Gastroenterological Endoscopy

Third Edition
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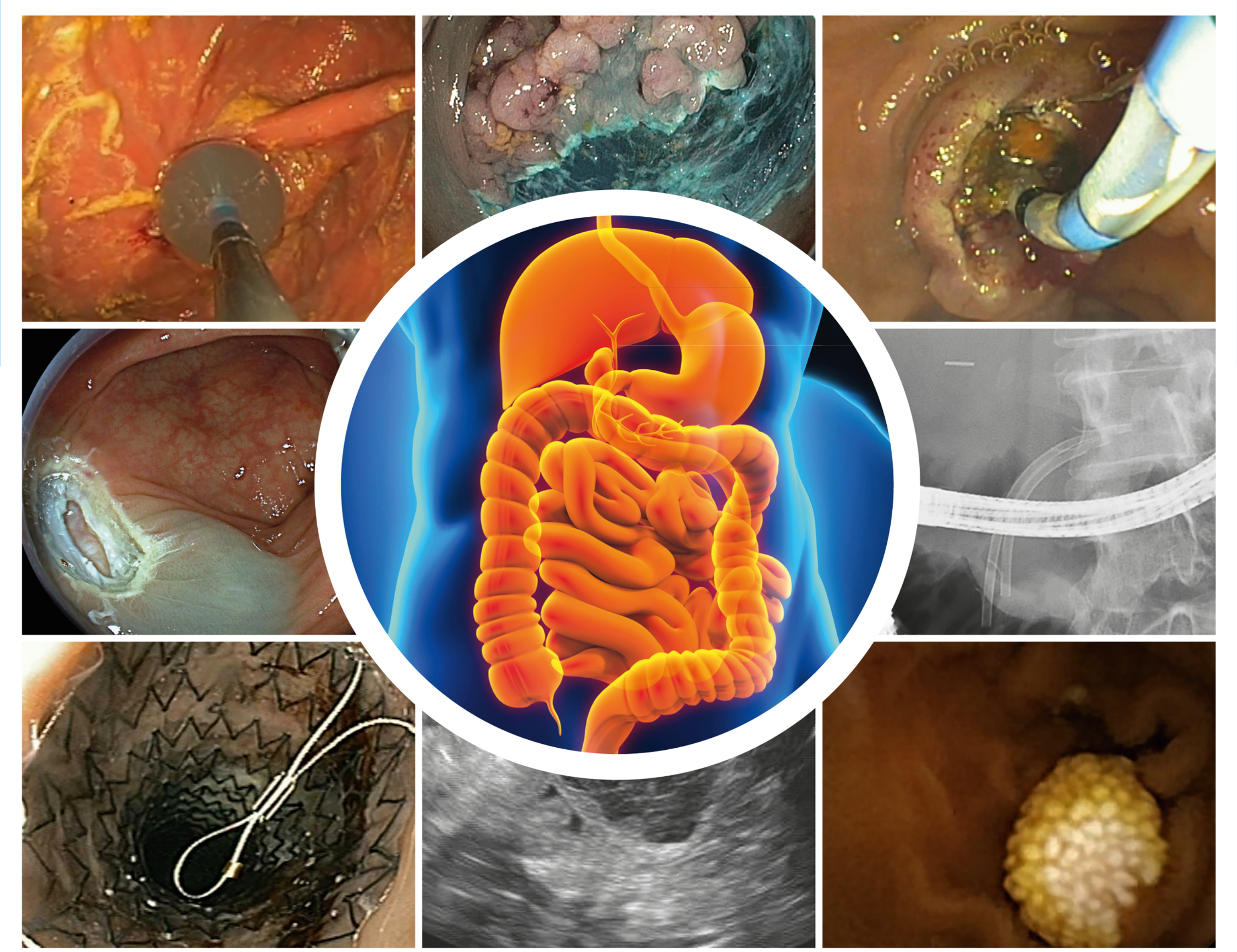

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Gastroenterological Endoscopy

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Third edition

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Dedication

In Memory of Dr. Lauren Battat Gerson

We mourn the untimely demise of our colleague Dr. Lauren Battat Gerson, who passed away on July 21, 2017. Lauren contributed to the field of *gastrointestinal endoscopy* in so many ways, including as an associate editor for this book. She will be remembered for all the lives she touched and patients she cared for. A memorial article was published in *Gastrointestinal Endoscopy*, volume 86, issue 4, pages 579–80.

Preface

We proudly present the third edition of *Gastroenterological Endoscopy*, 15 years after the first and 8 years after the second edition. This book, founded by Professors Classen, Tytgat, and Lightdale, now passes the torch to a second generation of editors. It nonetheless continues the tradition of excellence, depth, and breadth that its founding editors started. We strive to continue publishing the leading reference in the field of gastrointestinal endoscopy. Professors Fockens, Sung, and Wallace have brought together an outstanding team of associate editors: Todd Baron, Michael Bourke, Nicholas Shaheen, Nageshwar (Nagy) Reddy, and Lauren Gerson. After completion of the book, but prior to its publication, we were tremendously saddened by the sudden passing of Dr. Gerson, whose contribution carries on with the book. A memoriam to Dr. Gerson appears in the opening pages of this book.

The list of contributing authors is a who's who of endoscopy. We are fortunate to have both, senior masters and new innovators. In the preface to the second edition, the "new" procedures of the day were NOTES, ESD, and advanced imaging. Much has passed since 2010. NOTES (natural orifice transluminal endoscopic surgery) has largely waned, but it led endoscopy into the "third space," the submucosa between the lumen and the outside (intra-abdominal) world. Submucosal endoscopy enabled POEMS (per-oral endoscopic myotomy surgery) for achalasia and its new variations, gastric-POEMS (for gastroparesis) and STER (submucosal tunnel endoscopic resection), for subepithelial tumors. New devices such as over-the-scope clips have enabled safe closure of full-thickness defects. Initially, these were applied to unplanned perforations and bleeding, but as we became increasingly confident of closure, they enabled planned full-thickness resection of tumors and even tissue sampling of the gastroenteric nervous system, which further opens new methods of research and treatment. Endoscopic resection by EMR and ESD is now practiced worldwide with refinements in devices and techniques to make it easier and safer while still preserving its efficacy. A major recent advancement in endoscopy was the development of lumen-apposing metal stents (LAMS), initially for drainage of pancreatic fluid collections. Like NOTES, LAMS have opened a new world of possibilities to endoscopists including EUS-guided biliary drainage directly from lumen to bile duct (not retrograde through the papilla). Lumen-to-lumen apposition has opened the way for gastroenteric bypass in duodenal obstruction (or double biliary and duodenal bypass in the case of double obstruction from pancreatic head tumors). Creative endoscopists, driven by patients' needs, developed methods of biliary access in patients with surgically altered anatomy through a variety of transluminal routes. It is remarkable to witness the impact of new technology (LAMS, clips) and techniques (POEMS, NOTES) on unanticipated downstream innovations. These are truly disruptive events, all captured in the third edition.

In addition to the editors and authors, we wish to thank the outstanding staff at Thieme for editorial assistance in producing this large volume of work. We hope that endoscopists throughout the world will engage this new knowledge and, most importantly, apply it to improve the care of patients with gastrointestinal and other relevant diseases.

