Colorectal Cancer Screening

Quality and Benchmarks

Aasma Shaukat
John I. Allen
Editors

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ISBN 978-1-4939-2332-8 ISBN 978-1-4939-2333-5 (eBook)
DOI 10.1007/978-1-4939-2333-5

Library of Congress Control Number: 2014956665

Springer New York Heidelberg Dordrecht London

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

Dr. Shaukat: I would like to thank my husband Dan for his love and endless support, and my children Myra and Rayaan for their patience
Dr. Allen: I would like to thank my wife Carolyn, and my children Jennifer and Joshua

Foreword

Colorectal cancer (CRC) screening originated from the work of Dukes at St. Marks Hospital in London in the 1930s who developed a staging system for CRC and observed that survival correlated with early stage diagnosis and treatment. He and Lockhart-Mummery, unbeknownst to them at the time, also provided the basis for today's CRC screening goals of detecting both curable CRC and preexisting adenomas by demonstrating the link between the two. These concepts were challenged for decades until FOBT randomized trials showed that CRC screening reduced CRC mortality, the colonoscope was introduced into clinical practice, colonoscopic polypectomy was shown to be feasible, and CRC incidence was observed to be reduced by colonoscopic polypectomy.

This amazing series of developments, beginning in the 1970s, culminated in 2012 with the report of a reduced CRC mortality following colonoscopic polypectomy, which proved the concept of the polyp-cancer sequence and the effectiveness of screening for both CRC and adenomas. This resulted in the explosion of CRC screening worldwide which we are seeing today. In the USA, CRC screening is now being performed by about two thirds of the at-risk men and women, according to a recent CDC report. Most (90%) of those screened in the USA have been with colonoscopy, while the majority of those screened elsewhere have been primarily with FIT, and to a much lesser extent with flexible sigmoidoscopy. All roads lead to colonoscopy, whether as a screening test or for diagnosis in those with a positive first step screening test.

If screening is to be successful, it needs to be part of a multistep "package," which includes screening, timely diagnosis (pathology of polyps, cancer), timely treatment (cancer surgery, polypectomy) and follow-up surveillance. If one step in the process fails, the impact will be lessened or lost. At each step, quality in the performance is a critical factor. For screening colonoscopy, quality benchmarks correlate directly with the frequency of interval cancers. The good news is that interval cancers following average risk screening colonoscopy occurs at a rate of about 1/1000 exams. The bad news is that 5% of the cancers are missed. The interval cancer rate is even greater in the high risk post-polypectomy patients (1/200), and is related most often (70%) to missed lesions and incomplete polypectomy. Clearly, quality performance is required. When the "simple" FOBT card was introduced in

the 1970s, there was no quality control. A quality control window was added later but interpretation was often inaccurate. Quality performance is also critical for FIT since a false positive triggers off an unnecessary colonoscopy, and a false negative has other consequences. Newer tests such as CTC and stool DNA testing have their own unique quality performance considerations.

With the field of CRC screening moving dramatically from its early rudimentary stage to the present widespread high technology stage, we need to be certain that maximum effectiveness is achieved by high quality performance at each step. In this book an experienced and thoughtful group of leaders in CRC screening have identified the key issues in quality performance. The authors have cast a wide net in this area, with comprehensive presentations for every screening modality. In addition, issues related to surveillance, sedation, pathology, medical-legal aspects, and cost-effectiveness have been addressed. Concrete examples of various programs and initiatives provide excellent "nuts and bolts" tools for guidance in this increasingly complex field.

It has become clear that we need to step back and take stock of how we are to move forward in CRC screening. The latest data indicates that there has been a progressively downward trend in CRC incidence and mortality in recent decades. The annual "Report to the Nation" demonstrated that a major factor in this trend is screening. In the USA it is "opportunistic" rather than within the framework of a nationally organized program, which makes quality performance programs more compelling. The US screening rate is the highest in the world and the incidence/mortality reduction is also the highest worldwide. A campaign has been initiated nationally by the ACS and CDC to further increase the US screening rate to 80% by 2018 and to help eliminate the current racial disparities. This accelerated screening needs to be accompanied by quality performance in order to achieve maximum effectiveness. Each man and woman who accepts screening should be offered a test of the highest quality that provides the greatest probability to have CRC diagnosed at an early stage, or even to have CRC prevented altogether. Everyone who has been touched by cancer in a loved one understands the human tragedy that can be averted. We need to screen. Any test is better than none, and the best test is the one that gets done, and done well! This book tells us how to do it and what gaps there are to be filled in the future. It is a state-of-the-art treatise on quality performance of the entire range of screening and surveillance and their related issues. It is a must read for everyone engaged in this effort.

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Preface

Colorectal cancer (CRC) is the third most common cancer in men and women, and the second leading cause of cancer-related death in the USA. Screening is highly effective in reducing the risk of developing and dying from CRC. There is a menu of screening options that includes tests that detect cancers (stool-based tests, imaging) and tests that detect both cancers and precancerous lesions with the option of concurrent removal and thus cancer prevention (colonoscopy). Regardless of modality, the most effective screening program is one that is high quality, safe, cost-effective, readily accessible, highly acceptable, and actually performed. Establishing quality metrics and benchmarks for all types of CRC screening and surveillance tests is important for delivering high value care.

This textbook will provide a comprehensive overview of quality metrics and methods used to improve quality for all major modalities of CRC screening. It will introduce the readers to the evidence of effectiveness behind various CRC screening modalities: stool-based tests (Fecal Occult Blood, Fecal Immunochemical and Fecal DNA tests), flexible sigmoidoscopy, colonoscopy, and CT colonography. It will review the latest guidelines for CRC screening, compare differences among the five major national guidelines and highlight the need for valid quality and cost indicators. The main focus will be colonoscopy since most quality indicators and analyses have focused on this modality of screening and surveillance, but one chapter will be devoted to quality indicators of other screening modalities. Differences between process and outcome measures will be highlighted and a small but valid set of recommended national measures will be listed.

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Dr. Shaukat is a gastroenterologist and a clinical researcher. She received her medical degree at The Aga Khan University Medical College in Pakistan. She then matriculated to Johns Hopkins School of Public Health where she received an M.P.H. in International Health and Epidemiology. She conducted a gastroenterology fellowship at Emory University School of Medicine. She is currently Associate Professor in the Department of Medicine, Division of Gastroenterology at the University of Minnesota and Section Chief of Gastroenterology at the Minneapolis Veterans Affairs Healthcare system.

Dr. Shaukat has numerous publications on epidemiology, molecular markers and outcomes of colorectal cancer, quality of colonoscopy and colon cancer screening. She is an invited speaker at national and international scientific meetings on quality of colonoscopy and benefits of colon cancer screening. Dr. Shaukat has an active research program through federal funding, and continues to study colon cancer screening and prevention.

Dr. Allen grew up in New Jersey, upstate New York and Albuquerque, New Mexico. He graduated from Rice University in 1973 and the University Of New Mexico School Of Medicine 1977. He completed internship, residency in Internal Medicine and Gastroenterology Specialty training at the University of Minnesota (Minneapolis). He then spent 10 years on the Academic Faculty in the Department of Medicine in Minnesota attaining the rank of Associate Professor of Medicine while conducting clinical and laboratory research in the fields of alcoholic hepatitis and colon cancer. In 1991 he was recruited to be Associate Director of the Virginia Piper Cancer Center at Abbott Northwestern Hospital (Minneapolis) and joined a private gastroenterology practice. From 1991–2013 Dr. Allen helped build this single specialty GI practice into Minnesota Gastroenterology, one of the largest GI practices in the country and helped develop their nationally known Quality Improvement program. He also worked closely with leadership in Allina Health, a large Integrated Delivery System in the Twin Cities. He currently Chairs the Quality Committee of Allina Health and is on their Board of Directors. In April 2013, he left community practice to become Clinical Chief of Digestive Diseases and Professor of Medicine at Yale University School of Medicine.

For the last decade, Dr. Allen has worked in a leadership position with the American Gastroenterological Association (AGA). He was selected to Chair the Clinical Practice and Quality Management Committee of the AGA and led development of clinical quality measures for gastroenterology. He has written extensively on quality improvement in GI and has chaired or co-chaired Task Forces that created many of the GI measures currently in Medicare's Physician Quality Reporting System. He has published and spoken widely about the impact of health care reform on the specialty of gastroenterology and continues to publish about evaluation and management of inherited colon cancer syndromes. In 2014 he became President of the AGA Institute.

Chapter 1
History and Overview of the National Quality Strategy

John I. Allen

Introduction

In March 2011, the Agency for Health Care Research and Quality (AHRQ) published a report detailing a "National Quality Strategy" (NQS) for US health care, as mandated by the Patient Protection and Affordable Care Act (ACA). NQS provides an official blueprint for achieving a high-value health-care system. This blueprint has profound implications for all medical providers and health-care systems in this country and physicians need to understand the basic elements of the strategy and their role in the evolving world of health-care delivery. This chapter provides a background on the history of quality improvement (QI) efforts in medicine, the development of the NQS, and elements that impact the practice of gastroenterology, especially colonoscopy and colorectal cancer (CRC) prevention.

Some of the best medical care in the world is available in USA, yet there is a growing body of evidence that our commitment to deliver coordinated, effective health care to all citizens is below the standards of many other developed countries. The USA spends more per capita than all other countries, yet we lack universal health care and we lag behind other developed countries in terms of life expectancy and many major health outcome measures [1]. Our "healthy life expectancy" (a measure of overall population health accounting for both length of life and levels of ill health) places us 26th among developed countries, a testament to our lack of a national coordinated system of disease and preventive care [1].

To enhance national discussions about coordinating USA's health-care delivery, the Commonwealth Fund established a Commission on High Performance Health Systems in 2005. The commission [2–4], composed of 16 nationally recognized health-care leaders, issued a series of reports beginning in 2006 that defined a

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A. Shaukat, J. I. Allen (eds.), *Colorectal Cancer Screening,*
DOI 10.1007/978-1-4939-2333-5_1

framework for a high-performing health-care system, a series of organizing principles and finally a "roadmap" for reforming health insurance to achieve universal medical coverage.

In their initial report, the commissioners provided background on how we misallocate resources, fail to provide universal medical care, and fall short of delivering maximum value (defined as health outcomes per unit cost). The overarching recommendations from this report include (1) a commitment to a defined national strategy for achieving highest value, (2) a process to implement and refine that strategy, (3) proposals for care delivery through systems that emphasize clinical coordination, and (4) a movement to value-based reimbursement based on metrics that reflect health outcomes, quality of care, access to care, population-based disparities, and efficiency [2–4].

These reports, among many others, provided a foundation for discussions about restructuring health-care delivery in the USA and accelerated the commitment toward a "National Quality Strategy" that was ultimately codified within the ACA signed into law by President Barack Obama in March 2010. With passage of the ACA, the demand for providers and health systems to produce performance and health outcomes measures that are understandable to the lay public, readily available and tied to reimbursement has finally been woven into the core fabric of US medicine.

