradiotherapy. To reach sufficient sample size, multi-institutional collaborations or registry analyses are encouraged. Analyses of male patients, patients who underwent neoadjuvant chemoradiotherapy and level (height) up to which transanal dissection was performed are expected to address the outcomes of TaTME in these subgroups.

TaTME v. robotic TME: Available evidence is extremely limited and the same research considerations apply here as well. Critical and important outcomes as listed in the Methods section are expected to be addressed.

Monitoring

Use of the guideline by EAES members will be monitored through an online survey 2 years after publication. Feedback from target users in the form of email communication, letters to the editor, and comments in social media will be documented to be addressed by future versions.

Validity period

A scoping search of ClinicalTrials.gov, EU Clinical Trials Register, WHO International Clinical Trials Registry Platform, EORTC and ISRCTN registry identified at least 5 ongoing RCTs comparing TaTME with laparoscopic (n=4) or robotic (n=1) TME, including two mega-trials (planned to recruit >1000 patients each) [54][55][56][57][58]. Completion dates range from June 2021 to July 2025. Under consideration of the reported follow up duration of critical outcomes, substantial new evidence is expected by 2025 for Q1 and by 2026 for Q2. The validity of the present version of this rapid guideline is set until December 2025. Please read the Disclosure for further information regarding validity.

Update

An update of this rapid guideline is planned to take place in 2025. However, one could anticipate a change in the direction or the strength of the recommendation when data from cohort studies or registries become available, under the condition that their methodological quality will be high. The EAES Research Committee/Guidelines Subcommittee will keep monitoring new evidence and update this document if such data become published.
6. Conclusion

This rapid review summarizes highest quality evidence and provides evidence-based and trustworthy recommendations on the use of TaTME for low rectal cancer.
7. Competing interests statement

Marco Milone, Michel Adamina, Alberto Arezzo, Nona Bejinariu, Luigi Boni, Nicole Bouvy, Francesco Borja de Lacy, Elleke Dresen, Konstantinos Ferentinos, Nader K. Francis, Joe Mahaffey, George Theodoropoulos, Marta Penna, Katerina Maria Kontouli, Dimitris Mavridis, Per Olav Vandvik and Stavros A Antoniou have no direct conflicts of interest or financial ties to disclose. Indirect conflicts of external advisors were documented and managed as per G-I-N standards. Detailed conflict of interest statements of all contributors can be found in http://osf.io/65vkq
8. Funding statement

This project was funded by United European Gastroenterology and the European Association for Endoscopic Surgery. The funding bodies had no influence on the development of this protocol or this rapid guideline. There is no grant number linked to this research.
9. Acknowledgements

The steering group would like to thank Mrs. Lyudmil Ninov and the European Patients Forum for assisting in finding a patient representative to act as panel member in this guideline.
10. Appendix

COMMENTS TO THE LITERATURE SEARCH PROCESS

First-level and second level screening were performed by two reviewers independently (SAA, MM) using the platform Rayyan. Both reviewers were blinded to the other reviewer's judgement. Conflicts were encountered in 0.9% of the records (n=7), which were resolved by discussion.

For a substantial proportion of records we could not identify the full texts. This was typically because they referred to abstracts of congress presentations, rather than lack of access to the full text. We did not consider data provided in abstract form, because these do not provide sufficient information to allow for risk of bias assessment, hence they would be excluded from further analysis as per ROBINS-I (critical risk of bias due to insufficient information) [23]. Detailed reasons for exclusion can be found online [20].

Particular care was taken to avoid inclusion of studies reporting on overlapping patient populations, by cross checking the country and institution, the authors' names, any registries where patient data were provided to, years of patient recruitment, etc. Pathological outcomes (TME completeness, clear DRM) of a number of reports were excluded [31][33][35][36][43], due to overlapping patient populations with a multicenter study, as indicated by the primary author of the latter [44]. Outcomes from these original studies that were not reported cumulatively by the multicenter study were properly included in the analyses. For the outcome clear CRM, we included the original studies and not the multicenter study, because the cumulative number of patients was smaller in the multicenter study. More detailed information is provided in the data extraction sheet in the online appendix [20].

AMENDMENTS TO THE PROTOCOL

First and second level screening was carried out by two investigators, instead of one and cross-checking by another investigator, to increase the sensitivity of the search.