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Abbreviations

automated endoscope reprocessors	AER
argon plasma coagulation	APC
American Society for Gastrointestinal Endoscopy	ASGE
adenosine triphosphate	ATP
complementary metal oxide semiconductor	CMOS
carbapenem–resistant enterobacteriaceae	CRE
dual antiplatelet therapy	DAPT
esophagogastroduodenoscopy	EGD
endoscopic mucosal resection	EMR
endoscopic retrograde cholangiopancreatography	ERCP
endoscopic submucosal dissection	ESD
European Society of Gastrointestinal Endoscopy	ESGE
endoscopic ultrasound	EUS
fine-needle aspiration	FNA
gastric antral vascular ectasia	GAVE
gastrointestinal	GI
high- level disinfection	HLD
instructions for use	IFUs
Japanese Gastroenterological Endoscopy Society	JGES
liquid chemical germicide	LCG
multidrug-resistant organism	MDRO
Mallory–Weiss tear	MWT
not recommended	NR
polymerase chain	PCR
percutaneous endoscopic gastrostomy/jejunostomy	PEG/PEJ
peptic ulcer disease	PUD

Section I

Introduction to Endoscopy

1 Education and Training in Endoscopy

Jürgen Hochberger, Jürgen Maiss, and Jonathan Cohen

1.1 Introduction

Optimal patient care and quality outcomes are becoming increasingly important in clinical medicine. Specialist medical societies have produced guidelines and recommendations for minimum quality requirements for performance of endoscopic techniques (▶Table 1.1).[1] However, in most of these guidelines, terms such as "self-reliance" and "under supervision" are not clearly defined. Optimal methods, duration, and proper endpoints of training are still topics of debate.[2] There has been a growing trend to de-emphasize the number or procedures performed in favor of demonstration of competent and independent performance.[3]

Recently, endoscopy simulators have rekindled debate on whether training in basic manual skills is better provided outside the patient.[4,5,6,7,8] Despite the growing availability of various training models, practical skills are still routinely acquired by performing actual procedures under the supervision of a senior endoscopist. This chapter presents an overview of training issues and the role of simulators in training.

1.2 Clinical Education

A few general principles can be applied to the entire field of endoscopic training:

- The endpoint of training is the acquisition of competency to perform the examinations without supervision at a level comparable to that achieved by practitioners in the community.
- While certain general endoscopic basic skills are crucial to many procedures, training must be procedure specific. Competency in one technique does not necessarily guarantee competency in another technique.
- Procedures performed for diagnostic purposes should also enable related tissue sampling or therapies associated with that procedure.

1.2.1 Clinical Training to Competency in Esophagogastroduodenoscopy and Colonoscopy: Studies, Guidelines, and Assessment

Since the early 1980s, trainees have been required to keep a record of all procedures performed,[1] in particular for colonoscopy. The ability to reach the cecum is the most common criterion by which colonoscopies have been judged.[9] Data from early studies showed variable learning curves and led to the concept of minimal numbers of procedures required.[1] Sedlack et al presented in 2011 a new assessment tool, the so-called Mayo Colonoscopy Skills Assessment Tool (MCSAT), to describe learning curves for colonoscopy.[10] They evaluated forty-one GI fellows who performed 6,635 colonoscopies. Independent cecal intubation rates of 85% and cecal intubation times of 16 minutes or less were achieved at 275 procedures on average, which is more than previous gastroenterology training recommendations required.

In 2014, the Training Committee of the American Society for Gastrointestinal Endoscopy (ASGE) presented the "Assessment of Competency in Endoscopy" (ACE) tool as a refinement of the MCSAT.[9] The ACE tool added important quality parameters such as a metric assessment of fine-tip control and polyp detection rates. In 2016, a prospective, multicenter trial was published evaluating the ACE tool at 10 institutions across the United States including 93 gastrointestinal (GI) fellows.[11] A total of 184 senior endoscopists assessed 1,061 colonoscopies, which included 6 motor and 6 cognitive skills on a 4-point scale. The average fellow reached required cognitive and motor skills endpoints by 250 procedures, with over 90% of fellows surpassing these thresholds by 300 procedures.[11] Procedure times, polyp detection rates, and polyp miss rates with increasing experience are shown in ▶Fig. 1.1 and ▶Fig. 1.2.

Barton et al[12] described in 2012 the value of the Direct Observation of Procedural Skills (DOPS) method developed by an expert group of colonoscopists and clinical educators in the United Kingdom. Colonoscopists wishing to participate in the British National Health Service National Bowel Cancer Screening Programme (BCSP) were assessed. Assessments from 147 candidates and 28 assessors were analyzed. Candidates had to prove experience in a minimum of 500 colonoscopies with a self-reported cecal intubation rate of ≥ 90% and a polyp detection rate of ≥ 20%. The assessment had high reliability using generalizability theory (G) with $G = 0.81$ and correlated highly with a global expert assessment. Both, candidates and assessors, believed that the DOPS was a valid assessment of competence.

Anderson[13] recently described how DOPS evaluation has been successfully integrated for trainees as well as for independent endoscopists into the "UK National Bowel Cancer Screening Programme." The Joint Advisory Group (JAG) sets the standards for endoscopy training and the accreditation of endoscopy units as base training

Table 1.1 Recommendations regarding the minimum numbers of procedures required for competence.*

Organization	EGD	Colonoscopy	ERCP
American Society for Gastrointestinal Endoscopy	100	100	100
British Society of Gastroenterology	300	100	150
Conjoint Committee for the Recognition of Training in Gastrointestinal Endoscopy (Australia)	200	100	200
European Diploma of Gastroenterology	300	100	150

Abbreviations: EGD, esophagogastroduodenoscopy; ERCP, endoscopic retrograde cholangiopancreatography.

Source: Hochberger et al 2010.[1]

*Numbers often under debate.

units.[14,15] A Global Rating Scale web-based system is used for continuous assessment of performance and DOPS is regularly applied in order to monitor continuously individual performances. An individual web-based logbook and e-portfolio of each endoscopist is created via a national database system that is the base for credentialing and certification. Feedback of data to individuals helps in benchmarking and identification of those with suboptimal performance and a need for extra training and close audits. The system has recently been extended to upper GI endoscopy and other techniques.[16]

1.2.2 Training in Endoscopic Retrograde Cholangiopancreatography

Proficiency in all aspects of endoscopic retrograde cholangiopancreatography (ERCP) requires several years of practical training and continuous refinement of knowledge and skills.[8] With the advent of noninvasive tests such as magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasonography (EUS), ERCP is an almost purely therapeutic procedure. This is creating a new challenge in the training of young endoscopists, as ERCP procedures are becoming more complex and are concentrated in large- or mid-volume endoscopy centers.[17,18]

In most fellowship training programs, traditional ERCP training follows education in diagnostic gastroscopy and colonoscopy and is often begun when the trainee has been introduced to polypectomy, hemostasis, or EUS training as part of a "learning pyramid" (▶Fig. 1.3).[1]

Jowell et al[19] found that a minimum of 180 to 200 ERCPs are needed to be performed before a trainee could attain competency in ERCP.[19] (▶Fig. 1.4) Approximately, 80 to 100 ERCPs per

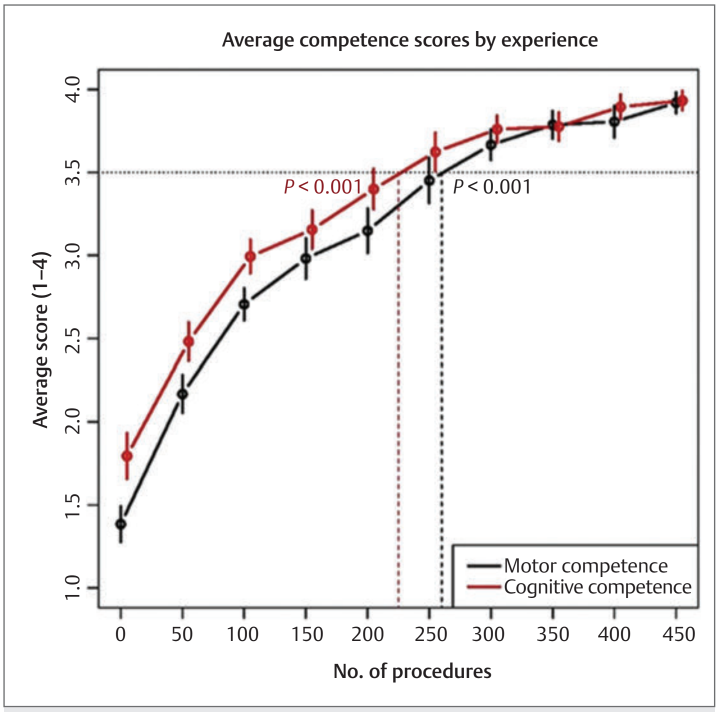

Fig. 1.1 Procedure time by experience. (Reproduced with permission from Sedlack et al 2016.[11])

