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USPSTF issues draft recommendations on screening for colorectal cancer

November 2020

On October 27, the U.S. Preventive Services Task Force (USPSTF) posted a draft recommendation statement suggesting that colorectal cancer (CRC) screening should start at age 45. This is a classified as a “B” recommendation, meaning that the USPSTF recommends the service and that there is high certainty that the net benefit is moderate. These draft recommendation apply to all adults without symptoms and who do not have a personal history of colorectal polyps or family health history of genetic disorders that increase the risk of developing CRC.

The Task Force continues to strongly recommend that people who are 50 to 75 years old undergo screening. This is an “A” recommendation, indicating that the USPSTF recommends the service and that there is high certainty that the net benefit is substantial.

For individuals aged 76 to 85, the Task Force continues to recommend that the decision to be screened should be made on an individual basis. This is a “C” recommendation, meaning that clinicians may suggest the service to selected patients depending on individual circumstances, but for individuals without signs or symptoms there is likely to be minimal benefit from this service.

Why the updated recommendations?

CRC remains the third-leading cause of cancer death in the U.S. Despite very strong evidence that demonstrates the effectiveness of screening, many people aged 50-75 have never been screened. Trends in CRC incidence show that CRC is increasingly occurring among younger adults, especially African-Americans who experience higher mortality from the disease.

The draft recommendation recommends direct visualization tests such as colonoscopy and stool-based tests such as FIT to screen for CRC. The pros and cons of each test should be discussed between primary care physicians and their patients to help decide which test would best attend each individual’s needs.

Take home message:

Trends in CRC incidence have driven the change to USPSTF screening guidelines, which recommend that screening should now begin at age 45 instead of 50. These guidelines apply to individuals without CRC symptoms who do not have a personal history of colorectal polyps or a family health history of genetic disorders that increase the risk of CRC.
AI-powered clinical trial tool connects young, underserved patients with CRC to treatments and research
November 2020

*Clinical Trial Finder* is an artificial-intelligence (AI)-powered web-based platform that helps patients with colorectal cancer (CRC) connect to relevant clinical trials that fit their unique disease profile. The platform is the result of collaboration between the non-profit organization Colorectal Cancer Alliance and the digital health company, TrialJectory.

The platform uses a series of questions in order to help customize and populate a list of clinical cancer trials that are relevant to each patient. *Clinical Trial Finder*’s AI technology is able to curate, structure, and personalize data and literature produced from clinical cancer research and help orient patients to find the most appropriate clinical trial. The platform is also capable of connecting patients to clinical trial specialists who can help them navigate the clinical trial process.

According to Colorectal Cancer Alliance, while large research hospitals are better able to offer patients with cancer the latest and most effective treatment options through clinical trials, younger patients or patients who are treated mainly through community health centres might not be exposed to the same treatment options. About 70% of people who use the platform are being treated in community cancer centres, which typically refer patients to clinical trials as treatment options only about 10% of the time. As such, using the platform could help to improve awareness and access to advanced treatments and better therapeutic options.

**Take home message:**

Depending on where a person with cancer is being treated, they may not be exposed to clinical trials as a possible treatment option. The emergence of AI-powered platforms such as *Clinical Trial Finder* can be helpful in connecting individuals with the latest and most effective treatment options through clinical trials regardless of their primary treatment centre.

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Should patients with a complete response to neoadjuvant chemoradiation for rectal cancer also undergo surgery?
November 2020

According to findings from a new study presented at the virtual 2020 American Society for Radiation Oncology (ASTRO) Annual Meeting, the non-surgical management or “watch-and-wait” approach for rectal cancer that preserves quality of life may be a safe treatment option for rectal cancer patients with a complete response to neoadjuvant chemoradiation.
selected patients.

Currently, the standard treatment for most rectal cancers in the US and Canada begins with neoadjuvant chemoradiation given before the primary treatment, followed by surgery to remove the rectum and surrounding tissues, followed by adjuvant chemotherapy given after the primary treatment to kill any remaining cancer cells.

The “watch-and-wait” approach, in contrast, begins with chemoradiation followed by strict patient surveillance to monitor cancer recurrence for a determined period of time. Surgical removal of the rectum and surrounding tissues is omitted, therefore avoiding potential life-changing side effects including loss of control bowel movements and bladder function, sexual dysfunction, and the strong possibility of requiring a permanent colostomy. Senior study investigator Vikram Attaluri, MD, notes that while rectal cancer surgery is very good for a cure, the side effects can have a massive impact on a patient’s quality of life: “…someone could be living with a bag outside their body for the rest of their life...Some patients have indicated they would rather live with cancer.”