Interrogation of medical databases identified cohort studies only. ROBINS-I suggests that studies at critical risk of bias should not be included in evidence synthesis [23]. We considered studies that did not adjust for important confounders to be at critical risk of bias due to confounding (hence, at critical overall risk of bias), and we did not consider them further for qualitative and quantitative analysis. These confounders were:

1. Sex
2. BMI
3. Tumor stage
4. Neoadjuvant CRT

This approach has the drawback that we cannot assess the possibility of substantial effect in spite of residual bias. Nevertheless, in our experience this is an extremely rare scenario and we have never encountered this in the surgical literature. Furthermore, evidence from studies adjusting for the above confounders (in the TaTME v. lap. TME comparison) does not suggest that effect despite residual confounding would be a plausible scenario in this context.

Following feedback from EAES members, we planned to perform the following subgroup analyses (in addition to the pre-specified ones), however no relevant data were available:

1. Male patients
2. Patients with neoadjuvant radiotherapy
3. Level of transanal dissection

COMMENTS TO DATA EXTRACTION AND OUTCOME ASSESSMENT

Outcome data were extracted from one author (MM) and cross checked by a second author (SAA). Disagreements were resolved by discussion. Risk of bias assessments were performed by one author (SAA).

Stoma construction was considered both as co-intervention and as confounder in risk of bias assessment, in studies where stoma construction rates differed substantially between the intervention and the comparator groups.

We considered patients with either protective ileostomy or Hartmann's procedure as cases with stoma, whenever this information was provided.

Completeness of TME was assessed using the Quirke criteria across studies [59]. There was no substantial variability among studies with regard to circumferential and distal resection margin assessment; the authors typically considered a distance of >1mm between the tumor (or the deepest tumor invasion) and the circumferential or distal resection margin to indicate no margin involvement.

We added the outcome 2-year local recurrence based on panel's and EAES members' input. The importance of this outcome was determined during the consensus meeting. The minimal importance difference was decided upon after panel's online anonymous voting.

Risk of bias summary tables and graphs were constructed using the robvis tool [60].

COMMENTS TO STATISTICAL ANALYSES

We conducted a random effect meta-analysis to synthesize quantitatively the evidence for the two guideline questions since we expected much variation in the PICO criteria across trials [25]. All the included outcomes are dichotomous. From each study, we extracted the number of events and the sample size of each group, and we estimated for each outcome the odds ratio along with the corresponding 95% confidence interval. We used the method of moments estimator, also known as the DerSimonian & Laird estimator for the between study-variance (heterogeneity) [61]. A continuity correction was applied to the studies with zero-cell counts. We explored heterogeneity via the $I^2$ statistic that describes the percentage of the variability of effect estimates, that is due to heterogeneity rather than sampling error. We further
explored heterogeneity by computing the Q-statistic and the 95% predictive intervals that show the plausible range of effect size values for a future trial. It has been suggested that at least ten studies are needed for the Eggers’ test to be applied [62]. It was not possible to check for small study effect either visually by inspecting the symmetry of the funnel plot or statistically by applying the Egger’s test because of an inadequate number of studies for the majority of comparisons. The fixed effect (also known as common effect) model was applied for all the analyses as a sensitivity analysis. Yet, there were not important differences observed between the results of fixed and the random effects model. All the analyses were performed in R statistical package version 4.0.3 using the meta, metafor packages.

COMMENTS TO ASSESSMENT OF THE CERTAINTY OF EVIDENCE

For time-to-event outcomes, we planned to use the GRADE guidance on rating the certainty in time-to-event outcomes [63]. One study only provided data on loco-regional recurrence and survival outcomes, with a follow-up of 3 years. The predefined outcomes were considered critical at 5-year follow-up, we therefore downgraded for indirectness. Further considerations are provided in the footnotes of the evidence tables.

COMMENTS TO THE EVIDENCE-TO-DECISION FRAMEWORK

Panel members were made aware that some outcomes are overlapping. Anastomotic leak is overlapping with Clavien-Dindo grouped outcomes. Negative circumferential margins and distal margins are contained within the outcome TME completeness. These ‘subgroup’ outcomes were not considered in the evidence-to-decision framework, relevant data are however provided because we considered they they would be valued by guideline users.
11. Appendix figures

PRISMA 2020 flowchart

Q1 Risk of bias summary 30-day complications Clavien-Dindo ≥3 (cohort studies)

Q1 Risk of bias graph 30-day complications Clavien-Dindo ≥3 (cohort studies)

Q1 Risk of bias graph 30-day complications Clavien-Dindo ≤2 (cohort studies)

Q1 Risk of bias summary 30-day complications Clavien-Dindo ≤2 (cohort studies)