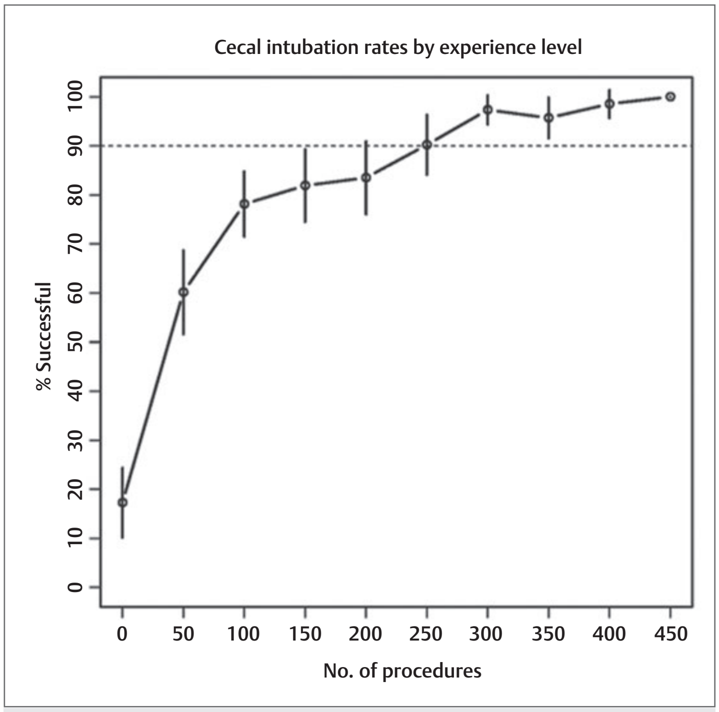

Fig. 1.2 Polyp detection and miss rates by experience. (Reproduced with permission from Sedlack et al 2016.[11])

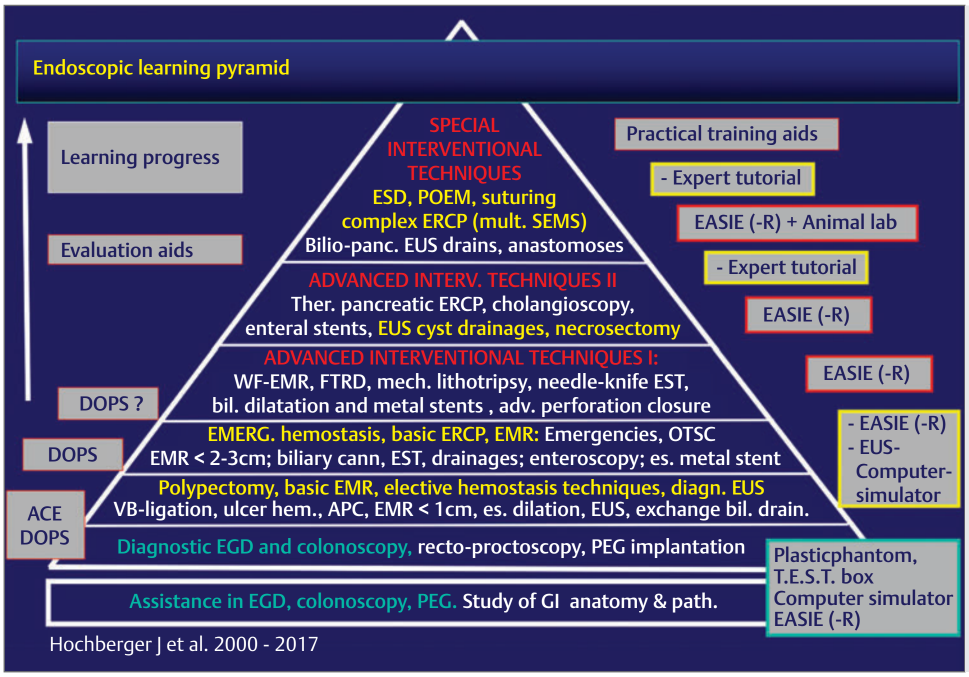

Fig. 1.3 The "learning pyramid" as an example of stepwise clinical training in interventional endoscopy. (Adapted from Hochberger et al 2010.[1])

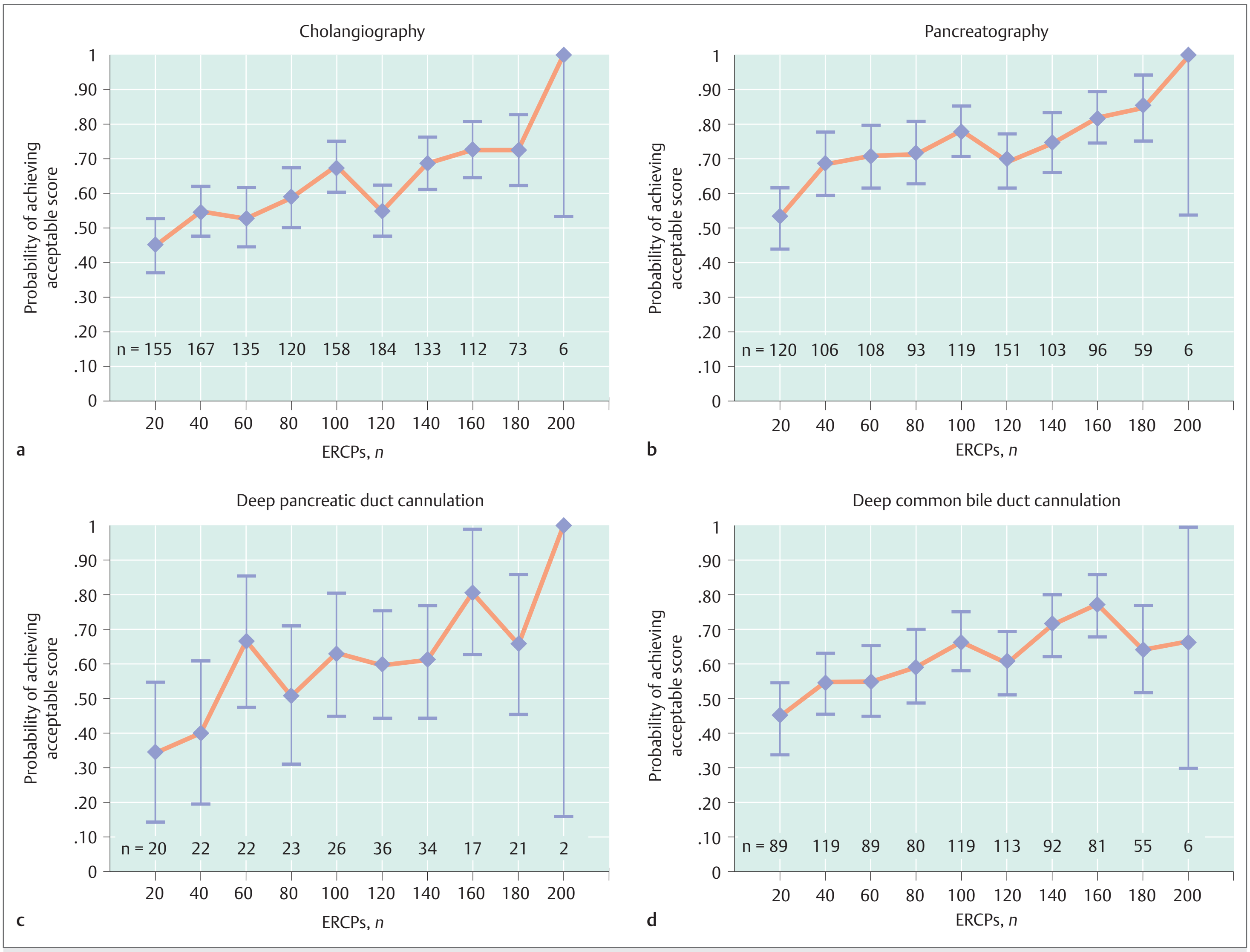

Fig. 1.4 The probability (with 95% confidence intervals) of achieving an acceptable score for cholangiography **(a)**, pancreatography **(b)**, deep pancreatic cannulation **(c)**, and deep biliary cannulation **(d)** during training of fellows in endoscopic retrograde cholangiopancreatography (ERCP), as reported by Jowell et al[19] for 17 gastroenterology fellows during 1,450 ERCP procedures.

