2.1: Hi. I’m Paul Limburg, the Chief Medical Officer, for Screening at Exact Sciences.

2.2: I’m a board-certified gastroenterologist with over 20 years of experience in clinical practice. I also received training in preventive oncology, and have research interests in cancer screening, chemoprevention, and epidemiology.

2.3: I have a particular passion for colorectal cancer screening, and I’m proud to serve Exact Sciences, providers, and patients by leading our medical affairs screening endeavors.

2.4: It’s unnerving to know that, with proper screening, colorectal cancer is preventable[[1]](#footnote-1) , yet millions of adult Americans are not being screened as recommended. [[2]](#footnote-2)\*† As a result, colorectal cancer has remained the second leading cancer killer in the U.S.[[3]](#footnote-3)

2.5: I’m in the Exact Sciences Laboratories clinical facility, bearing witness to the enormity of efforts underway at Exact Sciences to screen eligible patients for colorectal cancer.

2.6: Recently, there was a recommendation update published by the U.S. Preventive Services Task Force regarding colorectal cancer screening. As with previous recommendations from this group, multiple colorectal cancer screening strategies are included, including colonoscopy, CT colonography, flexible sigmoidoscopy, FIT/HSgFOBT, and sDNA-FIT[[4]](#footnote-4), also known commercially as Cologuard®.

3.1: Before I go into the details of how the USPSTF recommendation has changed, it’s important to understand a bit of background on the Task Force.

3.2: The U.S. Preventive Services Task Force, or USPSTF, is an independent, volunteer panel of 16 national experts recognized in prevention, evidence-based medicine, and primary care. They are appointed by the Director of the Agency for Healthcare Research and Quality (AHRQ) and serve 4-year terms.[[5]](#footnote-5)

3.3: According to the U.S. Preventive Services website, the Task Force works to improve the health of all Americans by making evidence-based recommendations about clinical preventive services.[[6]](#footnote-6) They provide recommendations on preventive services including counseling, preventive medication, and screening, which aims to update topics every 5 years unless major new evidence warrants a faster cycle.6

3.4: When making a preventive service recommendation, the USPSTF assigns a letter grade (an A, B, C, or D grade or an I statement) based on the quality of the evidence and the balance of benefits and harms of a preventive service offered in the primary care setting or services referred by a primary care clinician.[[7]](#footnote-7),[[8]](#footnote-8)

3.5: While the main audience for Task Force recommendations is the primary care clinician, the recommendations also have relevance for and are widely used by policymakers, managed care organizations, public and private payers, quality improvement organizations, research institutions, and patients.8

3.6: Most private insurance plans are required to cover preventive services that receive a grade of A or B from the Task Force without cost-sharing, but coverage and costs are not considered in assigning grades to preventive services. Coverage decisions are determined by payors and policymakers.[[9]](#footnote-9)

4.1: The USPSTF released their final 2021 recommendation statement in May this year. The last update was in 2016.

4.2: Here is what changed…

4.3: The biggest shift is the age to begin screening. The USPSTF recommends that colorectal cancer screening begin at age 45 for individuals at average risk for developing colorectal cancer.[[10]](#footnote-10)

4.4: This recommendation is a part of a growing trend as other national organizations have made similar recommendations to reduce the age to begin screening in adults at average risk to 45 because colorectal cancer incident is increasing in patients younger than 50 and patients are diagnosed with more advanced stages of cancer.[[11]](#footnote-11),[[12]](#footnote-12),[[13]](#footnote-13)

4.5: It is also worth noting that USPSTF recommends multiple colorectal cancer screening tests. They are untiered and stand equitably as options for screening eligible adults.[[14]](#footnote-14)

4.6: According to the American Cancer Society Guidelines published in May 2018, there was approximately a 51% increase in colorectal cancer among patients younger than 50 years in a 20-year time period between 1994 and 2014.[[15]](#footnote-15)

4.7: A separate study showed that among patients younger than 50 years who were diagnosed with colorectal cancer between 2004 and 2015, more than half (51.6%) were diagnosed with more advanced stages of cancer (stage III/IV) vs patients older than 50 years (40%).[[16]](#footnote-16)

4.8: It is well documented that colorectal cancer survival rates can be impacted by the stage at diagnosis.[[17]](#footnote-17)

4.9: The evolution of a benign adenoma to early colorectal cancer is believed to typically take more than 10 years, which provides an important window of opportunity to find and remove adenomas or to find early-stage colorectal cancer.[[18]](#footnote-18)

4.11: Data from the National Cancer Institute’s Surveillance, Epidemiology, and End Results, or SEER database, show that 5-year relative survival rates change with the stage of diagnosis.[[19]](#footnote-19)

4.12: Localized colorectal cancer has ~90%\* 5-year survival rate, while colorectal cancer that has spread to distant parts of the body such as the liver, lungs, or distant lymph nodes has ~14% 5-year survival. [[20]](#footnote-20),[[21]](#footnote-21)\*

4.13: What’s the take-away here? The USPSTF nowrecommends to start screening patients at 45 and older.[[22]](#footnote-22) This is important because colorectal cancer incidences is increasing in patients younger than 50[[23]](#footnote-23) and patients are diagnosed with more advanced stages of cancer.[[24]](#footnote-24)

5.1: Despite efforts among public health officials, primary care providers, gastroenterologists, advocacy organizations, and many other allied health professionals to increase awareness about the importance of colorectal cancer screening, colorectal cancer remains the second leading cause of cancer mortality in the United States.[[25]](#footnote-25)

5.2: Stated differently, A preventable cancer remains the second cause of cancer mortality in our country.25† The American Cancer Society estimates that 52,980 people will die from colorectal cancer in 2021.25

5.3: We know that screening can make an impact on cancer mortality.[[26]](#footnote-26) Unfortunately, 44 million adults aged 45-74 years at average risk for colorectal cancer are eligible but not up to date with current screening recommendations.[[27]](#footnote-27)\* To put that into perspective, there are more, average risk adults whom are due for screening than the entire population of California, our country’s most populous state.[[28]](#footnote-28)

5.4: As a practicing gastroenterologist, it’s jarring to hear that millions of eligible adults are not getting screened, especially when the benefit of screening is well documented.[[29]](#footnote-29) Providers often offer screening during routine wellness visits, however the colorectal cancer screening rate hovers around 67%.[[30]](#footnote-30)† Why is this?