Q1 Risk of bias summary 30-day mortality (cohort studies)

Q1 Risk of bias summary 30-day complications Clavien-Dindo ≥3 (RCT)
Q1 Risk of bias summary stoma construction (cohort studies)

Q1 Risk of bias graph stoma construction (cohort studies)

Q2 Risk of bias summary stoma construction (cohort study)

Q1 Risk of bias summary pathological outcomes (cohort studies)

Q1 Risk of bias graph pathological outcomes (cohort studies)

Q2 Risk of bias summary pathological outcomes (cohort study)

Q1 Risk of bias summary local recurrence at 2 years (cohort study)
Q1 Risk of bias graph local recurrence at 2 years (cohort study)

Q1 Risk of bias summary 5-year overall survival (cohort studies)

Q1 Risk of bias summary 5-year disease-free survival (cohort studies)

Q1 Risk of bias summary low anterior resection syndrome (cohort studies)

Q2 Risk of bias summary quality of life (cohort studies)
12. Protocol

ABSTRACT

Background
Transanal TME (TaTME) has emerged as a new approach to address the anatomical limitations of the bony confines of the pelvis, specifically in case of bulky tumors and fatty mesorectum. The evolution of this technique has stimulated the interest of colorectal surgeons. Conflicting evidence has caused confusion around the short-term safety and the oncological effectiveness of TaTME.

Methods and analysis
A rapid guideline will be developed in accordance with GRADE and AGREE II standards. The steering group will consist of general surgeons, members of the EAES Research Committee/Guideline Subcommittee with expertise and experience in evidence outreach and synthesis, and guideline development, biostatisticians and a guideline methodologist. The guideline panel will consist of six general surgeons, an oncologist, a radiologist, a radiation therapist, a pathologist and a patient representative. Two PICO questions with subgroup analyses will address the safety and effectiveness of TaTME compared to laparoscopic and robotic TME in male/ female patients with T1/T2/T3 middle/low rectal cancer. A systematic review will be conducted, and results of evidence synthesis will be summarized in summary of findings tables. Recommendations will be finalized through a Delphi process of the guideline panel within a structured evidence-to-decision framework.

Ethics and dissemination
The funding body will not be involved in the development of this guideline. Conflicts of interest, if any, will be addressed by re-assigning functions or replacing participants with relevant conflicts.

Keywords
TaTME; Transanal; TM; rectal cancer; clinical practice guideline; rapid guideline; GRADE; AGREE II; EAES

INTRODUCTION

Background
The gold standard treatment for low-middle rectal cancer is total mesorectal excision (TME) as demonstrated by Heald in 1979 [64]. Completeness of TME is the cornerstone of curative treatment of rectal cancer. However, the “holy plane” defined by the embryological origin of the rectum is not always easy to obtained, specifically in patients with difficult anatomy.

Various surgical techniques have been proposed to obtain a clear specimen with negative circumferential resection margins. Transanal TME (TaTME) has emerged as a new approach to address the anatomical limitations of the bony confines of the pelvis, specifically in case of bulky tumors and fatty mesorectum [11]. The evolution of this technique has stimulated the interest of colorectal surgeons. Conflicting evidence has caused confusion regarding the short-term safety and oncological effectiveness of TaTME [65][66]. Consensus statements by individual groups have attempted to summarize empirical and research evidence and provide practice recommendations [11][13][12]. Evidence-informed and methodologically rigorous clinical practice guidelines addressing the use of TaTME are lacking [67].

A survey of European surgeons by the EAES Research Committee/Guideline Subcommittee reflected this lack of information and prioritized colon cancer surgery as a candidate topic to be addressed by a clinical practice guideline (56%) [15].

Objective
The objective of this rapid guideline is to provide transparently developed, reliable, and evidence-informed recommendations on the application of TaTME in rectal cancer.

METHODS

The present protocol adheres to AGREE II and PRISMA reporting standards [68][69]. It will be available on the EAES website for access by healthcare professionals, and EAES members will be asked to comment on the content. Relevant comments will be considered by the steering group.

Funding
The project is funded by the European Association for Endoscopic Surgery. The funding body will not have any influence on the guideline development process.

Steering group
The steering group consists of general surgeons, members of the EAES Research Committee/Guideline Subcommittee, and experts in guideline development, medical statistics and evidence synthesis.

Guideline methodologist
The senior author fulfills the criteria of a GRADE methodologist [70], has participated in the development of more than 10 clinical practice guidelines, has experience in evidence synthesis, and will serve as a guideline methodologist in this guideline.