endoscopist per year appear to be necessary to maintain adequate competence for biliary procedures and 250 ERCPs per endoscopist per year for complex therapeutic procedures in the pancreas.[20] The ERCP volume plays a role in complication rates. In various studies, a minimum of 40 to 50 endoscopic sphincterotomies (ESTs) per endoscopist per year was found to be associated with a lower complication rate in comparison to endoscopists with a lower EST frequency.[8,21] Rabenstein et al[22] showed that both prior experience and ongoing volume of ERCPs influence the success and complication rate.

Now that most ERCPs are performed for therapeutic purposes, it is a matter of controversy whether cannulation is the next technique for the trainee to learn after he or she is able to maneuver the duodenoscope competently to the papilla. For example, it is well known that for routine stent exchanges in the setting of a prior sphincterotomy, fewer procedures (*n* = 60) are needed to obtain competence than is the case with cannulation of a native papilla (*n* = 180–200), and it is also known that stent exchanges are associated with a lower risk profile compared to cannulation. Patients with benign biliary strictures, chronic obstructive pancreatitis, and recurrent bile duct stones in the setting of prior sphincterotomy are also associated with lower risk during training.

The ASGE published their latest core curriculum for training in ERCP in 2016.[8,23] Trainees who elect to perform ERCP should have completed at least 18 months of standard gastroenterology training, followed by at least 12 months of ERCP training.

Schutz and Abbott[24] developed an ERCP grading scale based on procedural difficulty using benchmarks such as cannulation rates to gauge competency. A modification of this score was adopted by the ASGE as part of their quality-assessment document. Absolute numbers of procedures partially performed by a fellow may not realistically reflect competence.[25] Where possible, trainee logbook records should specify particular skills completed by the fellow (cannulation, sphincterotomy, stent placement, tissue sampling), and should also indicate cases that the trainee completed without assistance. The ASGE guidelines state that most fellows require at least 180 ERCP cases before competency can be assessed, with at least half being therapeutic.[8] Although not all of the trainees may ultimately perform ERCP after the completion of their training, all fellows should at least develop an understanding of the diagnostic and therapeutic role of the procedure, including indications, contraindications, and possible complications.[26]

The decision by a program director as to whether to train one or more fellows each year to achieve sufficient competence will depend in some measure on the volume of ERCPs performed at the institution and the availability of experts in ERCP (▶Fig. 1.4).[19] For example, with an annual volume of 400 cases and three fellows, it would be reasonable to have one fellow perform 300 or more cases and provide the other two with an exposure to ERCP, rather than have all three individuals equally share cases, with a low likelihood that any of the three would reach competence by the end of the fellowship.

1.2.3 Complementary E-learning and Video Courses

Live endoscopy courses, interactive teaching programs, and video materials can help trainees to recognize pathology better and to understand the appropriate application of therapeutic techniques.[27] However, such passive activities cannot replace the performance of the actual procedures.

1.3 Incorporation of Simulators in Training

The Gastroenterology Core Curriculum, Third Edition in May 2007 states in section IV.A.6.(b): "Fellows must participate in training using simulation."[23] To date, no simulator experience alone has been validated as sufficient to replace actual patient experience. To guide adoption of simulators for specific roles in training and assessing skill, the ASGE initiated a PIVI (*Preservation and Incorporation of Valuable Endoscopic Innovations*) task force in 2011.[28] This group set the following two thresholds for justifying adoption of a particular simulator:

- *Threshold for incorporation into training*. For an endoscopy simulator to be integrated into the standard instruction for a procedure, it must demonstrate a 25% or greater reduction in the median number of clinical cases required for the trainees to achieve the minimal competence parameters for that procedure.
- *Threshold for assessing skill*. Simulator-based assessment tools must be procedure-specific and predictive of independently defined minimal competence parameters from real procedures with a kappa value of at least 0.70 for high-stakes assessment.[28]

The logistic and cost issues for a particular simulator would need to be weighed. For example, a high-cost computer simulator that had a 25% reduction in a learning curve might not make any sense for a program in which trainees typically had sufficient actual case experience to develop competency. In contrast, a lower cost simulator in which a program typically had insufficient cases would be well worth the investment.

1.4 Endoscopy Simulators and Training Models

1.4.1 Plastic Phantoms and Other Static Models

The initial experimental models for endoscopy training were made of plastic and textile tissues.[1] In 1974, Classen and Ruppin[29] in Erlangen presented an anatomically shaped plastic phantom that allowed examination of the upper GI tract. Christopher Williams and his group in London have been working on the first semi-rigid colonoscopy phantoms. A robust further development represents the Kyoto Kagaku Colonoscope Training Model, which presents greater technical difficulty to reach the cecum and allows a more realistic loop reduction ▶Fig. 1.6.[29] Grund and co-workers in Tübingen, Germany, developed a series of advanced static models for different training purposes.[32,33] They include artificial tissues for electrosurgical interventions and recently specific ERCP techniques. Unfortunately, those models are not commercially available so far and there are no published data validating their use in training.

In addition, a number of device manufacturers have produced their own models to facilitate training in the procedures in which their accessories are used. The Cook Medical ERCP Trainer recently developed by Costamagna et al[34] allows to practice cannulation and different ERCP techniques except sphincterotomy via a plastic papilla with varying ampullary anatomy, orientation, and cannulation difficulty.

Another promising simulator is the "T.E.S.T box simulator" (▶Fig. 1.5).[35] The model, designed by Christopher Thompson has demonstrated an ability to distinguish skills levels with significant

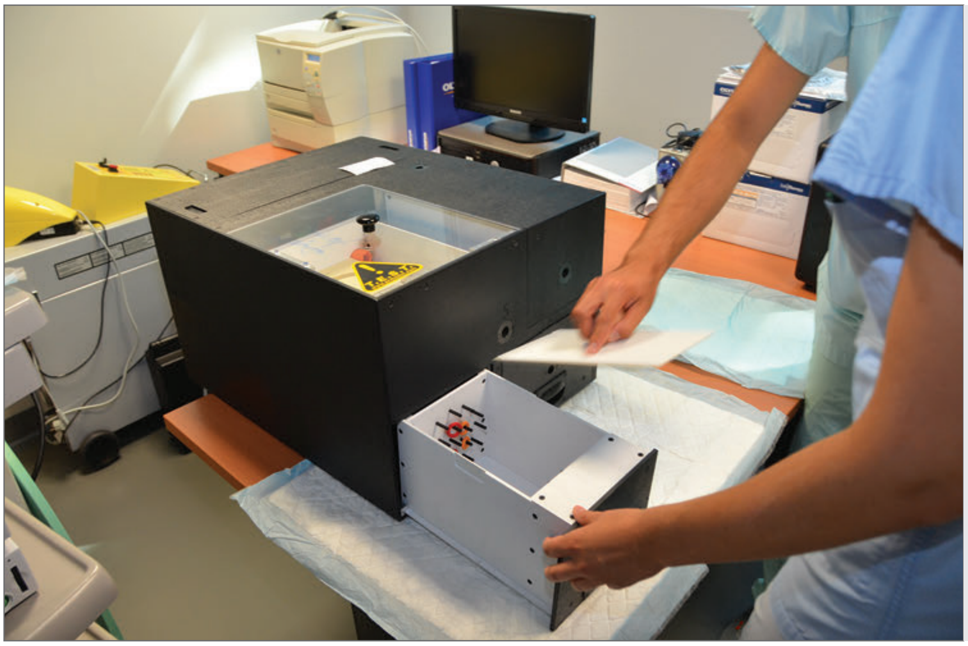

Fig. 1.5 The Thompson Endoscopic Part Task Simulator Training (T.E.S.T.) box containing five different training modules.[33]

differences between all categories from beginner to expert interventional endoscopist. One limitation of this and all static simulators to date is the limited exposure to pathology for training in image recognition and application of findings into management decisions.