History of QI in Medicine

A brief history of the QI movement within US medicine is instructive and will help the reader understand current initiatives contained within the ACA, especially the NQS and the "value-based modifier" (VBM) that will form the basis of reimbursement by the Centers for Medicare and Medicaid (CMS), State Medicaid agencies, and many commercial health plans. While innumerable individual initiatives have provided a basis for this QI movement, five key events are highlighted in this chapter.

Ernest Amory Codman

Ernest Codman (1869–1940) was a surgeon at the Massachusetts General Hospital (MGH), a prolific author and the first vocal advocate of the "End Result" system of measuring the quality of medical care (in 1910). His colleagues described him as "maniacally obsessed" with the simple idea that every hospital should follow every patient long enough to determine whether or not their treatment was successful and if not why not [5]. He became so disliked because of his insistence on end result analysis that he resigned from MGH and opened the Codman Hospital (literally down the street). He also advocated analysis of treatment effectiveness (clinical effectiveness analysis or CEA) and recommended tying a surgeon's pay

to outcomes (the original VBM). He even developed the first surgical outcomes registry focused on osteosarcomas based on standardized definitions of disease and containing long-term data on entered cases. His concepts concerning registries helped launch similar efforts in Europe but even today, the concept of registries linking treatment to outcomes remains relatively rare in the USA compared to other developed countries.

Avedis Donabedian

Unlike Codmen, Avedis Donabedian (1919–2000) found a more receptive audience for proposals concerning health outcomes research in the 1960s. An extensive review of his original works was published in the Milbank Quarterly in 2005 [6]. He is credited with founding studies of quality in health-care and medical outcomes research based on the "Donabedian Model" of care. This model described three boxes containing (a) structure, (b) process, and (c) outcome measures and linked by a unidirectional arrow. Health-care systems of any size use this conceptual framework to modify structures and processes to enhance health outcomes. During the 1970s, the Donabedian Model became one of the intellectual cornerstones leading to the rise of evidence-based medicine (EBM) and development of clinical guidelines and care algorithms so prevalent in today's health-care world.

Institute of Medicine

The committee on quality of health care, commissioned by the Institute of Medicine, released seminal reports in 2000, 2001, and 2007 in which they described the importance of medical errors, the dysfunctional health-care system in the USA, and a plan of a "learning health-care system" going forward [7–9]. These reports documented the cost and patient impact of medical errors, elevated the concept of patient safety to national attention, illustrated how our dysfunctional delivery systems add to this toll, and more recently provided a description of a high-value (learning) health-care delivery system. Each of these reports became important in shaping national health-care policy, re-emphasizing the original concepts of Ernest Codman of accountability, performance metrics, and outcomes measurement.

Donald Berwick and the IHI

In the late 1980s, Donald Berwick MD and a group of visionary leaders founded the Institute for Healthcare Improvement (IHI) to promote a systematic, scientifically rigorous approach improving outcomes in medical care. Their most important contribution may be defining the "Triple Aim" of medicine: enhancing patient experi-

ence, increasing the health of a population, and reducing medical costs [10]. IHI has become an influential force in developing health policy and a source of education about process improvement for the USA and many other countries.

CMS Programs and the ACA

CMS has long sought to alter current fee for service (FFS) reimbursement to one based on health outcomes. To that end, CMS created the Physician Quality Reporting System (PQRS: originally called the Physician Quality Reporting Initiative or PQRI) in 2007. PQRS now consists of more than 200 performance measures, mostly of recommended clinical processes, prevention, and care coordination [11]. PQRS is described in more detail later in this chapter and it is tied to the VBM. In the 6 years of existence, less than 30% of eligible providers have participated in PQRS despite reimbursement incentives and various methods of data entry (web interfaces, registries, and administrative claims). As detailed below, CMS can adopt specific measures on a time-limited basis but will sunset measures that do not go through the rigorous definition and vetting process set up by the National Quality Forum (NQF).

Finally, with passage of the ACA, the NQS was mandated by legislation and subsequently codified. It is based on a rich history of QI work as summarized above and has set the nation on a path of public transparency (both quality and cost) and provider accountability. With reimbursement tied to outcomes through both the VBM (direct CMS reimbursement to individual providers) and creation of accountable care organizations (ACO) described below, the need for providers to focus on measurement of their performance has been cemented into our everyday practice of medicine.

National Quality Strategy

The NQS (officially known as the "National Strategy for Quality Improvement in Health Care") is intended to align priorities and efforts of both government and private sector stakeholders to enhance the value of care provided in the USA [12]. NQS was initially published in March 2011 as a result of a legislative mandate included in the ACA and is overseen by the secretary of US Department of Health and Human Services (HHS). It was the culmination of many years of collective work by multiple stakeholders including the NQF, which the HHS enlisted to recommend goals and key measures for each of the six NQS domains. NQF is an independent nonprofit organization that calls for, refines, and endorses standards and measures of health-care quality through a sophisticated consensus approach based on scrutiny of consumers of health care, payers, purchasers, and content experts. Further discussion about the NQF can be found below.

The six domains (priorities) of the NQS include the following:

1. Safer care by reducing harm caused in the delivery of care
2. Engaging patients and family in care decisions
3. Promoting effective communication and coordination of care
4. Promoting effective prevention and treatment practices for leading causes of morbidity and mortality
5. Working with communities to promote healthy living
6. Making care affordable

The NQS's three overarching aims are essentially the "Triple Aim" described above: (a) better individual care, (b) healthier populations, and (c) affordability. A key objective of the strategy is to build a national consensus on how to measure quality so that alignment can occur throughout the health-care industry. To that end, HHS works with CMS reporting initiatives to be sure that data collection is simple, the number of measures is parsimonious, and programs such as PQRS and meaningful use (that defines electronic medical record or EMR standards) can crosswalk. More information about the evolving NQS is available at the www.ahrq.gov/workingforquality website [13].

NQF Contributions to the NQS: National Priorities Partnership and Measures Application Partnership

While the secretary of HHS oversees the NQS, it is shaped, owned, and implemented through the National Priorities Partnership (NPP), an organization with 52 partners from all aspects of the health-care industry. NPP is co-chaired by Bernard Rosof of the Physician Consortium for Performance Improvement (PCPI—a physician-led organization that helps develop performance measures and was convened by the American Medical Association) and Susan Frampton, president of Planetree (a company based in Derby Connecticut, founded in 1978 and organized to study patient needs in health care). Membership can be obtained at http://www.qualityforum.org/Setting_Priorities/NPP/NPP_Partner_Organizations.aspx. NPP provides annual input to the secretary of HHS and is a forum for multiple stakeholders to discuss practical implementation of the NQS. It collaborates with CMS as this agency rolls out multiple federal quality initiatives. Detailed information about NPP can be found in its Field Guide of Resources at www.qualityforum.org/Field_Guide.

The MAP is a public–private partnership convened by NQF created to review performance measures for potential use in federal public reporting and performance-based payment programs and to align measures across multiple federal, state, and private entities. MAP is the first entity of its kind developed to give input to the federal government prior to final rulemaking decisions for programs that affect clinical care measurement. This process is similar to the Relative Value Scale Update Committee that gives input to CMS prior to its final rulemaking decisions about payments for medical services. It is led by a Coordinating Committee and

has four main workgroups including (a) Hospital Workgroup, (b) Clinician Workgroup, (c) Post-Acute Care and Long-Term Care Workgroup, and (d) Dual Eligible Beneficiaries Workgroup.

The workgroups advise the Coordinating Committee on areas of needed measures and the Committee then develops time-limited Task Forces to call for measures. On December 1, 2013, MAP received from HHS a list of 234 measures then currently under consideration for use in 20 federal programs, a variety of public reporting and payment-based reporting programs that cover clinicians, hospitals, and post-acute/long-term care settings. MAP is in the process of aligning all these measures and reducing redundancy across all incentive programs. The MAP Clinician Workgroup specifically is tasked to provide input on measures for PQRS and whether these or other measures will be used in the Physician Compare and VBM initiatives.

Actual measure development occurs through the NQF's Consensus Development Process. Performance measures can be proposed after a call for measures (for a specific topic) is published by NQF. Any recognized medical society, agency, nonprofit, or for-profit company or health system can propose a measure or measure set. The Consensus Development Process involves eight principle steps as follows:

1. Call for Nominations (of measures)
2. Call for Candidate Standards
3. Candidate Consensus Standard Review
4. Public and Member Comment
5. Member Voting
6. Consensus Standards Approval Committee (CSAC) Decision
7. Board Ratification
8. Appeals

Endorsement by NQF now is required for measures to remain in PQRS, Physician Compare, and the VBM program.

Medicare Programs

Currently, there are a variety of CMS programs that are intended to move federal health-care reimbursement away from volume-based payment (FFS) to value-based payment. These include programs at a health system level, hospital level, and provider level. Examples of Medicare programs with measures evaluated by MAP are provided in Table 1.1

Table 1.1 includes examples of gastroenterology (GI)-related measures that might be useful to practices or implemented at a health system or ACO level and used to assess quality in a GI practice. Additional measures under consideration within this process include rate of repeat colonoscopy for poor preps, appropriate age for CRC screening colonoscopy, and several measures related to bundled payment for a colonoscopy episode. Recently, the American Gastroenterological

Table 1.1 Federal and state programs used to migrate to value-based payment

Level of accountability	Name	Description	Examples of GI measures in program
Health system	Medicare Shared Savings Program	Measures ACO care coordination	CG-CAHPS
	Medicare Advantage 5 Star Quality Rating System	Health plan quality incentive program	Rate of CRC screening among plan members
	Medicaid Adult Core Measure Set	Basic quality metrics for Medicaid patients	Flu shots, BMI, CG-CAHPS, monitoring of persistent medications
	Quality Rating System for Qualified Health Plans for Insurance Exchanges	Monitors health plans for meeting ACA standards	CAHPS, Access to specialists, cultural competency, CRC screening, weight management
Clinician performance	PQRS	1.5–2 % reduction in Medicare payments beginning 2015	CAHPS, CRC screening, polyp surveillance interval normal exam, surveillance interval in patients with prior adenoma. Adenoma detection rate added in 2014 (not NQF endorsed as yet)
	Meaningful Use	Penalties begin in 2015 and will continue	Stage 1, 2, and 3 with increasing standards for communication
	Physician Compare	Public reporting website on individual physicians—2014	Process and experience patient outcomes, Meaningful Use, PQRS participation
	VBM	Pay for performance—2017 for all. Composite of quality (NQF endorsed) and cost measures	CAHPS, CRC screening, polyp surveillance interval normal exam, surveillance interval in patients with prior adenoma. Adenoma detection rate not currently endorsed
Hospital performance	Hospital Compare	Public reporting and pay for performance	GI as part of a larger group

PQRS Physician Quality Reporting System, *VBM* value-based modifier, *ACO* accountable care organizations, *ACA* Affordable Care Act, *NQF* National Quality Forum, *GI* gastroenterology, *CG-CAHPS* Consumer Assessment of Healthcare Providers and Systems (CAHPS ®) Clinician & Group, CRC colonoscopy and colorectal cancer, *BMI* body mass index

Association Institute (AGA) published a framework to develop a colonoscopy bundle and CMS has expressed interest in testing payments tied to such a bundle [14].