Guideline panel and external advisors
The guideline panel will consist of six general surgeons, an oncologist, a radiologist, a radiation therapist, a pathologist and a patient representative. We will ask input by surgeons with vast experience in TaTME evident by their clinical and academic work in the field, however they will not participate in the evidence-to-decision framework due to by definition presence of indirect conflicts, as per Guidelines International Network guidelines [71]. The guideline panel’s and external advisors’ contribution will be acknowledged by fully Medline-citable standard or corporate authorship in the resulting journal publication of this guideline [72].
Guideline questions
Two PICO question will address the use of TaTME for the treatment of rectal cancer and subgroup analyses will address middle/low rectal cancer, T1/T2/T3 rectal cancer and rectal cancer in males/females:
1. Should TaTME versus laparoscopic TME be preferred for the treatment of rectal cancer?
2. Should TaTME versus robotic TME be preferred for the treatment of rectal cancer?

Thematic breakdown of questions and methodology to address these are presented in Table 1 available here.

Guideline development methodology
The guideline development process will adhere to AGREE II and GRADE guideline development standards, and methodology parameters of rapid recommendations [73]. Different thresholds for minimal important differences in the form of absolute effect differences will be set. The guideline panel will be asked to comment on the PICO questions and subgroup analyses, and to vote on the level of importance of each outcome, and on the most appropriate threshold for minimal clinically important differences through a web-based anonymous survey. Their responses will be summarized and direct the decision about the selection of outcomes and thresholds for minimal importance differences.

The literature search strategy will be developed by a member of the steering group with experience in outreach, knowledge, and evidence search. The Healthcare Databases Advanced Search (HDAS) interface developed by the National Institute for Health and Care Excellence (NICE) will be used to interrogate Medical Literature Analysis and Retrieval System Online (MEDLINE) Excerpta Medica database (EMBASE). The grey literature will be searched through OpenGrey (Exalead). Relevant terms will be selected to identify eligible reports. Thesaurus headings, search operators, and search limits in each of the above databases will be adapted accordingly.

Risk of bias of eligible studies will be assessed using RoB 2 for randomized trials [22] and ROBINS-I for cohort studies. Study selection, risk of bias assessment and data extraction will be performed by one investigator and independently cross-checked by a collaborator; disagreements will be resolved by discussion. Statistical analyses as outlined in Table 1 will be performed by biostatisticians using the methodology reported below.

GRADE evidence tables and summary of findings tables will be constructed and presented to the guideline panel in a web-based meeting. Draft recommendations will be formulated and strength of recommendations will be defined. The recommendations will be refined and their strength will be assessed and revised as judged by the guideline panel through an online Delphi process. Comments by the Delphi panel must be in accordance with the GRADE methodology in order to be considered. Formulation of recommendations will be informed by GRADE and AGREE-REX [74][75].

Evidence synthesis methodology
A random effects meta-analysis model will be applied as we expect some variation in the PICO criteria among trials [25]. Mantel-Haenszel pooled odds ratios will be calculated for binary variables and the standardized mean difference for continuous variables, with corresponding 95% confidence intervals. Time-to-event data, also known as survival data, arise when we are interested not only in the event of an outcome but also on the time elapsing before this event is observed. Participants for whom we did not observe the event but contributed some time will be part of the analysis. For trials including time-to-event outcomes, we will extract the hazard ratio and the standard error of the logarithm of the hazard ratio. If instead of the standard error, the corresponding 95% confidence interval or p-value is reported, we can used them to estimate the standard error (Cochrane handbook Chapter 6).

These are standard outputs from a Cox proportional hazards model. If these data are not given, we can approximately estimate the hazard ratio using statistics estimated from a long-rank analysis (Cochrane handbook Chapter 6). If some studies give the hazard ratio but other give risk ratios (or the number of events and sample size in each group), we will combine them in a sensitivity analysis.

Conceptual heterogeneity related to the PICO parameters and the study design will be assessed, and statistical heterogeneity will be tested for using the I² statistic and by comparing the estimated heterogeneity variance to its empirical distribution as estimated by empirical studies [76]. We will explore for small-study effects using funnel plots and statistical tests (e.g. Egger’s test) [62]. Statistical analyses will be performed using the meta library in R. We will compute the fixed-effect pooled estimate as a sensitivity analysis. Where means and p-values, or confidence intervals will be given, the standard error and the standard deviation will be obtained by using the formula suggested by the Cochrane Collaboration [77].