1.4.2. Computer Simulators

Various computer simulation systems have been developed since the early 1980s.[1] Rapid progress in computer technology and electronics at the early 2000s allowed the development of commercially available systems. The first of these models was the Simbionix GI Mentor (3D Systems Healthcare, Littleton, CO, United States, formerly Simbionix Corporation), at the time in the shape of a human torso mannequin.[34] The system creates a relatively realistic virtual endoscopy environment and allowed the simulation of various diagnostic and interventional procedures at different levels. During training, teaching modules with anatomy and pathology (▶Fig. 1.7) atlases are at the trainee's disposition. Beginners can train their dexterity in a "GI Fundamental Skills" module including navigation, targeting, retroflection, loop reduction, or in "Cyberscopy," a module to further enhance hand–eye coordination. Different modules such as upper and lower GI endoscopy, sigmoidoscopy, EUS, ERCP, and hemostasis training are available. EUS and ERCP modules allow parallel viewing of radiographic and endoscopic simulations. Virtual sphincterotomy, stone extraction, and other techniques have been implemented. In addition to the current GI Mentor model (3D Systems Healthcare), the EndoVR virtual reality endoscopy simulator (CAE Healthcare, Montreal, Canada, formerly "Accutouch" by Immersion Medical, Inc., Gaithersburg, MD, United States) has been used in multiple studies (see later). Recently, another system the so-called "Endo X" has been presented (Medical-X BV, EM Rotterdam, the Netherlands (▶Fig. 1.8). The system provides mainly upper and lower GI techniques, but also includes analyzing tools such as insufflation performance simulation and video recording of the procedure. All devices allow user-specific training curricula and reflect the user-specific learning curve. Modules are supervised by a virtual tutor and the whole system can be connected to a real supervisor via internet for additional personal feedback and to view learning curves of different trainees by the supervisor (▶Fig. 1.9). Various studies have demonstrated the benefits of additional computer simulator training in connection with colonoscopy.[1,28]

In a prospective simulation study, four fellows at the Mayo Clinic received 6 hours of simulator-based training, compared with four fellows without training. The simulator-trained fellows outperformed the traditionally trained fellows during their initial 15 to 30 colonoscopies in all performance aspects except for insertion time ($p < 0.05$). Beyond 30 procedures, there were no differences in performance between the two groups (evidence level B).

Fig. 1.6 The Kyoto Kagaku colonoscopy training model with different possibilities to vary the difficulty of passage of the sigmoid (Level 1-6). (Images are provided courtesy of Kyoto Kagaku, Kyoto, Japan.)

Fig. 1.7 Hands-on training using the compactEASIE simulator. **(a)** Groups of three or four fellows per simulator and teacher receiving instructions. **(b)** Individual practice, for example, for basic gastroscopy.[1]

Fig. 1.8 The EASIE-R model designed by Kai Matthes and based on the compactEASIE simulator.[1]

Fig. 1.9 A computer simulation model for gastroscopy and colonoscopy skills (Image is provided courtesy of Medical-X BV, EM Rotterdam, the Netherlands).

In a randomized controlled multicenter trial of 45 first-year GI fellows in New York comparing 10 independent hours of work on the Simbionix GI Mentor II versus no simulator training, trainees who worked on the simulator had significantly better objective technical and cognitive performance on their first 20 to 80 real supervised colonoscopy examinations but no difference in the time required to achieve competency nor in subjective proctor assessment of patient discomfort. These studies suggest that virtual reality simulator training prior to real cases accelerates early training, but improvement in final competency has not yet been established. Nor has there been any computer-based skills test that has been correlated with competent performance on actual endoscopic procedures.

1.4.3 Training Courses with Live Animals

Animal models offer a realistic learning environment; however, a substantial organizational, technical, and financial effort is required. Ethical considerations, animal welfare, and problems of hygiene, along with the need for dedicated endoscopes for animal use and substantial staff and financial expenditure, are major restrictions. Currently, training courses on live animals are performed for many different techniques including endoscopic submucosal dissection and peroral endoscopic myotomy.[36,37]

1.4.4 Ex Vivo Porcine Tissue Models (EASIE, Erlanger Endo-Trainer, EASIE-R)

Clean pig stomachs with a dedicated mold have been used for training in diagnostic gastroscopy for many years.[1] As in the pulsatile organ perfusion simulator described by Szinicz et al,[40] a roller pump can be used to simulate spurting arterial bleeding in hollow GI viscera.

The “compactEASIE” device is a simplified version of the original biosimulation model and was developed in 1998 (▶Fig. 1.10**a-c**). For ERCP interventions such as sphincterotomy and stent placement the hepatobiliary system with the liver, extrahepatic bile ducts, and gallbladder is dissected and added to the upper GI tract. Bile duct stones can be simulated by inserting pieces of plastic stents into the bile duct. Matthes and Cohen have reported an interesting model called the “neopapilla.”[41]

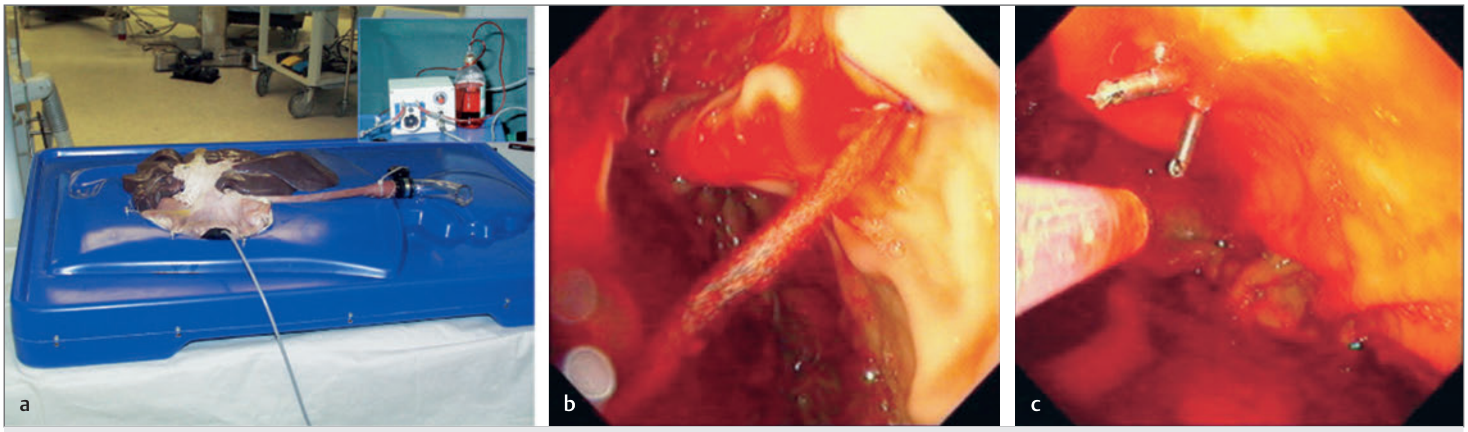

Fig. 1.10 **(a)** The compactEASIE model for hands-on training using specially prepared pig organs. **(b)** A roller pump drives artificial blood into vessels that have been sutured into a pig stomach, to provide training in hemostasis procedures in realistic conditions. **(c)** Practicing hemoclipping with the compactEASIE simulator.