There is new information about PQRS as it relates to GI as of 2014. Of note, the adenoma detection rate is included in the 2014 PQRS but as yet is not endorsed by NQF. CMS is going to retire a number of claims-based measures (such as those related to hepatitis C) in order to encourage more use of a qualified registry. It is also increasing the number of measures that need to be reported from three to nine in many cases. As of 2014, CMS is offering a new "qualified clinical data registry" (QCDR) reporting option requiring nine measures across three NQF domains and including at least one outcomes measure. These specific measures can contain a combination of PQRS and non-PQRS measures. CMS announced recently that there are two registries pertinent to gastroenterologists that will be "qualified". These include the Digestive Health Outcomes Registry (DHRP) maintained by the AGA and the GI Quality Improvement Consortium (GIQuIC) a registry maintained by the American College of Gastroenterology and the American Society for Gastrointestinal Endoscopy (ASGE). Reporting through a QCDR into PQRS can only be done at an individual level and must include more than 50% of eligible Medicare patients seen by a provider.

In summary, the following are current colonoscopy-related measures that are either endorsed or under consideration for use in a qualified registry (as a non-PQRS inclusion):

- Endoscopy/Polyp Surveillance: Colonoscopy Interval for Patients with a History of Adenomatous Polyps—Avoidance of Inappropriate Use (PQRS 185 NQF 0659)
- Endoscopy/Polyp Surveillance: Appropriate Follow-Up Interval for Normal Colonoscopy in Average Risk Patients (PQRS 320/NQF 0658)
- Screening Colonoscopy Adenoma Detection Rate (PQRS 343)
- Colonoscopy Assessment (Procedure adequacy)—Assessment of Bowel Preparation (non-PQRS measure)
- Colonoscopy Assessment (Cecum reached)—Cecal Intubation/ Depth of Intubation (non-PQRS measure)
- Unnecessary Screening Colonoscopy in Older Adults (non-PQRS measure)

Building a QI Program in Your Practice

Physicians who decide to build a QI program within their practices should understand clearly that performance is to be measured by their peers, compared to optimal practices, opportunities for improvement will be identified, and they will be held accountable for actively participating in these initiatives. When improvement opportunities are found, practices can follow the Donabedian Model described above to alter processes or structure and improve health outcomes. Several basic references are provided to help kick-start a QI program [15–18].

Variation in colonoscopy quality and outcomes exists and will likely continue until process and outcome measures for all colonoscopy examinations are either mandated (see later discussion) or become a routine part of practice for both gastroenterologists and nongastroenterologists who perform screening colonoscopy. The current FFS system of reimbursement, where payment is disconnected from health outcomes, will likely end in the near future. Current systems of credentialing occur at a facility level (a situation with inherent economic conflicts of interest) so factors other than quality and patient-centered health outcomes continue to be powerful influences in the community. Recent CMS efforts to begin identifying outliers within ambulatory surgical centers will continue and increase in intensity.

Recognizing variation in colonoscopy practice, physicians should feel compelled to demonstrate their own value as they perform colonoscopy and other endoscopic procedures. Uniform data collection and interpretation requires that measures be predefined and consensus gained on developing practice transparency and a commitment to improving. While measures used for federal or commercial incentive programs are rigidly standardized, those used for submission via registries or for practice (or ACO) improvement efforts can be less complex and more intuitive.

Optimal metrics should correlate with important clinical outcomes, be evidence based, reproducible, and easy to collect. Significant investments in infrastructure, staff time, and expertise are required for larger improvement efforts and fulfilling national expectations for performance and data submission. For short-term ad hoc improvement projects, manual data tracking and display are typically sufficient. Automated data accrual is helpful for larger settings and the repetitive nature of gastrointestinal endoscopy simplifies documentation if data can be collected using electronic report generators.

Every practice has opportunities for improvement in safety, efficiency, clinical outcomes, cost, or service. The capacity to undertake QI initiatives is usually constrained so practices should prioritize their efforts to (a) gaps in care that pose direct risk to patient safety or procedural outcomes, (b) measures required to ensure full reimbursement, (c) issues related to patient dissatisfaction, and (d) quality measures mandated regulatory agencies. Additional QI opportunities can be identified by attention to “near miss,” “never,” or sentinel events (all of which warrant investigation for structural or process failures); patient complaints; and employee or referring physician surveys.

Many practice changes can be addressed administratively, but substantive improvement or redesign in care processes usually requires a more formal process such as Lean or Six Sigma methodology. Here, process improvement is accomplished by assembling a team of responsible individuals who define a plan with clearly delineated goals, use of established techniques, and a timeline. Improvement teams should include both staff and managers with responsibility for the process or outcome being addressed, and individuals with skills and experience with database queries, data acquisition, statistical assessment, and process control charting.

Benchmarking is a method for comparing one’s performance and outcomes against those from similar individuals or institutions. External benchmarking can be accomplished by participation in a “registry” that typically provides comparison

against aggregate data from many groups. Risk adjustment for differences in populations and services can enable comparison between disparate groups. A prime motivation for participating in national registries for endoscopy or other focused practice areas within clinical GI (hepatitis and IBD care) is to facilitate automated submission of performance data on quality measures to CMS although current changes in CMS programs (see above) need to be considered as practices commit to a registry.

GIQuIC is a nonprofit national registry established by the ASGE and the ACG. This program provides comparative results on facility and physician-level quality measures pertaining to endoscopy. Measures of interest are electronically submitted following either manual abstraction or automated retrieval from an electronic endoscopic report generator. To date, this registry does not contain any PQRS measures, and through the QCDR process it must be reported at an individual level as summarized above.

DHRP developed by the AGA is actually two registries using differing data entry processes. Practices have the option of submitting measures to satisfy PQRS via the Group Measures process for either the inflammatory bowel disease or hepatitis C measures that are part of the "Group Measures" within PQRS. In this format, 20 consecutive patients with an IBD or hepatitis C are used for data extraction and submission using a web-based tool (at least half must be Medicare if used for PQRS submission). DHRP is currently available for IBD and hepatitis C practices and is linked to Bridges to Excellence recognition. A module is in development for colon cancer prevention. For more information, see www.gastro.org/practice/quality-initiatives/aga-digestive-health-recognition-program. In addition to the Group Measures process, DHRP also is a recognized QCDR so practices can submit using that format on 50 % of their Medicare patients. In this process, a colon cancer prevention (colonoscopy) set of measures is available.

Conclusion

What are the implications of all of these initiatives for national colonoscopy improvement efforts? Bluntly stated, the commitment of the USA to CRC prevention is huge and gastroenterologists who provide screening examinations will be held accountable for their outcomes. A commitment to enhancing value means a commitment to improving quality (known to be variable) and reducing total cost of care. Because we (gastroenterologists) led the effort to mandate population-based CRC screening with colonoscopy, we have an ethical commitment to be vigilant about our results and accountable for outcomes.

Gastroenterologists who understand future reimbursement and health-care trends are preparing their practices to meet new challenges of transparency and bundled payments. Pressures from large purchases of medical care (both employers and the federal government) will be sufficient to drive change. Robust measurement and public reporting of results both are firmly embedded in many regions of the country

and will become universal as we move to value-based reimbursement. The path is clear for those who study these issues, monitor process measures for internal improvement, push resource efficiency, connect to national registries to demonstrate quality externally, and constantly try to provide a service with the highest health value.

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Chapter 2
Current Screening and Surveillance Guidelines

Swati G. Patel and Dennis J. Ahnen

Introduction

Colorectal cancer (CRC) is a major cause of morbidity and mortality in the world. In 2008, there were more than 1.2 million new cases and approximately 610,000 deaths from CRC worldwide, making CRC the third most common cancer and the fourth leading cause of cancer-related death in the world [1]. Similarly, in the USA, CRC is the fourth most common malignancy and the second leading cause of cancer-related death; in 2013, there were an estimated 142,820 new cases and 50,830 deaths due to CRC [2]. An average-risk individual in the USA has a 4.8 % lifetime risk of developing CRC and a 2–3 % risk of death from CRC.

CRC mortality is stable or decreasing in most developed countries, but the USA is the only country in which both CRC incidence and mortality are steadily declining (about 2–3 % per year for the past 15 years). This decline is likely multifactorial (use of hormone replacement therapy among women, smoking cessation efforts, and widespread use of aspirin for cardiovascular health) and began well before screening was common in the USA (Fig. 2.1); however, reasonable estimates suggest that up to half of the recent trend can be attributed to CRC screening [3].

This chapter presents the historical basis for CRC screening, reviews the data available regarding current screening options for individuals at average and increased CRC risk, and reviews recommendations for surveillance after polyp removal; when possible, US and international guidelines will be compared. A detailed discussion of familial CRC syndromes or CRC associated with inflammatory bowel

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A. Shaukat, J. I. Allen (eds.), *Colorectal Cancer Screening,*
DOI 10.1007/978-1-4939-2333-5_2

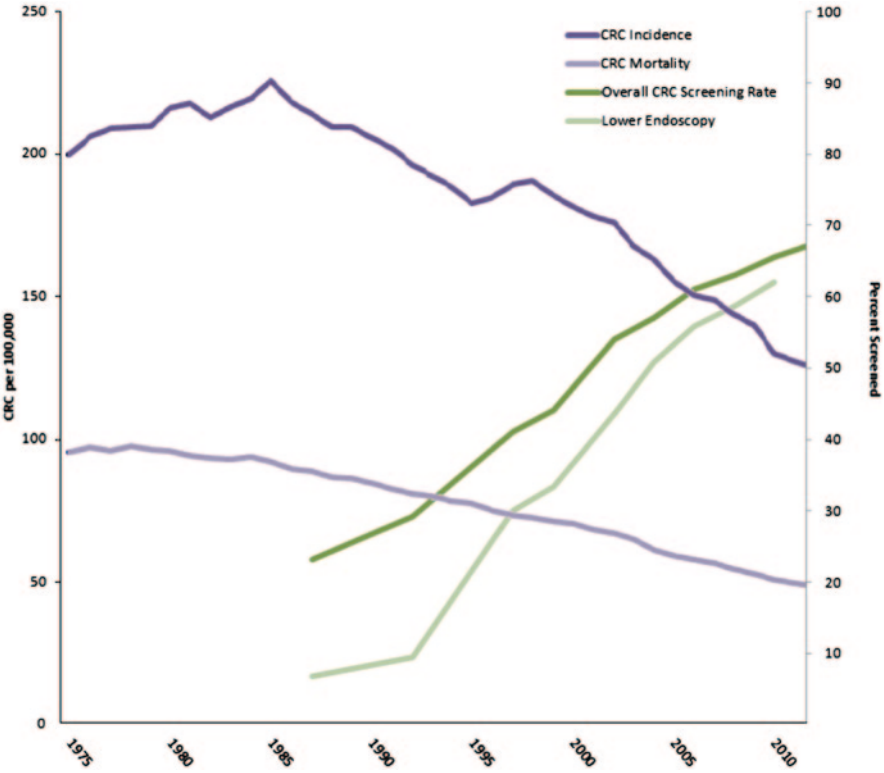

Fig. 2.1 Incidence/mortality of CRC and screening uptake rates over time. CRC incidence/mortality reported as rates among adults age 50 or older (Surveillance, Epidemiology and End Results database) to reflect the screening population. To cover the entire timeline, CRC screening test uptake rates derived from the National Health Information Survey were used for data before 1992 and Behavioral Risk Factor Surveillance System data were used for 1997–2010. The surveys did not differentiate between flexible sigmoidoscopy and colonoscopy for lower endoscopy; however, the sharp increase in lower endoscopy since 1995 is almost entirely the result of an increased use of colonoscopy.CRC colorectal cancer. (Adapted from Ref. [107]. With permission from Elsevier)

disease is outside the scope of this chapter; however, these topics are reviewed in detail elsewhere [4–6].