In order for patients to be eligible for “watch-and-wait”, they must achieve a complete clinical response, or have no visible tumour several months after their initial chemoradiation therapy. Dr. Attaluri says that the number of rectal cancer patients that qualify may be less than 20%, though this percentage is on the rise as more patients receive more effective neoadjuvant treatments.

Based on their findings, the investigators suggest that the watch-and-wait approach appears to be the safest among patients with stages I and II rectal cancer. Patients with stage III rectal cancer experienced higher mortality rates after 3 years, with the exception of those that received oxaliplatin-based intravenous chemotherapy. Rectal magnetic resonance imaging is recommended to confirm a complete treatment response. Despite being considered an experimental treatment approach, some specialists in colorectal surgery suggest that there is sufficient evidence to support the use of this alternative approach to eligible patients.

Watch-and-wait surveillance includes monitoring every 3 months for the first 2 years after initial chemoradiation therapy, then every 6 months for the next 3 years, and then annually thereafter.

Take home message:

The non-surgical or “watch-and-wait” approach to rectal cancer may be a valuable, quality of life-preserving alternative for patients with no visible remaining tumours following initial treatment with chemoradiation therapy.
“Test all patients with cancer”: 1 in 8 have inherited mutations  
November 2020

Findings from a recent study conducted by the Mayo Clinic found that while about 1 in 8 patients with cancer have an inherited genetic mutation that likely contributed to the development of their cancer, nearly half of these mutations would have been missed under current clinical guidelines.

The study was the largest of its kind, including approximately 3000 patients with a wide range of cancer stages and types. The findings demonstrate that current clinical practice guidelines do not sufficiently prioritize genetic testing, which can shed light on more effective management strategies specific to the individual.

In the study, 2984 patients with cancer who were receiving treatment for a variety of cancer types were included. All patients were tested for about 84 genes using Next Generating Sequencing (NGS), a type of DNA sequencing technology that rapidly scans the entire human genome for mutations. Patients who tested positive for known cancer mutations were offered genetic counselling, which was also offered to their family members. A significant advantage of genetic testing is that family members can be alerted to specific mutations that could lead them to participate in screening to detect early forms of cancer. Based on the results of their genetic testing, patients were offered changes to their treatment for which they may otherwise have not been eligible, including changes to surgical management, immunotherapy, or enrolment in a clinical trial.

Currently, genetic testing is underused in cancer care, often as a result of out-dated guidelines that limit testing to a narrow group of high-risk patients, such as those with inherited disorders such as Lynch Syndrome. Cost has also been a limiting factor to wider access, though with the advent of automatic genetic testing technologies such as NGS, the previously high cost of performing genetic testing manually has decreased significantly.

Lead researcher Niloy Samadder, MD, from the Mayo Clinic states that the Mayo Clinic will be changing its clinical practice at all four of its cancer centers, offering every cancer patient genomic evaluation, including genetic testing to screen for any underlying genetic mutations. This information will then be used to help clinicians decide how to design the best surgical and treatment options for that patient and their family.

**Take away message:**

In the era of precision medicine, genetic testing in cancer care should no longer be restricted to a small subset of high-risk patients. With the advent of automated technologies including Next Generation Sequencing that help to minimize cost barriers, all patients with cancer should undergo genetic testing to identify mutations that could enable them to access more tailored and effective treatments.
New predictive test gains momentum with 2 positive studies in localized colon cancer
November 2020

Immunoscore® is a novel test used to estimate a cancer patient’s prognosis based on how well the body’s immune cells, namely white blood cells, surround and enter a tumour. The technology can help to refine a patient’s prognosis, particularly among patients with stage II colon cancer with “high risk clinical features”, and offer further information to aid in decision-making about best treatment. When used together with the Tumour, Node, Metastasis (TNM) scoring system – the most common method used to assist in staging solid tumours - Immunoscore® appears to be a valid method of predicting a patient’s risk of recurrence, helping to develop a more personalized approach to treatment.

The test provides a score, which can be high or low. The resulting score may be referred to as a biomarker. A high Immunoscore indicates a high level of immune cell infiltration, which tells clinicians that a patient’s immune system is actively involved in fighting the cancer cells and there is a lower risk for cancer recurrence. In contrast, a low Immunoscore indicates that a patient’s
immune system is not as active in destroying the tumour and therefore suggests a higher risk of recurrence.