Training in more than 30 interventional endoscopic techniques can be provided (▶Table 1.2). It is generally recommended to use special animal endoscopes for the training with isolated ("ex vivo") pig organs. Sedlack et al[42] compared computer simulator, harvested porcine organ, and live anesthetized pigs for ERCP training. The authors concluded the harvested porcine organ model to be the most realistic model for instruction in both basic and advanced ERCPs.

1.4.5 Training Courses

Ways of Integrating Educational Material, Demonstration, Practice, Feedback, and Evaluation into a Comprehensive Workshop

Regular training workshops on endoscopic hemostasis using the compactEASIE simulator have been available since 1997. EASIE team training comprises the simultaneous training of doctors and nurses in different interventional endoscopic techniques using this type of simulator and was first described in detail in 2001.[1]

Basic skills. To assess an individual's capacity for brain–hand coordination, a practical simulator test for manual skills was developed. For this hand–eye dexterity test performed before the training course, four 2- to 3-mm dots are created on the anterior wall of the ex vivo porcine simulator using a thermal device. The dots are arranged in the form of a square standing on one corner, with a diagonal length of 2 cm. Precision in the brain–hand coordination test can be evaluated by asking the trainee to touch each mark with the probe in a clockwise fashion. The time needed to complete the task is also measured. In this exercise, precision is weighted more heavily than speed.

Studies on training using ex vivo simulators (e.g., compactEASIE) for fellows and the EASIE team-training method

Since the introduction of the EASIE simulator, considerable efforts have been made to assess the value of additional simulator training using the EASIE model in endoscopic hemostasis. Several prospective trials have been conducted in recent years to provide objective evidence that participants benefit from simulator training. A prospective randomized study conducted in collaboration with the New York Society for Gastrointestinal Endoscopy (NSYGE) was undertaken.[6] The results provided the first evidence of benefit from simulator training in the treatment of upper GI bleeding. In this prospective training project, 37 gastroenterology fellows from nine hospitals in New York were first evaluated in five endoscopic techniques using the compactEASIE simulator. These included manual skills, ulcer hemostasis using injection, a coagulation probe and hemoclipping, as well as variceal band ligation. Twenty-eight fellows with comparable skills were then randomly assigned either to an intensive training group attending three 1-day simulator hands-on workshops over a period of 7 months or to a control group only receiving traditional clinical training in endoscopy in their home hospitals (▶Fig. 1.11). During the 7-month study period, it was demonstrated that the additional simulator training in four endoscopic hemostasis techniques significantly enhanced the participants' skills in comparison with the fellows who only received a clinical training. In particular, the evaluation of clinical cases following the training period showed a higher initial hemostasis rate and a lower complication rate among simulator-trained fellows, although the difference in the complication rate was not significant. These results were confirmed in a national training project conducted in France on training in endoscopic hemostasis that started 1 year later, with a similar study design.[43] The efficacy of the EASIE simulator was also confirmed in another project including novice endoscopists, in which remarkable levels of skill in hemostatic techniques were achieved using intensified simulator training every second week.[7]

Table 1.2 Selection of endoscopic interventions for which training can be carried out using the compactEASIE simulator

Training goal	Technique
Ulcer hemostasis	Injection techniques
	Thermal probes
	Clip application
	Over-the-scope-clip (OTSC)
	others
Variceal treatment	Multiple band ligation Cyanoacrylate glue injection
	Sclerotherapy
Tissue resection techniques	Snare polypectomy, loop application Saline-assisted polypectomy/endoscopic mucosal resection (EMR) including piecemeal EMR, capEMR, "band and snare" technique Endoscopic submucosal dissection (ESD) Full-thickness resection (FTRD) Rotablation of tissue
Tissue coagulation and cryoablation	Argon plasma coagulation (APC) Radiofrequency ablation (RFA) Cryoablation, etc.
Stricture management and stenting	Balloon dilation, bougienage Stenting: esophageal, gastro-duodenal, enteral, colonic
ERCP	Cannulation techniques, sphincterotomy and precut techniques, (Over) Guidewire exchange techniques (long and short wire/Rx) Stone extraction (balloon, basket), mechanical lithotripsy, Dilatation and bougienage Stents, plastic, self-expanding metal stents (SEMS) Complex stenting techniques (multiple, bi-hilar stents) Fine caliber cholangioscopy
Complication management	Bleeding, perforation closure

1.4.6 Incorporating Simulator Training into Educational Programs and Maintaining Skills in Complex Procedures

Simulator training in interventional endoscopy provides an effective opportunity for endoscopy trainees to gain considerable experience in ERCP techniques without time limitations and patient risk. In the New York study on EASIE simulator training in

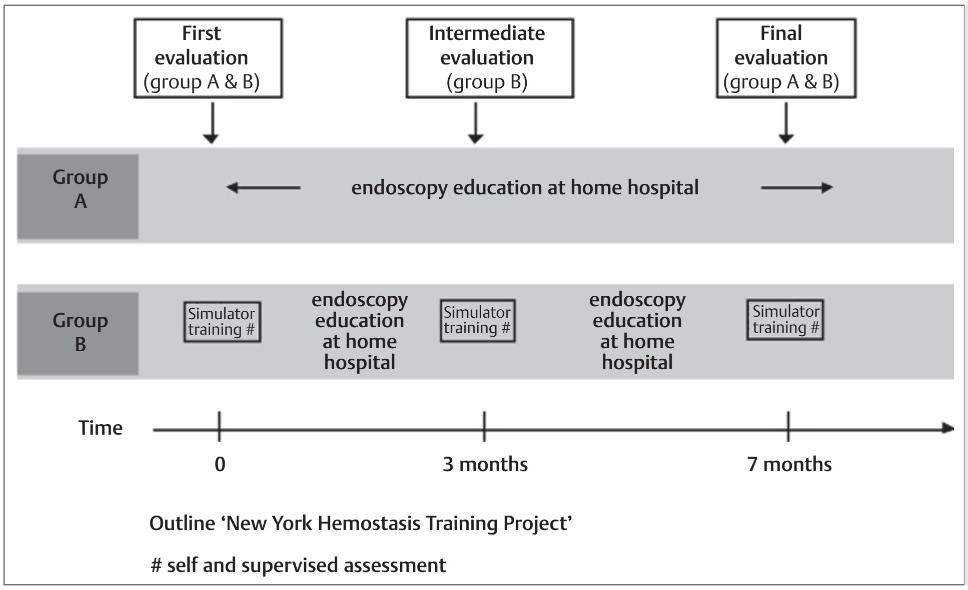

Fig. 1.11 Outline of a prospective and randomized study of training conducted in New York City, comparing conventional clinical education in endoscopic hemostasis provided for 14 gastroenterology fellows with 14 fellows who received additional hands-on training in simulators in three 1-day workshops. After a period of 7 months, the intensive training group had significantly improved in all disciplines, while the conventional clinical group had only improved in variceal band ligation. (Adapted from Hochberger et al 2005.[6])

hemostasis, the trainees achieved significant improvement in the performance of multiple skills on the simulator after only three workshops.[44] It appears that a structured educational program with access to simulator training, in addition to supervised real cases in the hospital plus DOPS evaluation, would increase the effectiveness of education in any interventional technique. The results of the real hemostasis cases performed in the New York study highlight this potential.[40] The analogous French training project confirmed that more complex techniques like clipping or injection/gold-probe application need repeat training courses to acquire and to maintain competence compared to easier techniques like band ligation.[39]

The role of simulators in training the proper application of new devices and new techniques is not really known. However, many manufacturers have already now made specific certified training and supervision of the first clinical cases obligatory for new suturing, closure, or resective devices.