History and Rationale for CRC Screening

In the USA, screening for CRC has been promoted since the mid-1970s but the tools that are currently used for screening have a much longer history. Although the *Corpus Hippocraticum,* dating back to the fourth and fifth centuries BC, recorded the first rudimentary attempt at endoscopy with a rectal speculum, most historians credit Philipp Bozzini (Fig. 2.2a) as the creator of the first "modern" endoscope in 1806—the *Lichtleiter* or light conductor (Fig. 2.2b). The device was constructed

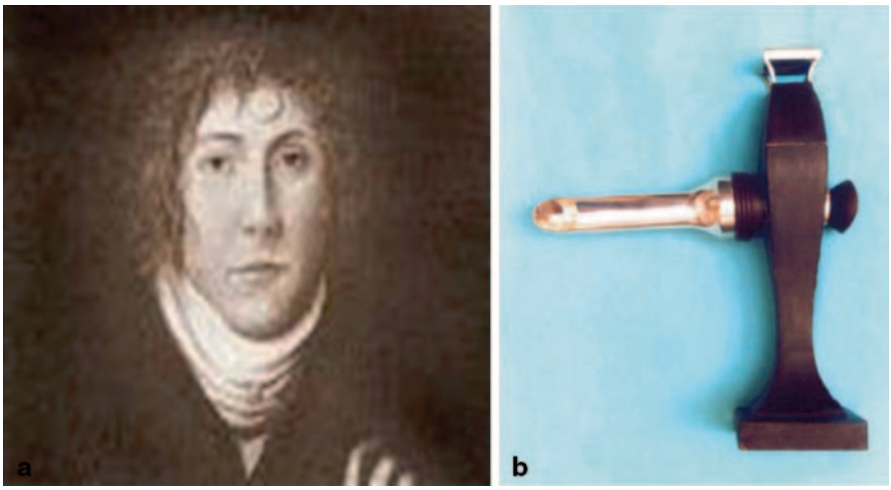

Fig. 2.2 **a** Philipp Bozzini (1773–1809) is credited with developing the first "modern" endoscope. **b** The *Lichtleiter* or light conductor. (Adapted from Ref. [108]. With permission from Nature Publishing Ltd.)

with double aluminum tubes (to be inserted in the body orifice being examined) and angled mirrors to project internal structures to the human eye, employing a single candle as a light source [7]. Rigid sigmoidoscopes have long been used diagnostically and screening sigmoidoscopy was developed in the 1950s [8].

Fecal occult blood testing (FOBT) also has a long history. In the 1850s, Christian Friedrich Schonbein first recognized the chemical reaction causing rapid bluing of guaiac (a resin from the West Indian gouyaca plant) when exposed to ozonized air [9]. Guaiac contains a phenolic compound that is oxidized to a quinone by hydrogen peroxide in a reaction catalyzed by peroxidases including hemoglobin. Von Deen developed a guaiac-based test for occult blood in 1863 [10]. Greegor stimulated widespread interest in FOBT when he reported, in 1967, that asymptomatic CRC could be detected by the presence of blood in the stool [11]. The immunologic tests to detect human hemoglobin were introduced in the 1970s [12], commercialized in the 1980s, and are now considered preferable to standard guaiac-based FOBT because of better performance characteristics (see below). Several FIT tests have now been approved by the US Food and Drug Administration (US-FDA).

As early as 1977, the American Cancer Society (ACS) recommended CRC screening with digital rectal exam and rigid proctoscopy as part of a *cancer-related health checkup* [13]. The rationale for screening was largely based on observations that patients with screen-detected CRCs had earlier stage disease and longer survival than those with symptomatic CRCs. Compelling evidence of the effectiveness of CRC screening emerged with the completion of large randomized screening trials beginning in the 1990s. On the basis of these trials, the US Preventive Services Task Force (USPSTF) initially recommended CRC screening with annual FOBT and/or sigmoidoscopy in 1995 with a grade B recommendation citing fair evidence of effectiveness [14]. In 2002, the USPSTF upgraded CRC screening to a grade A recommendation stating

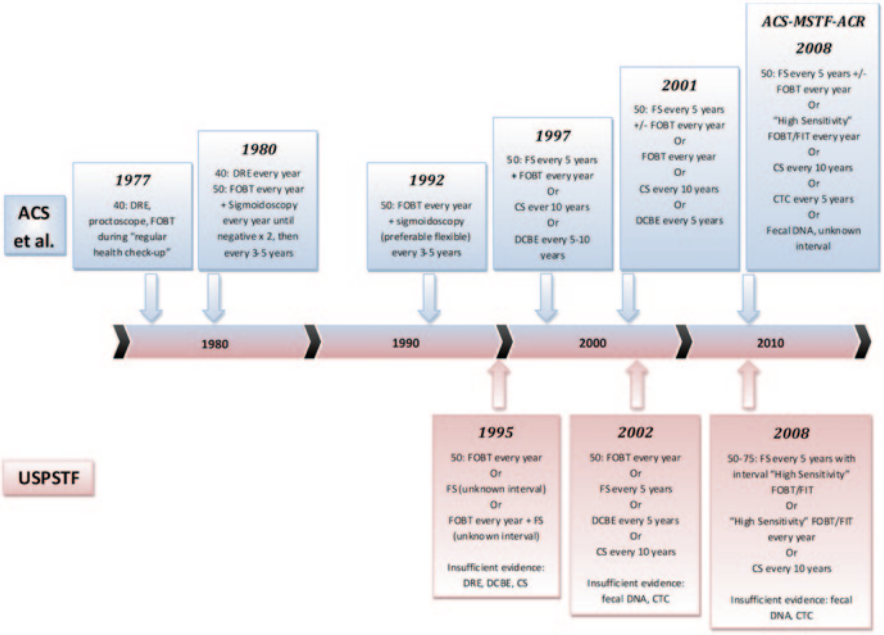

Fig. 2.3 Timeline of US colorectal cancer screening guidelines. ACS guidelines changed to ACS-MSTF-ACR guidelines in 2008. Prior to 2008, MSTF published independent guidelines [14, 35, 59, 109–111].ACS American Cancer Society, ACS-MSTF-ACR American Cancer Society-Multi Society Task Force-American College of Radiology. (Adapted from Ref. [108]. With permission from Springer Verlag)

that the USPSTF "strongly recommends that clinicians screen men and women aged 50 and older who are at average risk for colorectal cancer."In 2004,CRC screening became a Healthcare Effectiveness Data and Information Set (HEDIS) performance measure, essentially establishing that CRC screening is an accepted standard of care in the USA (HEDIS measures are used by more than 90% of US health plans to measure performance). CRC screening guidelines in the USA have evolved over time (Fig. 2.3), largely based on the results of the trials that are described in this chapter.

Average-Risk Screening Options

Current CRC screening options can be categorized into stool-based testing and structural radiographic or endoscopic imaging. Stool-based tests detect the consequences of colonic neoplasia (bleeding or shedding of neoplastic cells into the stool) and, as a one-time test, are better at detecting cancers than precancerous colonic polyps, while imaging modalities (endoscopy, radiology) can directly visualize both colonic polyps and cancers. The advantages, disadvantages, and performance characteristics of these tests are compared in Table 2.1.

Table 2.1 Summary of colorectal cancer Screening Modalities (Adapted from Ref. [108]. With permission from Springer Verlag)

Test	Advantages	Disadvantages	Sensitivity	Specificity	Screening interval	Guideline support	Cost per test
Imaging tests							
CS	Can visualize entire colon Performed every 10 years Can remove/biopsy lesions Can diagnose other diseases Single-step diagnostic and treatment Minimal patient discomfort	Invasive Sedation required, patient must be accompanied Time-consuming Expensive Full bowel preparation required Risk of bleeding, perforation Operator dependent, bowel preparation dependent	*Generally considered* "gold standard" 90 % (when using CTC as standard) for adenoma 5 mm, 97 % for advanced adenoma[a]	*Generally considered* "gold standard"	10 years	ACG ACS-MSTF-ACR USPSTF ASGE WGO	US$ > 1000[c]
FS	Simpler bowel preparation than CS Sedation not required Quick Performed every 5 years Does not require specialist or physician Lower risk than CS	Does not visualize entire colon Patient discomfort Risk of bleeding, perforation Two-step test Operator dependent, bowel preparation dependent	60–70 % for "clinically significant neoplasia"[b]	Equivalent to CS for region visualized	5 years	ACG ACS-MSTF-ACR USPSTF ASGE WGO CCA/CAN	US$150–300[c]
DCBE	Can visualize entire colon No sedation required Performed every 5 years Lower risk than CS	Insensitive for lesions 1 cm Less training for technicians/radiologists administering and interpreting exam Full bowel preparation required Two-step test	50 % for adenomas 1 cm 39 % for all polyps	96 % for adenomas > 10 mm	5 years	ACS-MSTF-ACR	US$300–400[c]

Table 2.1 (continued)

Test	Advantages	Disadvantages	Sensitivity	Specificity	Screening interval	Guideline support	Cost per test
CTC	Can visualize entire colon Less time consuming than endoscopy No sedation required Performed every 5 years Lower risk than CS	Can miss polpys 1 cm Full bowel preparation required Unclear how to follow extra-colonic findings Expensive Two-step test Radiation exposure Variability in performance	6–9 mm: 23–86 % /=10 mm: 52–92 %	86–95 %	5 years	ACG ACS-MSTF-ACR USPSTF WGO	US $>1000[c]
Stool-based tests							
gFOBT	Low risk, noninvasive Widely available No bowel preparation Inexpensive Home testing	High false-positive rate Insensitive for adenomatous lesions Requires frequent testing Two-step test Pretest dietary limitations	For CRC: Single test: 30 % Multiple nonrehydrated: 50–60 % Multiple rehydrated: 80–90 %	For CRC: 87–98 %	1 year	ACG ACS-MSTF-ACR USPSTF ASGE EU WGO CCA/CAN BSG/ACPGBI	US$ 13 [115]
FIT/iFOBT	Low risk, noninvasive Widely available No bowel preparation Inexpensive Home testing No dietary restrictions More specific to lower GI bleeding Detects human globin	High false-positive rate Insensitive for adenomatous lesions Requires frequent testing Two-step test	81.9–94.1 % for CRC 25–27 % for advanced adenoma 67 % for “clinically significant neoplasia”	87.5 % for CRC97–93 % for advanced adenoma 91.4 % for “clinically significant neoplasia”	1 year	ACG ACS-MSTF-ACR USPSTF ASGE WGO CCA/CAN BSG/ACPGBI	US$ 20 [115]