New findings from a study presented at the 2020 ASCO Quality Care Symposium demonstrated that Immunoscore could improve a patient’s care by reducing unnecessary adjuvant chemotherapy by providing more tailored treatment to individuals. Further evidence to support the clinical value of the test was published in the *Journal of Clinical Oncology*. Immunoscore was also found to provide valuable insight into disease recurrence and the use of adjuvant chemotherapy among patients with stage III colon cancer.

The effectiveness of the Immunoscore test continues to be evaluated in ongoing clinical trials assessing its role as a prognostic tool in patients’ response to treatment across various tumour types.

**Take away message:**

The Immunoscore test is a tool that can help clinicians gain valuable insight into a patient’s disease outcomes (prognosis) by examining how well the body’s immune cells are able to surround and infiltrate the tumour microenvironment. Multiple studies have provided evidence to support its use as a prognostic factor, especially in stage II and low-risk stage III colon cancer.
Based on the long-term results from the phase III randomized OSLO-COMET trial, minimally invasive laparoscopic surgery appeared to be just as effective as open surgery among patients with colorectal liver metastases. Additional benefits of laparoscopic surgery include fewer surgical complications, improved quality of life following surgery (reduced postoperative pain and reduced hospital stay), reduced cost and resulted in similar 5-year life expectancy compared to open surgery. 5-year overall survival for patients who underwent open liver resection was 55%, compared to 54% among those who underwent laparoscopic resection. Relapse-free survival was 36% for patients who underwent open surgery, compared to 30% among those who underwent laparoscopic surgery.

The OSLO-COMET study is the first of its kind to examine laparoscopic liver resection in a randomized setting. Further research will aim at exploring new aspects of minimally invasive liver surgery, to help make complex surgeries less invasive as possible to improve patients’ quality of life.

**Take away message:** Minimally invasive laparoscopic surgery to remove colorectal cancer liver metastases appears to be just as effective as open surgery, with similar disease outcomes, fewer surgical complications, improved patient quality of life, and better cost-effectiveness.
• Increase efficiency of the drug development pathway and timely access to cancer therapies for patients, promoting patient-centered care in the era of precision medicine
• Promote collaboration between patient groups, health agencies, and stakeholders such as pharmaceutical and tech companies
• Support effective patient group participation in clinical trial design and implementation, encouraging their input and active participation
• Encourage the collection and use of real world data (RWD) and real world evidence (RWE) to generate more generalizable data to reflect the true effects of therapies in everyday clinical practice (the “real world”, compared to the highly controlled environment of clinical trials)

Key questions:

• How can the Charter help to inform an organization’s patient engagement model?
• How can the way an organization operates be better influenced by patient engagement?

Speakers: Judy Needham and Stephen Sundquist

Take away message:

Patient engagement in cancer research is two fold: patients as participants, and patients as partners, with the focus today leaning increasingly towards the latter. The future of cancer research should be involving patient partners throughout all phases of research, from determining how the research question can be delivered to collecting more patient-oriented evidence – evidence that measures things that a patient would care about such as symptoms, quality of life, costs, morbidity and mortality, length of stay.

Speaker: Stephen Lemery
International Regulatory Collaboration

Take away message:

Project Orbis is an example of an international collaboration in drug development. Benefits include reducing costs of development, fostering similar standards of care globally, as well as faster clinical trial processes, especially for rare diseases or mutations. It is a framework for parallel submission and review of oncology products among participating international partners (so far, Project Orbis is a collaboration between the US, Canada, Australia, Singapore and Switzerland).

Speaker: Murray Aitkin
Advancing RWE use in support of Precision Medicines

Take away message:
The migration towards precision medicine has created greater demand for evidence from small and more diverse subgroups of patients. Today, there are increasing options available to meet these demands for high quality data, with a greater number of data sources (ex. digital health records and patient-reported evidence) and more sophisticated data technologies to integrate RWD and RWE to better inform drug development decisions.

**Speaker: Michael Seewald**  
*Using RWE to inform value-based agreements*

**Take away message:**

RWE can be used to better understand real world treatment patterns to confirm the value of patients’ access to drug therapies. Encouraging strong stakeholder collaboration can help to improve patient outcomes and deliver better value to the healthcare system.

**Speaker: Melissa Hunt**  
*Health Canada’s experience with Project ORBIS*

**Take away message:**

The goal of Health Canada is to improve access to prescriptions medications by expanding collaboration with health partners to facilitate more timely access to drugs and devices. Through international collaborations such as Project Orbis, there is increased global alignment and the expediting of the availability of critical drugs to patients when they need them. Furthermore, international collaborations enable better sharing of information and resources, a reduction of duplicated submissions to sponsors, and faster review times without compromising high international standards.