There is little doubt that the knowledge and skills gained once may decline over time. Apart from sphincterotomy volume, little is known about deterioration of skill or outcome with infrequently practiced techniques. British experience with web-based e-portfolio of trainees and independent endoscopists highlights that central monitoring of practice may play a role in the future.

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2 The Value of Clinical Research

Michael B. Wallace and Peter D. Siersema

2.1 Introduction

In this review, we will cover major topics relevant to the performance and communication of clinical research, including key issues such as the value to clinical care, keys to conducting research, and how to build teams of successful researchers within institutions and between institutions. We will provide a basic overview on how to design clinical trials, generate research ideas, write grants, and conduct day-to-day clinical research. We will provide valuable information on how to present at national and international meetings and write and publish manuscripts. Finally, we will cover issues such as ethics and the future of scientific publications.

Clinical research provides value through guiding physicians and other caregivers on how to choose the optimal method of diagnosing and treating diseases. It is fundamentally different from basic research, which focuses on mechanisms of diseases as well as normal and abnormal biological processes. Clinical research particularly focuses on the patient. In our daily practice, we struggle through decisions in virtually all patients including, which diagnostic tests to perform, what the optimal treatments are, and how to deal with the costs and adverse effects of our diagnostic and treatment approaches. It is widely acknowledged that there are major gaps in our knowledge. High-value clinical research should include several key elements including:

- Selecting clinically relevant interventions for comparison to current standards of care.
- Inclusion of relevant and diverse populations.
- Collection of health-related outcomes important to patients, physicians, and payers.

All clinical trials should be performed in a rigorous scientific manner that adheres to several key principles to provide accurate and reliable information.[1] Studies performed in a highly selected group of patients, who are fundamentally different from the patient we are currently caring for, do not provide reliable guidance. The value of clinical trials is only as great as the extent to which those results are communicated and made available to patients, colleagues, and providers. The process of scientific publication has long been the mechanism by which we communicate these results, although many other options are increasingly available; such as communication at scientific conferences, internet, and social-media based methods of data sharing.

2.2 Keys to Success

Clinical research is both tremendously rewarding and challenging. Over many years of conducting research we have defined four key elements to success:

- A tough skin.
- A team approach.
- Attention to detail and a questioning approach.
- Having long-term as well as short-term goals.

2.2.1 A Tough Skin

Even the most successful clinical investigators face many hurdles while conducting and publishing clinical research. Most competitive medical journals have acceptance rates of well under 20%. Large federal grants are even more competitive with funding rates now less than 10%. Thus, even excellent research proposals and papers may be rejected for funding and publication. To ultimately succeed, clinical investigators must be willing to accept the short-term failures and persist in conducting and publishing the research they believe in.

2.2.2 Building Teams

Building teams enables each member of the team to bring unique talents and ideas to a research project. Many of the best research projects occur at the boundary zones between different areas of expertise. A specific example of this is our research on the role of endoscopic ultrasound in lung cancer.[2,3] Both the field of endoscopic ultrasound and the field of lung cancer were represented by very different groups of physicians; however, working together identified unique contributions of each team. Beyond physicians, a successful team should include senior mentors, junior investigators, statisticians, experts in clinical trial design, study coordinators, and editorial assistants.

Fellows play one of the most important roles in the team. For the fellow, the goals are to perform the research and to learn the process. The only way to do this, is to practice. Most academic medical centers include research activities as a part of their core curriculum. In addition to clinical fellows, who spend part of their time doing research, many programs offer dedicated research fellowships in clinical investigation. These programs often include dedicated training in research methodologies and advanced degrees such as a Master or Doctoral degree. Such didactic training has been shown to increase the likelihood of long-term research success.[4]

Research collaboration, both within an area of interest and across disciplines, fosters long-term academic productivity. In addition, collaboration with colleague researchers in other centers, both on a national and international level, often increases the clinical value of observations. Developing a long-term plan to integrate with other colleagues is critical. Key elements of this include shared authorship and shared responsibilities, both of which are best outlined at the beginning of a study. A challenging issue for many large groups is authorship on manuscripts. Overall, it is best to acknowledge the contributions of each member either throughout authorship, if they meet guidelines, or through acknowledgment. It is important to recognize that it is not necessary to include a division chair on every manuscript. The International Committee of Medical Journal Editors (ICMJE) provides widely accepted definitions of authorship.[5]

Study coordinators do the majority of the day-to-day work of clinical trials. Clinical coordinator should be chosen based on the skills necessary for each trial. In some cases, a nurse is required when important clinical decisions need to be made. In other circumstances, data coordinators can collect clinical trial information in a reliable and efficient manner. Coordinators should be respected members of the team who are included in research planning discussions and acknowledged in manuscripts.

Statisticians play a key role in the design and analysis of studies. A common mistake is to involve statisticians only at the end of the study when analysis is needed. A much more effective strategy is to involve statisticians at the planning stages. In this way, variables can be carefully defined and chosen in a way that will optimize data analysis. Statisticians can also significantly improve the overall study design. For example, simple changes in study design can substantially alter the sample size needed.[6]

Finally, partnering with editorial assistants may be highly valuable for some investigators. The skill of writing manuscripts is very different than the skill of conducting research. Many large academic centers have medical editors who can facilitate how we communicate our scientific discovery with the broader community.

2.3 Designing Clinical Trials

The field of endoscopy has matured substantially over the past 20 to 30 years. From one where simply describing our observations and experience was enough to be published, to now where competitive journals typically only publish well-designed controlled clinical trials and cohort studies. In order to be published, such high-quality clinical studies should be carefully designed to achieve our primary goal of seeking scientific truth. Designing clinical trials follows a general pattern from generating ideas, to study design, to grant writing, and finally completion of the study. Each of these is discussed further.

2.3.1 Generating Ideas

Generating ideas should be the easiest of all research activities. All those involved in patient care know that many decisions we make, for both diagnosis and treatment, have only a limited amount of scientific evidence. Thus, in almost every patient encounter, we can identify opportunities for research.

2.3.2 Refining Ideas

Many studies can take months or even years to complete, so the long list of possible research topics needs to be refined based on several key factors:

- Is the topic of high interest to the investigator?
- Are the resources to study the question available to the investigator, including adequate numbers of patients, access to large databases, collaborators with sufficient expertise, and funding sources?

Research questions should be further defined based on a very detailed review of the current literature. Ultimately, research is aimed at extending the envelope of knowledge beyond what is currently known. Many resources are available (PubMed, Google Scholar, Medline, etc.) to identify current knowledge and its gaps including review of published research and consultation with other experts. Almost all published studies end with a statement such as "further research is necessary to confirm/clarify…." These statements offer excellent clues on how to further refine a specific research question. Moreover, some outcomes need to be confirmed or even excluded because they seem clinically not rational.

2.3.3 Clinical Trial Design

Clinical trial design balances precision and accuracy of a particular research question with available resources. Theoretical and practical issues must be taken into consideration. For treatment trials, the definitive randomized control trial is often not feasible, cost-effective, or even ethical.

Studies of new diagnostic technologies, which are particularly common in the field of endoscopy, often begin with a pilot study assessing the general safety and efficacy of a new device such as a new endoscopic imaging technology. This should initially be compared to historical controls. If promising, further studies should then be performed comparing the new method to the current standard in a controlled cohort or randomized study. Many diagnostic trials follow a crossover design where each patient undergoes both procedures, either back-to-back or in a sequential crossover design. Such methods may reduce by 10- to 20-fold the number of patients needed compared with a simple randomized design since each patient serves as his/her own control, thus minimizing variability.[6] Nonetheless, particularly back-to-back studies are prone to bias if not well conducted, for example, when the same investigator performs both procedures in the same subject.