Table 2.1 (continued)

Test	Advantages	Disadvantages	Sensitivity	Specificity	Screening interval	Guideline support	Cost per test
Stool DNA	Low risk, noninvasive No bowel preparation Home testing No dietary restrictions Higher sensitivity than other stool tests	Need to collect an entire stool sample More expensive than other stool tests Unclear how to manage false-positive results Uncertain surveillance interval Two-step test	25–51 % for CRC 20–41 % for advanced adenomas+CRC	94–96 % for CRC	Unknown ACG recommends 3 years	ACG ACS-MSTF-ACR WGO	US$ 350[c]

FS flexible sigmoidoscopy, *CS* colonoscopy, *DCBE* double contrast barium enema, *CTC* computerized tomography colonography, *gFOBT* guaiac fecal occult blood testing, *FIT* fecal immunochemical testing, *iFOBT* immunochemical fecal occult blood testing, *ACG* American College of Gastroenterology, *ASGE* American Society for Gastrointestinal Endoscopy, *ACS-MSTF-ACR* American Cancer Society-Multi Society Task Force-American College of Radiology, *USPSTF* United States Preventative Services Task Force, *EU* European guidelines for quality assurance in CRC screening and diagnosis, *WGO* World Gastroenterology Organization, *CCA/ACN* Cancer Council Australia/Australian Cancer Network, *BSG/ACPGBI* British Society of Gastroenterology/Association of Coloproctology for Great Britain and Ireland

[a] Advanced adenoma: significant villous features (>25 %), size of 1.0 cm or more, high-grade dysplasia, or early invasive cancer

[b] Clinically significant neoplasia advanced adenoma or CRC

[c] American Cancer Society Colorectal Cancer Facts & Figs. 2008–2010

Stool-Based Tests

Stool-based CRC screening tests include guaiac-based and immunochemical FOBTs, and more recently, stool DNA tests. The concept of stool testing is based on the observation that colonic neoplasms can both bleed and shed cells into the stool. FOBT is the most widely used CRC screening modality in the world [15] and has been the most rigorously evaluated (see Table 2.2).

Guaiac FOBT

Guaiac-based tests detect heme in the stool by the presence of a peroxidase reaction, which turns the guaiac-impregnated paper blue. Most screening protocols require collecting stool samples from three consecutive bowel movements at home to optimize sensitivity. Patients are typically instructed to avoid aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) for 7 days and vitamin C, red meat, poultry, fish, and raw vegetables for 3 days prior to testing to improve specificity. However, a systematic review indicated that a recommended restricted diet did not decrease FOBT false-positivity rates, but did decrease compliance to testing [16]. There are a variety of commercial FOBTs available. The initial tests such as Hemoccult and Hemoccult-II have been shown to be effective in large prospective screening trials (Table 2.2) and are the standard by which subsequent FOBTs have been compared, but they have substantially lower sensitivity for CRC than Hemoccult SENSA (see below).

Performance Characteristics

The performance characteristics of guaiac FOBTs (gFOBTs) can be assessed as a one-time test for the detection of CRC or adenomas of the colon but gFOBTs are recommended to be repeated every 1–2 years, so the performance of a program of gFOBT testing is also important (this distinction highlights the critical importance of ongoing compliance as an issue for stool testing). The performance characteristics of gFOBTs vary with the prevalence of CRC and the age of the population screened and there is even greater performance variability among the types of gFOBTs [17–21]. Of all of the commercial kits available, Hemoccult SENSA has the highest one-time sensitivity for CRC (64–80%), but a lower specificity (87–90%) than the other gFOBTs (sensitivity <50%; specificity ~95%) [22].

Efficacy

The clinical efficacy of FOBT has been established by controlled trials using the lower sensitivity Hemoccult or Hemoccult II tests. The first trial, reported by Man-

Table 2.2 Summary of randomized controlled trials for fecal occult blood testing (FOBT) (Adapted from Ref. [108]. With permission from Springer Verlag)

Trial	Screening	Follow-up (years)	Testing	Participants	Attendance (first screen‖at least 1‖subsequent rounds)	Sensitivity[a]	PPV[b] CRC	PPV adenoma	CRC incidence	CRC mortality[c]	All-cause mortality
Minnesota [23], [112]	Annual (A) and biennial (B)	18	Hemoccult Rehydrated	46,551	– ‖ 75% ann, 78% bi ‖ –	92.2%	0.9–6.1%	6–11%	A: 0.8 (0.73–0.94, p 0.001) B: 0.83 (0.73–0.94, $p=0.002$)	A: 0.67 (0.51–0.83, p 0.05) B: 0.79, 0.62–0.97, p 0.05)	342 (334–350)[d] A: 340 (333–348) B: 343 (336–351) *NS*
Nottingham [24]	Biennial	11.7	Hemoccult Not rehydrated	152,303	53.4% ‖ 59.6% ‖ –	57.2%	9.9–17.1%	42.8–54.5%	1.51 versus 1.53/1000 person yr *NS*	0.87 (0.78–0.97, $p=0.010$)	1.01 (0.96–1.05) *NS*
Funen [21]	Biennial	17	Hemoccult II Not rehydrated	61,939	66.8% ‖ – ‖ 91–94%	55%	5.2–18.7%	14.6–38.3%	1.02 (0.93–1.12) *NS*	0.84 (0.73–0.96, $p<0.05$)	0.99 (0.97–1.02) *NS*
Goteborg [25]	Biennial[e]	15.75	Hemoccult II Rehydrated	23,916	63% ‖ 70% ‖ 60%	82%	4.8%	14%	0.96 (0.86–1.06)	0.84 (0.71–0.99, $p<0.05$)	1.02 (0.99–1.06) *NS*

NS non-significant results

[a] Proportion of all CRC that were detected by screening, where "all CRC" was the sum of screen-detected cancers (TP) and interval cancers within 1 or 2 years of screening (FN)

[b] Positive predictive value

[c] Reported as odd ratio with 95% confidence interval

[d] Mortality per 1000

[e] Three cohorts: all screened for initial prevalence, cohort 1 and 2 rescreened at 21–24 months, cohort 3 rescreened at 1 year and 2 year after initial screening. Cohort 1 rescreened at approximately 10 years

del et al. [23] from the University of Minnesota, randomized 46,551 patients to annual FOBT, biennial FOBT, or a control arm. Mortality due to CRC was decreased by 33% at 13 years in the annual screening group and 21% at 18 years in the biennial screening group when compared to the control arm. Subsequently, three European trials also demonstrated a CRC mortality benefit ranging from 13 to 16% using biennial screening [21, 24, 25]. Longer-term follow-up of the US study showed that gFOBT screening led to a 17–20% lower incidence of CRC [23] (Table 2.2) and that the mortality benefits have been maintained through 30 years of follow-up [26].

There is no direct evidence that screening with FOBT decreases all-cause mortality (Table 2.2). Although none of the trials were powered to assess an effect on all-cause mortality, a meta-analysis of the three major controlled trials [27] found that screening was associated with a significant decrease in CRC mortality, a significant increase in non-CRC mortality and no impact on overall mortality.

Fecal Immunochemical Tests

Immunochemical tests for blood in the stool have several advantages over gFOBTs. Fecal immunochemical tests (FITs) specifically detect human globin so they do not require dietary restriction of meat or peroxidase-rich food and FITs typically require one to two stool samples rather than the three recommended for gFOBTs. Not surprisingly, participation rates have been reported to be significantly higher for FIT than gFOBT; 61.5 versus 49.5% in a study by Hol et al. [28]. In addition, globin protein is digested in the stomach and proximal small bowel so FIT should be more specific for bleeding from the colon than gFOBTs. There are multiple FDA-approved FIT kits commercially available; the major technical differences among the tests are whether they can report quantitative as well as qualitative results and whether they can be performed in an individual laboratory or require central processing. The analysis of reported data with FITs is complicated by the fact that the level of sensitivity can be adjusted and the number of tests recommended is not uniform; the performance characteristics of the tests vary substantially by adjusting either or both of these parameters. FIT is typically more expensive than gFOBT but, for a single test, both are substantially less expensive than the imaging modalities described below.

Performance Characteristics

FIT is thought to have a similar sensitivity for CRCs and advanced adenomas (≥10 mm, presence of high-grade dysplasia or villous features) as Hemoccult SENSA and both have improved sensitivity over other gFOBTs like Hemoccult II. Allison et al. [18] reported that FIT sensitivity was higher than Hemoccult SENSA for distal CRCs (81.9 vs. 64.3%) but lower for advanced adenomas (29.4 vs. 41.3%). Hundt et al. [29] found great variability in the performance of six FIT kits for detec-

tion of adenomas; the two best performing tests (immoCARE-C (CARE diagnostica, Voerde, Germany) and FOB advanced (ulti med, Ahrensburg, Germany)) had sensitivities for the detection of advanced adenomas of 25 and 27 % with specificities of 97 and 93 %, respectively.

Efficacy

There are no long-term data regarding the impact of screening with FIT on CRC mortality or incidence; however, there are several trials underway with results expected in the 2020s. Results from the initial round of screening of one of the trials comparing colonoscopy with FIT (hemoglobin threshold of 75 ng/mL) showed higher compliance with the FIT arm, higher adenoma detection in the colonoscopy arm, and, after one round of FIT testing, no difference in CRC detection rates [30].

Fecal DNA Testing

Fecal DNA testing is a new and evolving stool-based screening test based on the observation that colonic neoplasms have altered DNA compared to normal cells, that colonic neoplasms shed cells into the stool, and that their DNA can be detected in stool. Fecal DNA testing has the theoretical advantage of identifying a marker thought to be in the causal pathway to CRC (mutations or mutation-like events) rather than the less specific finding of blood in the stool. Typically, an entire bowel movement is collected and shipped to a laboratory for the fecal DNA tests.

Performance Characteristics

Fecal DNA testing is a very active area of ongoing research and there are numerous studies reporting high sensitivity and specificity of various stool DNA tests in selected patient populations. In two studies using colonoscopy as a standard, a fecal DNA test (PreGen Plus®; no longer commercially available) had a sensitivity of 25–51 % for CRC and 20–41 % for clinically significant neoplasia (CRC plus advanced adenomas) with specificities of 94–96 % [31, 32]. A combination stool DNA/FIT assay (Cologuard®) was recently reported to have a 92 and 42 % sensitivity for CRC and advanced adenomas, respectively, with a specificity of 86 % [33]. This test has been submitted to the FDA for premarketing approval.

Efficacy

There are no long-term data available upon which to draw conclusions regarding the efficacy of fecal DNA testing on CRC mortality or incidence.