**Speaker: Margaret McCusker**  
*Real World Evidence and Precision Medicine*

**Take away message:**

Complexity of oncology treatment necessitates new and better sources of high quality evidence including RWE. It is estimated that only 8% of US adult patients with cancer enrol in clinical trials, leaving a large, unmet need among patients who are not enrolled. It is essential to understand the benefits and harms of drugs in everyday practice in real world populations. The Flatiron Network of community and academic practices aims to build an evolving database of RWD and RWE to help advance health care delivery and increase both the extent and rate of drug access for specific patient populations.

**Speaker: Mackenzie Wildman**
Novel approaches to precision medicine: Data collection in the wild

Take away message:

Patients and their outcomes have historically been characterized using limited, visible-to-the-system data, such as those collected in clinical trials. “Invisible data” or RWD, includes those that are collected passively and continuously in everyday life, collected directly from individuals that are universal but remain largely inaccessible to healthcare systems. Patient generated health data (ex. data collected using wearable devices) provides new ways of measuring health to better diagnose, predict and treat disease.

Speaker: Lillian Siu
Rethinking Clinical Trials in the Era of Precision Cancer Care

Take away message:

As oncology continually evolves towards increasingly tailored approaches to treatment, it is important that clinical trials reflect the diversity of patients and their needs (“smart” clinical trials). Rare diseases make it very hard to conduct large randomized clinical trials, stressing the importance of RWD/RWE to investigate patient access and treatment effectiveness. Clinical trial navigators are a critical feature of a precision medicine approach, helping to best coordinate care among patients and their local oncologists.

Speaker: Kam Kafi
Artificial intelligence: turning data into knowledge

Take away message:

Artificial intelligence (AI) has the potential to increase our human capacity in accelerating operations and informing healthcare procedures by saving time, cost and effort. AI together with the increasing adoption of virtual health approaches, including telemonitoring to improve patient adherence to therapies, can be integrated to produce better digital analytics including RWD collected via patient reported outcomes or wearables. Improved databases and computer systems can be used to make better predictions or decisions about a specific health-related task, with minimal cost and human effort.

Speaker: James Creeden
Impacting patients with innovative data products

Take away message:

While the gold standard of clinical data remains that which is collected from randomized controlled trials, this data is not largely generalizable and does not represent the majority of cancer patients’ experiences. RWD carries less scientific strength and validity, it is able to include larger sample sizes, longer follow-up, better side effect profiles in real world settings, and more realistic expectations of how a drug will affect specific patients. Organizations such as Foundation
Medicine or Flatiron Health aim to provide harmonized and curated molecular and clinical data (Clinico-Genomics Database), combining the genomics of patients with their clinical therapeutic regimen to increase the efficiency of healthcare delivery, better treatment access and disease prediction capacity.

**Speaker: Aaron Leibtag**  
**Pentave AI technology**

**Take away message:**  
AI can help to change economics and possibilities, to benefit patients and support regulatory decisions. It can enable evidence and insight at very large scales that might not have been possible previously due to human constraints. With the advent of precision oncology, there is a large unmet need for studies dedicated to rare diseases and tumor types – something that would demand incredible amounts of time in order to gather sufficient results through traditional pathways. AI can help to drive down the currently unsustainable costs of bringing drugs to patients, opening doors to diverse stakeholders united to drive solutions.

**Speaker: Christopher McCabe**  
**Research oriented market access**

Drug programs face increasing budgetary pressures and strong evidence helps to support investment and disinvestment decisions. Cost-effectiveness analyses help to inform these decisions, but available evidence often leaves decision makers highly uncertain and further evidence is often expensive to generate. The Institute of Health Economics proposes a research-oriented market access (ROMA) protocol to assess the value of generating RWE within a life cycle health technology assessment framework, which builds upon existing health technology assessment methods for the assessment of the value of new technologies.

**Final takeaway message:**

The era of precision medicine in oncology is uncovering the large, unmet need for a greater diversity of high-quality data that more accurately reflects the real world experience of patients, especially those with rare mutations and diseases. Positioning patients at the centre of cancer care means involving them as partners in cancer research and throughout the clinical trial continuum. Novel technologies for real world data collection used in tandem with innovative stakeholder collaborations could help to improve the overall efficiency of healthcare delivery, increase patient access to necessary medications and advance disease prediction capacity.