Treatment studies also began typically as an initial safety study. Ideally, these should be compared to historical controls and, if the data are promising, lead to prospective randomized controlled trials. The classic randomized controlled trial is well-suited in this area and can be done efficiently, particularly when there are significant improvements with a new technology compared to existing technology. Such studies have led to major landmark publications and have set new standards of care for endoscopy.[7]

Trials of causation and association, such as the link between *Helicobacter pylori* and gastric ulcers and gastric lymphoma,[8] often cannot be addressed through prospective clinical trials. In these cases, large cohort or case–control studies may be better suited. Cohort studies are valuable for common conditions such as the association between nonsteroidal anti-inflammatory drug use and peptic ulcer disease. However, for more rare conditions, case–control study design is more efficient. This includes studies such as the association between gastroesophageal reflux disease and esophageal adenocarcinoma.[9]

2.3.4 Grant Writing

The skill of grant writing is similar to the skill of publishing clinical trials. A well-written grant must convince the funding agency that:

- the question is important.
- your methods are well-suited.
- the question and approach is novel.
- your team is the best one to answer the question.

Most successful research teams build on a long arc of successful investigation in the specific area. Because of their established record, they can achieve each of the elements mentioned above and continue to push the frontier of knowledge forward. Having said this, it also means that the initial steps on the research path are often not easy!

2.3.5 Conducting Clinical Trials

Once the study is designed and funded, the day-to-day work of completing the study is often assigned to study coordinators, with oversight from the principal investigator. If the idea was well formed and refined, the trial carefully designed, and the team of collaborators well chosen, clinical trial conduct usually proceeds without difficulties. However, even in these circumstances, regular meetings to review enrollment and identify any problems with study data collection are very important. In some studies, where the outcomes are highly uncertain, a planned interim analysis should be considered to allow for appropriate adjustment.

2.3.6 Presentation and National Meetings

Once the study is complete, or during a planned interim analysis, the communication of study results is often done in a multifactorial way including presentation at national meetings. This is often the first opportunity to communicate important results to colleagues and to receive feedback. By their nature, presentations at national meetings are very short relative to the full publication. Most large meetings include options for either oral or poster presentation. Oral presentation typically involves a slide review of the study aims and hypothesis, and a short review of the background, followed by methods, results, and conclusions. This must be communicated in a short period of time, typically 8 to 12 minutes. The message should be kept relatively simple with two to three main points that are communicated. Fewer slides that are carefully worded and presented communicate much more than very densely written slides and rapid speech. The presenter should always be highly respectful of his or her time allocation and allow for a question and answer session.

2.3.7 Manuscript Writing

Many investigators fall short at the final stage of the scientific process. The classical writers' block has prevented many excellent studies from being fully published. Each investigator has his or her own style of writing and overcoming writers' block. One of the most valuable methods is to remind ourselves that the manuscript does not have to be perfect on the first draft. It is often easier to *edit* a manuscript than to *write* a manuscript. For this reason, simply getting the ideas down on paper can overcome the most challenging obstruction. With current voice recognition technology, this can be done simply by dictating a manuscript. Begin by assembling all the key elements of the study, such as tables, figures, and the previous grant submission. Large aspects of the manuscript may have been previously written, such as the background section of the grant, which should change little other than a timely update of the most recent literature. The methods section should largely be identical to the methods written in the original grant application. The results also should largely reflect the key data elements including figures and tables. The discussion is perhaps the most difficult to write. A discussion section should generally follow a general sequence as outlined in the following:

- Summarize your key findings.
- Discuss how your findings compared to literature that supports the results.
- Discuss how your findings extend knowledge compared to other studies.
- Discuss how your findings may conflict with other published results and explain why these differences exist.
- Discuss the strengths and limitations of your study.
- Discuss the implications and conclusions of your study.
- Discuss what future research should be done.

2.4 Ethics

Scientific exploration, particularly studies that involve commercial devices, has potential for conflicts of interest. Scientific misconduct occurs when we lose sight of our primary goal, to discover new knowledge, and instead focus on personal gains. We have recently published a summary of the key ethical issues in scientific publication and how to prevent them.[10,11] Common ethical problems include the following.

2.4.1 Conflict of Interest

Conflicts of interest should be clearly declared and should err on the side of overdisclosure even if the author feels there may not be a direct conflict of interest. It is better to allow the reader to decide if the conflict of interest is present and how it might influence the scientific study. Examples include consulting fees or equity interest in a commercial product or company related to the study.

2.4.2 Registration of Clinical Trials and Underreporting of Negative Trials

The ICMJE guidelines, to which many journals adhere, require clinical trials to be registered at the outset of the study.[12] According to the ICMJE, a clinical trial is defined as "any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes."[12] Some studies, such as a retrospective chart review, do not require registration. All studies that meet this definition should be listed on one of the many acceptable registration sites such as:

- www.anzctr.org.au
- www.clinicaltrials.gov
- www.ISRCTN.org
- www.umin.ac.jp/ctr/index/htm
- www.trialregister.nl
- https://eudract.ema.europa.eu/

2.4.3 Falsification of Data

Although this is the most dangerous of all ethical issues, it is often very difficult to detect. Most issues of data falsification come to light through collaborators who have questions about the authenticity of data and raise these concerns to either institutional leadership or journal editors.

2.4.4 Plagiarism

The ability to copy and paste text material and the broadly available content throughout the World Wide Web have made plagiarism an increasingly common practice. On the other hand, software tools to search text within any manuscript and compare it to other published work have made it very easy to detect plagiarism.[10,11]

A more challenging issue is the reuse of text by the same author, so called "text recycling." Authors must remember that the copyright of published manuscript belongs to the journal and cannot be reused verbatim. Direct reuse should be quoted and referenced with permission from the original source or preferably rewritten in new words.

2.5 Manuscript Submission and Review Process

Most medical journals follow a standard process for submission and review, although new online open access journals are changing this process. For most journals, the approach is to submit a manuscript, typically through a website. The journal's managing editors and chief editor typically screen manuscripts to identify those that should be sent for full peer review. Many competitive journals may not send some manuscripts out for review.

Once an article clears the initial screening, it is typically sent for review to two or more independent experts in a field. They provide a critical review of the manuscript and often make a recommendation regarding whether manuscripts should be published and what improvements should be made. The decision on whether manuscripts should be published is ultimately made by the editorial team and chief editor. Most journals prioritize studies that are novel, well designed, well written, and appropriate for the audience of the journal. For this reason, the authors should carefully select the most appropriate journal. It is a common mistake to choose a journal simply based on the reported impact factors. Ultimately, the goal of publishing manuscripts is to communicate the new knowledge with the audience that is most likely to benefit, as opposed to the most widely read or cited journals.

2.5.1 Expanding the Reach

Many journals now expand their reach beyond just the print publication including online publication and even online-only publication. Professional and public social media sites, such as such as Facebook, Twitter, WeChat, ResearchGate, Doximity, and LinkedIn, allow peer-to-peer and journal-to-peer sharing of articles and online discussion and will likely continue and gain more popularity.

2.5.2 The Future of Scientific Publications

Publication through printed journals, which are distributed to individuals and libraries in monthly issues, has been the preferred method of scientific publication for more than a century. Scientific publication is rapidly evolving and includes open access journals, with or without peer review. While some well-respected open access journals (e.g., F1000, PLoS) publish high-quality scientific articles,[13,14] others are fraught with opportunities to publish poorly designed or even plagiarized material.

The mechanism of editorial review is changing toward a more open and peer-to-peer communication. While anyone can post their scientific discovery online, the role of journals and editors will continue to be valuable. For many busy scientists and physicians, it will remain valuable to have an expert editor identify the most important new studies relevant to their needs among rapid explosion of studies being performed and published. The journal itself will likely evolve into a refined portal of information linking each study with the physicians and scientist who can most apply that new knowledge. Despite these very rapid and uncertain changes, there is no doubt that clinical research and the communication will be valuable to physicians, scientists, and patients alike, with the role of editors to ensure that knowledge is effectively and accurately conveyed.

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