Blood Tests

A reliable blood test for colon cancer screening would have substantial advantages over stool collections. A large prospective study of methylated septin 9 in patients scheduled for screening colonoscopy demonstrated that a CRC marker can be detected in blood; the assay had a 48% sensitivity for CRC [34]. A septin 9 CRC screening assay (ColoVantage®) has been submitted to the FDA for premarketing approval.

Structural Tests

Colonic imaging tests used for screening include radiologic (barium enema and CT colonography) as well as endoscopic (flexible sigmoidoscopy (FS) and colonoscopy) tests. Although barium enema is still supported as a screening modality in the multi-society guidelines [35], there are no studies evaluating its effectiveness in CRC screening and it is rarely used for screening.

Computerized Tomography Colonography

Computerized tomography colonography (CTC) emerged as a CRC screening tool in the mid-1990s, and the technology has rapidly evolved since. CTC is an attractive screening approach in that, like colonoscopy, it visualizes polyps as well as cancer throughout the colon but it does not require sedation, it takes less time, and is associated with a lower complication rate than colonoscopy. Current protocols require patients to undergo a standard bowel preparation and the colon is inflated using a rectal catheter prior to imaging, which can cause discomfort.

Performance Characteristics

Defining the sensitivity and specificity for CTC is more complicated than for any of the other screening modalities since the current radiologic practice is to not report polyps less than 5 mm in size. The reported sensitivity for polyps sized 6–9 mm has ranged from 23 to 86% and from 52 to 92% for polyps > 10 mm and 75–100% for CRC [36–39]. This wide variability has been attributed to differences in technology and operator experience and training.

There is a concern that operator dependence could be even a bigger issue in the general community than that reported in the controlled trials. The trials reporting the best CTC performance [36, 39] went to great lengths to ensure that their study radiologists were highly trained and experienced with CTC. Thus, these study results may not be generalizable to the community.

Despite these concerns, the best CTC studies reported sensitivities for cancer and for polyps larger than 10 mm of 94 and 90 %, respectively, with specificites for polyps > 10 mm of 86–95 % [36–38].

Barriers to the widespread use of CTC screening include residual angst about the ability of CRC to detect diminutive and flat polyps. Even though only a small percentage of polyps less than 5 mm have advanced histology (only 1 of 966 diminutive polyps found in Pickhardt's trial had villous features), it is unclear if leaving these polyps undetected and unremoved is acceptable to patients and their providers. There are little data about the performance of CTC for the detection of flat lesions in the colon which are increasingly reported as having a substantial cancer risk [40]. Small flat lesions are also missed frequently by endoscopy, however, and the overall sensitivity of CTC and colonoscopy for polyps > 6 mm is similar [41].

CTC is less expensive than colonoscopy but there are conflicting data regarding the cost-effectiveness of CTC compared with colonoscopy [36, 42–45]. Most of these modeling studies assumed that patients would only be referred for colonoscopy if polyps greater than 10 mm were found. In practice, Shah et al. [46] found that both patients and physicians preferred to follow even small polyps with colonoscopic examination. If all detected polyps led to colonoscopy, the cost of primary CTC screening would increase substantially.

Efficacy

There are no long-term data available to assess CTC screening on CRC mortality.

Flexible Sigmoidoscopy

FS is generally performed with a 60-cm sigmoidoscope, which typically allows visualization to the descending colon or splenic flexure (less than half of the colonic length). The bowel preparation for FS is usually enemas alone; although simpler, the preparation may not be as good as with the more extensive preparations used for CTC or colonoscopy. FS typically does not require sedation and can be performed by nonphysicians (nurses, mid-levels), but it causes more patient discomfort than sedated procedures.

Performance Characteristics

The sensitivity of FS for advanced adenomas and CRC of the entire colon is approximately 60–70 % (when compared to colonoscopy as gold standard) if colonoscopy is recommended for any adenoma detected in the distal colon [47]. Provided that the bowel preparation is good, the sensitivity and specificity for detecting lesions in the distal bowel is thought to be equivalent to colonoscopy.

Efficacy

Although earlier studies had been conflicting, three recent large controlled trials from the UK [48], Italy [49], and the USA [50] (Table 2.3) reported decreases in both incidence (18–23%) and mortality (22–31%) in patients randomized to FS. The benefit of FS was due to a decrease in left-sided CRCs with no significant effect on right-sided CRCs. None of the FS trials has found a statistically significant reduction in overall mortality.

Colonoscopy

Colonoscopy is thought by many to be the most effective CRC screening test available given its ability to both visualize and remove/sample lesions throughout the entire colon. There are, however, no controlled trials to establish the effect of colonoscopy on CRC incidence and mortality. It is important to recognize that colonoscopy quality is highly operator dependent and varies greatly due, in large part, to differences in the training, experience, and skill of the endoscopist and the quality of the endoscopic equipment and the prep. In one study of endoscopists at an academic medical center, adenoma detection rates (ADRs) varied almost threefold (17–47%) and serrated polyp detection rate varied even more (1–18%) [51]. Cecal intubation rates, withdrawal times (WTs), and ADRs are accepted measures of colonoscopy quality [52], the goal of colonoscopy is to prevent CRC. Longer WTs are generally associated with higher ADRs and two studies [53, 54] have shown that higher ADRs are associated with lower interval (post-colonoscopy) CRC rates.

Colonoscopy is the most expensive and highest risk CRC screening test with a perforation rate of about 0.6 per 1000 (higher in patients undergoing polypectomy) and a bleeding risk as high as 8.7 per 1000 procedures in which a polypectomy is performed [55]. Bowel preparation is critically important for colonoscopy and typically includes clear liquids the day prior to the procedure and ingestion of a large volume of a polyethylene containing liquid with half the dose the night before and the other half the morning of the exam. The exam is generally performed with conscious sedation or anesthesia, which provides an amnesic benefit so that most patients report that the preparation is the most unpleasant part of the procedure.

Performance Characteristics

Because colonoscopy has been viewed as the gold standard in CRC screening, there are no robust estimates of test characteristics in terms of sensitivity and specificity. Initially, tandem colonoscopy studies (two complete colonoscopies by different endoscopists during the same session) [41] estimated miss rates of 2% for adenomas 10 mm or greater, 13% for adenomas 5–10 mm, and 25% for adenomas less than 5 mm, with a 22% overall miss rate for all polyps. Studies performing both CTC and colonoscopy estimate that the miss rate for colonoscopy is substantially higher

Table 2.3 Summary of randomized controlled trials for flexible sigmoidoscopy: CRC incidence, mortality, and all-cause mortality (Adapted from Ref. [108]. With permission from Springer Verlag)

Trial	Participants	Follow-up (years)	CRC incidence (RR[b] or number)	CRC mortality (RR[b])	All-cause mortality (RR or number)
Telemark [113] Norway	799	13	0.2 (95 % CI, 0.03–0.95)[a]	No patients died of CRC in either arm	1.57 (95 % CI, 1.03–2.4)[a]
NorCCaP[c] [114] Norway	55,736	7	134.5 versus 131.9/100,000 person yr	0.73 (95 % CI, 0.47–1.13) ITT[d] 0.41 (95 % CI, 0.21–0.82) per protocol[a]	1.02 (95 % CI, 0.98–1.07)
UK FS trial [48]	113,195	11.2	0.77 (95 % CI, 0.70–0.84) ITT[a] 0.67 (95 % CI, 0.60–0.76) per protocol[a]	0.69 (95 % CI, 0.59–0.82) ITT[a] 0.57 (95 % CI, 0.45–0.72) per protocol[a]	0.97 (95 % CI, 0.94–1.0)
SCORE[e] Trial [49]	34,272	11.4	0.82 (95 % CI, 0.69–0.96) ITT[a] 0.69 (95 % CI, 0.56–0.86) per protocol[a]	0.78 (95 % CI, 0.56–1.08) ITT 0.62 (95 % CI, 0.40–0.96) per protocol[a]	660.3 verus 641.0/100,000 person yr
PLCO[f] Trial [50] US	77,445	11.9	0.79 (95 % CI 0.72–0.85)[a]	0.74 (95 % CI 0.63 to 0.87)[a]	0.98 (95 % CI, 0.96–1.01)

CI confidence interval, *CRC* colorectal cancer, *RR* relative risk

[a] Denotes statistically significant

[b] Relative risk

[c] Norwegian Colorectal Cancer Prevention

[d] Intention to treat

[e] Sigmoidoscopy in colorectal cancer screening working group

[f] Prostate Lung Colorectal Ovarian Cancer Screening Trial

(12 % miss rate for polyps greater than or equal to 10 mm) [36]. Reports of the range of ADRs among endoscopists [53] suggest the average endoscopist may miss up to half of patients with adenomas.

Efficacy

There have been no randomized controlled trials of colonoscopic screening with CRC incidence or mortality endpoints, but there is substantial indirect evidence to support its use as a screening tool. The efficacy of colonoscopic polypectomy was initially highlighted by the National Polyp Study (NPS) which estimated a 76–90 % reduction in incidence of CRC after polyp removal compared to historic controls [17]. Similarly, a veterans affair (VA)-based case–control study by Muller et al. [56] reported that having had a lower endoscopy within the previous 6 years was associated with a 60 % reduced CRC mortality (odds ratio (OR) 0.41, 95 % confidence interval (CI) 0.33–0.50). Efficacy can also be extrapolated from randomized controlled trials performed for other screening modalities that eventually referred patients for colonoscopy. The reduction in CRC incidence in the FOBT trials [26] is attributable to the colonoscopy and polypectomy performed for positive FOBT results.

It seems intuitive that colonoscopy would be a better screening test than sigmoidoscopy since it can visualize the entire colon. Recent studies, however, have called into question the ability of colonoscopy to prevent CRC throughout the entire colon. Case–control studies from Canada and Germany [57] reported that colonoscopy resulted in a significant decrease in CRC mortality (OR 0.33, CI 0.28–0.39) and in metachronous advanced adenoma rates in the left colon but neither found a risk reduction in the right colon. A US case–control study [58] using the Surveillance, Epidemiology, and End Results (SEER)-Medicare database found a protective effect of colonoscopy for CRC; the magnitude of the benefit was substantially greater for left- than right-sided CRC (OR 0.24 (95 % CI, 0.21–0.27) vs. 0.58 (95 % CI, 0.53–0.64). These marked regional differences could reflect a different biology of right-sided tumors, a higher proportion of flat and indistinct lesions, and/or a higher likelihood of poor bowel preparation in the right colon, among other reasons.

At least three randomized controlled trials are currently underway to directly examine the efficacy of colonoscopy in reducing CRC incidence and mortality. Both the US Department of Veterans Affairs CONFIRM (Colonoscopy vs. Fecal Immunochemical Test in Reducing Mortality from Colorectal Cancer) trial and a Spanish trial [30] will be comparing colonoscopy to FIT, while the Nordic-European Initiative on CRC will compare colonoscopy to no screening. These trials are expected to take another decade to complete.