Target users
This guideline is intended to be used by general surgeons, multidisciplinary team members, hospital administrators, policy makers, and patients. The guideline publication will contain a short abstract in plain language to be used by patients.

Publication and dissemination strategy
As a EAES Research Committee/Guideline Subcommittee project, this guideline will be submitted for publication in Surgical Endoscopy, official journal of the Association.

Feedback
The steering group will consider constructive feedback received during the conduct of the project via various routes and sources such as letters to the editor and social media. Such feedback will be taken into account in the guideline development process or a future update of the guideline.

Monitoring, update and future steps
Use of the guideline by EAES members will be monitored through an online survey 2 years after publication. The timing of the update of the guideline will be decided by the steering group on the basis of new research data on this topic.

DISCUSSION

Implications for practice and research
Stringent criteria defined by GRADE and AGREE II will be applied
to collate, appraise and analyze the available evidence. The
guideline is expected to inform decision making, and guide clinical
practice and health policy. Guidance will be provided on direction
and implications for future research in light of identified evidence
gaps.

**Strengths and limitations**
The strengths and limitations of rapid guidelines have been
previously reported [73][81][77]. The merits of rapid guidelines,
including trustworthiness, credibility, and time efficiency have to
outweigh the shortcomings, such as the narrow scope and possible
missing of resources due to the rapid review process.

**Research ethics**

Conflicts of interest statements will be collected by all participants
before and upon completion of the project. Participants with
substantial conflicts will be either re-assigned functions or
replaced as per Guidelines International Network
recommendations [78]. Authors of studies considered for
development of evidence summaries will not be involved in risk of
bias appraisal of these studies and discussion of the relevant
evidence to decision framework.

**CONCLUSION**
This rapid guideline will address the use of TaTME in the treatment
of rectal cancer and aspires to constitute a useful information
source for key stakeholders.
13. Authorship and contributions

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14. Patient version of UEG and EAES Rapid Guideline: TaTME for Rectal Cancer
14.1 Contact information

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14.2 Key points

- Resection of bowel cancer that lies very low in the pelvis using the so-called TaTME may confer some benefits.
- This is a demanding technique that requires surgeon's expertise for optimal outcomes.

14.3 Introduction to the target topic

Complete removal of the last part of the bowel, which is called rectum, along with the surrounding fatty tissue is important to prevent cancer relapse. Complete removal is challenging when the tumor lies very low in the pelvis.

Removal through laparoscopic surgery, also known as keyhole surgery, is standard of care in many institutions. A technique called “transanal total mesorectal excision” or “TaTME” involves performing part of the resection through the anus using keyhole instruments. It was developed to address the difficulties with resection of bowel tumors that lie very low in the pelvis.

14.4 Purpose, scope and target users

This document aims to provide information to patients with cancer of the lowest part of the bowel, the rectum, who are being proposed to be treated by a technique called transanal total mesorectal excision.

14.5 Link to the source guideline

The full guideline is available here:
https://app.magicapp.org/#/guideline/4767

14.6 Recommendations

- Keyhole surgery and keyhole surgery with the assistance through transanal total mesorectal excision are both options for the treatment of rectal cancer.

- Transanal total mesorectal excision may confer some benefits in very low cancers of the rectum, including lower risk of perioperative death and lower risk for the tumor coming back in the future.

- This is a demanding technique, requiring prior training and experience of the surgeon.

- A weak recommendation was issued for the use of transanal total mesorectal excision, if surgeon’s experience is available.

- A weak recommendation means that most patients would likely want this intervention, and benefits may outweigh harms for the majority of patients, but not all.

14.7 Questions to ask
Questions you may want to ask your surgeon:

- Do you have experience with transanal total mesorectal excision?
- Do you prefer this technique over keyhole surgery without the assistance through transanal total mesorectal excision and why?
- Are there infrastructures and expertise among the OR team in place for this technique?

14.8 Funding

This project was funded by United European Gastroenterology and the European Association for Endoscopic Surgery; both are not-for-profit organizations. A patient representative was involved as panel member throughout the development of this guideline.

14.9 Conflicts of interest

The steering group and the guideline panel members declared no conflicts of interest throughout the development of this guideline. Indirect (intellectual) conflicts of external advisors were managed in accordance with principles set by the Guidelines International Network. Importantly, external advisors were not involved in the decision about the direction, the strength and the wording of the recommendations. The funding organizations had no influence on the development of this guideline.
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