PillCam Colon

There are little published data on the use of the colonic capsule endoscopy for CRC screening in the USA. PillCam Colon® has received FDA approval for use in pa-

tients with incomplete optical colonoscopy but not yet for screening and it has not been incorporated into any CRC screening guidelines.

Guidelines for Average-Risk Screening

The most frequently cited colon screening guidelines in the USA are those developed by the USPSTF which focus on average-risk screening [59], those developed jointly by the ACS, the American College of Radiology, the US Multi-Society Task Force (MSTF; includes the American Gastroenterology Association Institute, the American College of Gastroenterology (ACG), and the American Society for Gastrointestinal Endoscopy) [35], and the National Comprehensive Cancer Network (NCCN), which include screening recommendations for average- and high-risk groups (see Table 2.4) and polyp/cancer surveillance recommendations [60]. The British Society of Gastroenterology (BSG) and the Association of Coloproctology for Great Britain and Ireland (ACPGBI) published guidelines in 2010 [61] that update recommendations on screening, polyp surveillance, and cancer surveillance. The guidelines published by the European Commission [15] and the Australian guidelines [62] focus their recommendations on screening.

Diet and Lifestyle

There is little mention of diet or lifestyle modifications for the prevention of CRC in the US and European guidelines. The MSTF, ACG, NCCN, European Union (EU), and UK guidelines do not mention these interventions at all whereas the USPSTF guidelines point out that interventions such as avoidance of red meat and alcohol or consumption of a high-fiber diet have not been substantiated in trials, therefore cannot be recommended. In contrast, the Australian guidelines "strongly recommend" limiting alcohol consumption and restricting caloric intake, "recommend" engaging in physical activity, maintaining healthy body mass index, avoiding tobacco smoke, and restricting dietary fat to prevent CRC.

Average-Risk Screening

All guidelines define the "average risk" population as asymptomatic adults age 50 years or older without a personal or family history of colonic neoplasia or inflammatory bowel disease. There is a stark contrast in the approach to screening average-risk individuals in the US guidelines versus the non-US guidelines. In the USA, the general approach has been to support offering a variety of options, acknowledging differences in patient preferences and variable access to the different modalities. In the European and Australian guidelines, there is more of an emphasis

Table 2.4 Summary of US screening guidelines

		USPSTF	ACS/MSTF/ACR	ACG	NCCN
Average risk (no family history)	Age to screen	50–75 75–85: suggest stopping 85: stop screening	50-Individualized	50-Not specified	50-Not specified
	Test(s) (interval)	HS FOBT (annual) FS (q 5 year) + interval FOBT CS (q 10 year)	HS FOBT (annual) FS (q 5 year) CS (q 10 year)	CS preferred (q 10 year)	CS preferred (q 10 year)
FDR with early onset CRC (or adenoma)	Specifications	N/A	1 FDR with CRC or any adenoma age <60 or 2 or more FDR with CRC or any adenoma at any age	1 FDR with CRC or *advanced* adenoma age <60 or 2 or more FDR with CRC or any adenoma at any age	1 FDR with CRC age <50 or 2 or more FDR with CRC at any age
	Age to screen	N/A	40 or 10 years before CRC	40 or 10 years before CRC	40 or 10 years before CRC
	Test(s) (interval)	N/A	CS (q 5 years)	CS (q 5 years)	CS (q 3–5 years)
FDR with CRC (or adenoma) any age	Specifications	N/A	1 FDR with CRC or adenoma at any age	1 FDR with CRC or advanced adenoma at any age	1 FDR with CRC > 50
	Age to screen	N/A	40	50	50 or 10 years before CRC
	Test(s) (interval)	N/A	Any (average-risk interval)	CS (q 10 years)	CS (q 5 years)
SDR with CRC	Specifications	N/A	2 SDRs with CRC at any age	N/A	1 SDR with CRC < 50
	Age to screen	N/A	40	N/A	50
	Test(s) (interval)	N/A	Any (average-risk interval)	N/A	Per colonoscopy findings

USPSTF US Preventative Services Task Force, *ACS/MSTF/ACR* American Cancer Society/Multi Society Task Force/American College of Radiology, *ACG* American College of Gastroenterology, *NCCN* National Comprehensive Cancer Network, *HS FOBT* high sensitivity fecal occult blood test, *FS* flexible sigmoidoscopy, *CS* colonoscopy, *FDR* first-degree relative, *CRC* colorectal cancer, *SDR* second-degree relative

on participation in a "screening program" with a single option or limited options offered through their national health services.

The modalities supported by the ACS/MSTF/ACR guidelines include annual high sensitivity FOBT (HemeSensa or FIT) or stool DNA (the interval for stool DNA is not clearly specified). In terms of structural exams, the MSTF supports FS every 5 years, colonoscopy every 10 years, double-contrast barium enema (DCBE) every 5 years, or CTC every 5 years. The USPSTF does not recommend DCBE and concludes that there is insufficient evidence to support CTC or fecal DNA testing for routine screening but endorses annual HS-FOBT, FS every 5 years preferably with an interval high-sensitivity FOBT or colonoscopy every 10 years. Although the ACG supported the MSTF guidelines, they stated their updated society guidelines [63] that colonoscopy is the "preferred strategy," and lists FS (every 5–10 years), CTC (every 5 years), FOBT (annual), and fecal DNA (every 3 years) as acceptable alternatives. The NCCN also lists colonoscopy as a preferred option if it is available with annual FOBT, sigmoidoscopy (every 5 years), or the combination as alternatives.

FOBT every 2 years is the primary screening test recommended by the EU guidelines, the UK Bowel Screening Program, and the Australian guidelines. The Australian guidelines also include the option of adding FS every 5 years to an FOBT program. The non-US guidelines also emphasize quality metrics for overall screening programs such as invitation coverage, uptake rates, timeliness of testing/results, and compliance with colonoscopy after positive test.

The USPSTF guidelines do not recommend routine screening for individuals 75–85 years of age and explicitly recommend against routine screening in individuals older than 85. The MSTF advises that in older individuals, decisions about screening should be individualized balancing risk, benefits, and comorbidities. The other guidelines do not specifically address when to stop screening.

High-Risk Screening

Family History

Rationale

Approximately 30% of all CRCs have some familial component [64]. Two meta-analyses [65, 66] on this issue have reported a strikingly similar result with about a twofold increase in the risk of CRC in individuals with a single first-degree relative (FDR) with CRC and about a fourfold increased risk for those with at least two affected FDRs. The relative risk also increased as the age of the CRC in the relative decreased.

It is less clear if FDRs of individuals with adenomatous polyps are at a significantly increased risk of CRC. In the meta-analysis cited above [65], the relative risk

of CRC in FDRs of people with adenomatous polyps was increased (1.99; 95% CI 1.55–2.55) but these studies have been criticized as being flawed in design [67]. Since adenomas are so common, it seems unlikely that FDRs of anyone with an adenoma is at a substantially increased CRC risk but risk does appear to be increased in relatives of individuals with large or histologically advanced adenomas [68].

Data to Support Screening

There are no controlled studies available establishing the impact of screening individuals with a family history of CRC or adenomas on CRC incidence or mortality.

Guidelines

The USPSTF [59] does not make specific recommendations for screening in high-risk populations. The ACS/MSTF/ACR guidelines [35] categorize several groups as "high risk" based on family history. This group recommends that individuals with an FDR with either CRC or an adenomatous polyp before the age of 60 start CRC screening with colonoscopy at age 40 (or 10 years before the CRC diagnosis in their FDR) and the interval for follow-up should be every 5 years. Individuals with an FDR with CRC or an adenoma greater than age 60 or two second-degree relatives with CRC or adenomas are advised to initiate screening at age 40 using any MSTF recommended screening modality at standard intervals.

In contrast, the ACG [63] recommends that individuals with a single FDR older than 60 with CRC or adenomas undergo average-risk screening. For those with a single FDR with CRC or an *advanced* adenoma diagnosed under the age of 60 or two FDRs with CRC or advanced adenomas, the ACG recommends colonoscopy screening at age 40 (or 10 years younger than the youngest affected family member) with a 5-year surveillance interval. Additionally, the ACG identifies African Americans as a high-risk group and recommends initiating screening at age 45. The NCCN guidelines [60] are similar to those of the ACG except the age cutoff for high risk is CRC in a relative is 50 rather than 60 years.

The UK guidelines [61] differ substantially from the US guidelines. For individuals with one FDR with CRC diagnosed younger than age 50 or two FDRs diagnosed after age 60, the UK guidelines recommend colonoscopy once at age 55 and if normal, no follow-up. For those with two FDRs diagnosed with CRC younger than 60 or three FDRs diagnosed with CRC at any age, the UK guidelines recommend colonoscopy at age 50 and surveillance every 5 years.

The Australian guidelines recommend average-risk screening for individuals with a single FDR with CRC diagnosed after the age of 55. For individuals with one FDR diagnosed with CRC younger than 55, or two first- or second-degree relatives with CRC at any age, the Australian recommendation is to perform colonoscopy at the age of 50 or 10 years before the youngest family member's diagnosis at an interval of every 5 years.

Polyp Surveillance

Rationale

Individuals with colonic adenomas are at increased risk for developing metachronous adenomas or cancer compared with individuals without adenomas.

Data to Support Surveillance

Surveillance intervals should ideally be based on data demonstrating an impact on CRC incidence and mortality but the majority of data supporting surveillance focuses on findings of adenomas and advanced adenomas at follow-up examinations. Saini et al. [69] performed a meta-analysis of five studies and identified baseline colonoscopy findings associated with increased risk of advanced adenomas at follow-up. Individuals with three or more adenomas at baseline (when compared to those with one to two adenomas at baseline) and those with high-grade dysplasia (compared to those with low grade dysplasia at baseline) had an increased risk of advanced adenoma at follow-up (2.52; 95% CI, 1.07–5.97 and 1.84; 95% CI, 1.06–3.19, respectively). A pooled analysis [70] of eight prospective studies including 9167 patients with adenomas at baseline and follow-up colonoscopy within 3–5 years also found that the number of adenomatous polyps at baseline is associated with increasing risk of advanced adenoma at follow-up (one adenoma—8.6%, two adenomas—12.7%, three adenomas—15.3%, four adenomas—19.6%, 5+adenomas—24.1%, trend <0.001). Size of the largest adenoma at baseline (for polyps ≥20 mm OR 2.99; 95% CI, 2.24–4.00), presence of proximal adenoma (OR 1.68; 95% CI, 1.43–1.96), and baseline villous histology (1.28; 95% CI 1.07–1.52) were also independent risk factors for advanced adenomas at follow-up.

Although the data are limited, detection of an advanced adenoma on surveillance is a consistent risk factor for finding an advanced adenoma on the next examination, regardless of findings on index examination. After an index exam showing a "high-risk adenoma" (HRA; three or more adenomas, adenoma ≥10 mm, with villous features or high-grade dysplasia), "low-risk adenoma" (LRA; 1–2 tubular adenomas<10 mm), or no adenoma and a follow-up exam showing AA in each case, Pinsky et al. [71] reported a 19.3, 15.6, and 11.5% incidence of AA on second surveillance, respectively. In contrast, if both the baseline and surveillance colonoscopy showed no HRAs, the risk of advanced adenoma on the next surveillance examination was very low (3.1%) [71]. Laiyemo et al. [72] and Robertson et al. [73] reported similar results.

Sessile serrated polyps (SSPs; synonymous with sessile serrated adenomas (SSAs)) are increasingly being recognized as important malignant precursors. Approximately 20–30% of CRCs arise through the CPG island methylator phenotype (CIMP) pathway in which SSPs are thought to be the precursors [74]. CIMP-posi-

tive tumors account for a disproportionate percentage of interval cancers (cancers arising at or before next scheduled surveillance examination), particularly in the right colon [75]. Endoscopic features, such as bland color, flat contour, and poorly defined borders have rendered SSPs more difficult to detect and completely resect than conventional adenomas [76].

Schreiner et al. [77] demonstrated that patients with at least one nondysplastic serrated polyp in the proximal colon carried a significantly higher risk of synchronous advanced neoplasia (OR 1.90, 95% CI 1.33–2.70) and those with a serrated lesion ≥10 mm carried a 3.37 (95% CI 1.71–6.65) odds of synchronous advanced neoplasia. In addition, those with proximal nondysplastic serrated polyps at baseline were more likely to have advanced neoplasia at surveillance 5.5 years from the index exam (2.17, 95% CI 1.03–4.59).

Guidelines

The ACS/MSTF updated guidelines for colonoscopy surveillance in 2012 [78] and included, for the first time, guidelines for serrated polyps. The ACS/MSTF guidelines recommend a 5–10-year follow-up interval for individuals with one to two small (<10 mm) tubular adenomas at baseline. For individuals with three to ten small tubular adenomas at baseline or at least one adenoma ≥10 mm or an adenoma with villous features or high-grade dysplasia, the recommended surveillance interval is 3 years; those with more than ten adenomas are advised to have surveillance in less than 3 years and be evaluated for the possibility of a polyposis syndrome. The recommendation for patients with SSP(s) <10 mm with no dysplasia is to repeat colonoscopy in 5 years and those with SSP(s) ≥10 mm, those with dysplasia or any traditional serrated adenomas should undergo surveillance at 3 years. In terms of follow-up after initial surveillance, the MSTF recommends that patients with an LRA at baseline and HRA, LRA, or no adenoma at surveillance should undergo second surveillance at 3, 5, and 10 years, respectively. Those with HRA at baseline and HRA, LRA, or no adenoma at surveillance should undergo second surveillance at 3, 5, and 5 years, respectively. The NCCN surveillance guidelines are similar to those of the ACS/MSTF.

In contrast to the US guidelines for polyp surveillance summarized above (see Fig. 2.4), the BSG divides baseline findings into "low risk" (one to two adenomas <10 mm), "intermediate risk" (three to four adenomas <10 mm or at least one adenoma ≥10 mm), and "high risk" (≥5 adenomas <10 mm or ≥3 adenomas with at least 1 ≥10 mm) findings. The guidelines recommend that individuals with low-risk findings undergo either no surveillance or a repeat examination in 5 years, individuals with intermediate risk findings undergo surveillance at 3 years, and those with high-risk findings undergo surveillance in 1 year.

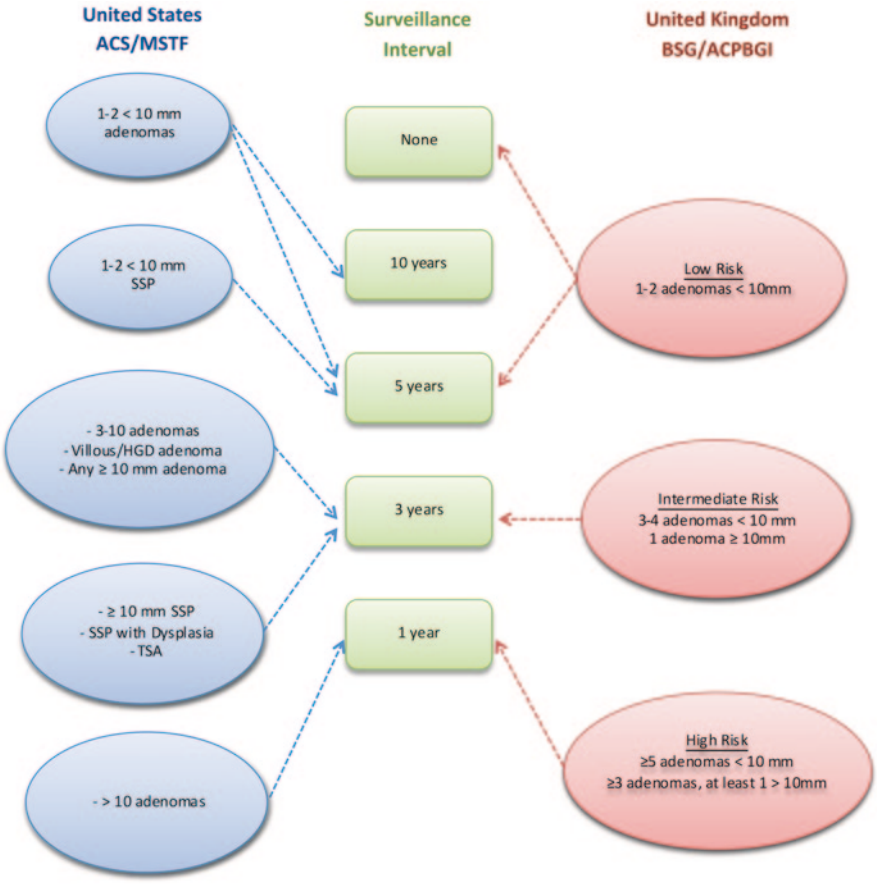

Fig. 2.4 Comparison of the US and UK polyp surveillance guidelines. Recommended colonoscopy surveillance interval based on findings on index colonoscopy

Cancer Surveillance

Rationale

Synchronous cancer (two or more simultaneous primary tumors not due to direct extension/metastasis) occurs in 2–5% of patients diagnosed with CRC [79, 80] and synchronous adenomas are present in at least 30% of these patients. Metachronous lesions (nonanastomotic new lesions developing at least 6 months after initial diagnosis) develop in 1.5–3% of patients in the first 3–5 years after surgical resection [79, 81–88]. More than half of these lesions arise within the first 2 years post resection [82, 84, 86], suggesting that they may have been missed synchronous cancers. Anastomotic recurrence occurs in 2–4% of patients with CRC, with higher rates of

recurrence in patients with rectal cancer [82, 84, 89–93]. More than 80% of anastomotic recurrences occur within the first 2.5 years post resection [84, 85].

Data for Surveillance

There is a clear benefit for colonoscopy surveillance post-cancer resection for detecting metachronous cancers and adenomas. The majority of metachronous cancers detected by surveillance are early stage (65% are Dukes stage A or B) [82, 84–86, 94–97], asymptomatic (56%) [82, 84, 85, 90, 94, 98, 99], and potentially surgically curable (87%) [84, 85, 89, 90, 94–98].

On the other hand, neither prospective randomized trials [82, 89, 100] nor meta-analyses [101] have found a benefit of shorter colonoscopic surveillance intervals (1 year) compared to longer intervals (3–5 years) for CRC recurrence after resection. This is likely because anastomotic recurrences are uncommon and most patients with anastomotic recurrence also have other sites of metastatic disease.

Guidelines

The ACS/MSTF published guidelines for colonoscopy surveillance after cancer resection in 2006 [102]. These guidelines recommend "clearing colonoscopy" preoperatively if possible or within a few months of resection. Colonoscopy should subsequently be performed 1 year post resection then 3 years later then every 3–5 years depending whether adenomas are found. Given the higher risk of recurrence in rectal cancer, rectal surveillance (usually via sigmoidoscopy) should be performed every 3–6 months for the first 2–3 years post resection. The NCCN guidelines are similar to those of the ACS/MSTF except that they recommend another annual colonoscopy if an advanced adenoma is found at the 1 year postresection colonoscopy.

In contrast, the UK guidelines recommend colonoscopic surveillance 5 years after surgery and every 5 years thereafter.

Current Screening Practices Around the World

The approach to screening in the USA is very different from approaches in the rest of the world. Screening in Europe and Australia is usually included as part of a national health program which typically offers a single or limited screening strategy, in most cases FOBT. In the USA, a variety of options are included in national guidelines with an emphasis on individualizing the screening approach based on local expertise, access to specialty care, and patient preference. Despite these options, about 80% of all screening in the USA is done by colonoscopy, in part because

there are substantial incentives for colonoscopic screening for both the primary care provider (PCP) and endoscopist. Colonoscopy is the one screening test that examines the entire colon and allows polypectomy during the same procedure and many PCPs believe that it is superior to the other CRC screening approaches [103]. If colonoscopy is negative, no further CRC screening is needed for 10 years and the responsibility for follow-up is shared with the endoscopist. There are strong financial incentives for the endoscopist to offer colonoscopic screening since screening colonoscopies are covered by almost all insurance plans in the USA and they are well reimbursed. Colonoscopy accounts for a large proportion of the average US gastroenterologist's revenue stream.

In contrast, there are few disincentives to colonoscopy screening in the USA. One would think that cost would be a major issue; however, cost-effectiveness models have argued that the increased cost of colonoscopy is justified by its estimated increased effectiveness. There are, however, a number of trends in the use of colonoscopy that are impacting its cost-effectiveness in a negative manner. The increase in ADRs will identify a larger portion of the screened population that will require more frequent surveillance and increase the pathology costs associated with colonoscopy. The tendency of endoscopists to schedule follow-up colonoscopies at intervals substantially shorter than the guidelines recommend [104] and the increasing use of monitored anesthesia care for routine colonoscopies also increases overall cost. Interestingly, all screening and preventive approaches look more attractive [105] and even cost-effective [106] as the cost of CRC treatment with the addition of biologics has skyrocketed.

Conclusions

Colon screening is arguably one of the greatest cancer prevention success stories of the past 25 years. Although CRC mortality is falling in many Western countries, the USA is the only country in which both incidence and mortality have been steadily falling for the past 30 years and much of this is likely due to screening. Screening rates are currently more than 60% in the USA and are continuing to increase (Fig 2.1). Conceptually, the field appears to be moving from early detection of CRC to identification and removal of precancerous colonic polyps. There is robust evidence to support FOBT and FS as primary screening modalities and indirect evidence to support colonoscopic screening. International guidelines focus on a screening program as a whole and generally support a single screening strategy (FOBT in most cases) while US guidelines support a variety of options including stool-based tests (FOBT, FIT, fecal DNA) and structural tests (DCBE, CTC, FS, colonoscopy). Colonoscopic screening has become the dominant screening modality in the USA. There are several trials underway to investigate the efficacy of colonoscopy but will not be completed for at least another 10 years. Despite drawing on the same evidence, the US guidelines tend to be more aggressive in screening and surveillance when compared to international guidelines.

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