5.5: In one study of 483 patients conducted prior to the COVID pandemic 198, described some type of barrier when asked the open-ended question, “what barriers or things got in the way of being screened” [[31]](#footnote-31)‡

5.6: Nearly a third of respondents (29.5%) mentioned fear or worry, which ranged from general fear to more specific concerns about the procedure, sedation and the possible test outcome.31‡

5.7: Other responses included logistic challenges with screening (19.1%), that screening was a low priority (15.8%), discomfort or disgust with the procedure (11.5%) or the bowel preparation for colonoscopy (6.6%).31‡

5.8: Perceived barriers may lead to nonadherence,it’s important to identify a screening option that is appropriate for each individual based on their own preferences.31‡

6.1: There are multiple test options for colorectal cancer screening, and published evidence has shown that when patients are given a choice of two screening options, adherence rates nearly double.[[32]](#footnote-32)

6.2: Dr. John Inadomi and his colleagues published a study involving patient choice in *Archives of Internal Medicine* in 2012. They randomized 997 patients ages 50-79 with average risk of colorectal cancer to one of three study arms.

6.3: Patients were given an initial colorectal cancer screening recommendation of fecal occult blood test (FOBT), colonoscopy, or their choice of the two tests.

6.4: When patients were offered colonoscopy alone, just 38% were screened at 1-year.32\*

6.5: In the choice arm, sixty-nine (69%) percent (n=221/321) patients who were given a choice between two different colorectal cancer screening modalities (FOBT or colonoscopy) completed their screening within 1 year.

6.6: Of patients who were recommended FOBT stool testing, sixty-seven (67%) percent (n=231/344) were adherent with screening.

6.7: There was a thirty-one percent (31%) absolute increase in patient adherence in the choice arm vs. for patients who were offered colonoscopy alone.

6.8: It is interesting to note that the investigators thought patient adherence would decrease if patients were given a choice of tests, but this hypothesis did not bear out.32

6.9: These results support offering test choices to patients when making colorectal cancer screening recommendations.

7.1: Since the mt-sDNA test, or Cologuard, was launched, more than five million patients have been screened with this test nearly half of whom self-report that they have never been screened before.[[33]](#footnote-33)† I want to share one example of a previously unscreened patient, recounted firsthand

7.2: “This story reflects one individual’s experience. Not every person will have the same treatment, experience, outcome, or result. Cologuard is prescribed by a health care provider.

Visit www.Cologuard.com for important risk information and more information about Cologuard. “

I wanted to come down and write this letter because their work matters so much. And I just want to thank everyone at Exact Sciences and Cologuard for what they do.

Last year, a friend and I attended the Cologuard Classic. As a 52-year-old male, I knew I’d need a colonoscopy at some point, but had heard the stories of the prep, etc. I wasn’t very excited to get one and had been putting it off. When my doctor and I were talking during a checkup last Fall, he suggested a Cologuard test since I was resistant to a full colonoscopy. I take the Cologuard test, it comes back positive. Not to worry, said the doctor, but you do need a full colonoscopy. I found out I had a big tumor completely blocking my colon.

December 7th was my surgery. The tumor was so large, sorry, the tumor was large, so the laparoscopic procedure became a regular surgery. After the surgery, I woke up and I asked the doctor, “how did it go?” He said, “we’ll know when the pathology comes back.” I said “you’ve gotta give me more than that, doc. How did it go?” And he said, “quite frankly Scott, we have concerns.” And that’s when it really got dark. The pathology came back and it was negative for spread. They got all the cancer. Not kidding, this screening changed the course of my life. I may not be here. I might have been in radiation or chemo right now. And because of Cologuard, I’m not.

I’m so thankful for what you do. Wishing you all great success at your event this week, and with utmost respect and gratitude. And I signed my name, Scott.

7.3: I’ve tried to share my passion for the importance and the impact of colorectal cancer screening. The message I want to deliver is simply this:  The evidence is clear.  It’s time to think differently about colorectal cancer screening, we should be offering choices starting at age 45 to average risk patients. Think about the incredible difference we can make by better enabling patients to make an informed decision about how they prefer to get screened.[[34]](#footnote-34),[[35]](#footnote-35)\* When we give patients options, they are far more likely to choose, and complete, a colorectal cancer screening strategy that works for them.[[36]](#footnote-36) Conversely, when we use a “one size fits all” approach, too many patients make no screening choice34, and not screening can lead to incident, and sometimes even fatal, colorectal cancers that might have otherwise been avoided.[[37]](#footnote-37),[[38]](#footnote-38)†

7.4: At Exact Sciences we aim to help minimize the burden of cancer, motivated by trying to improve the health of the people that we serve. We want to empower people with information, so they can make more informed decisions.

7.5: Thanks for watching this presentation. We invite you to join us in our mission, helping to spread the message that there is more than one option for effective colorectal cancer screening, and encouraging patients to choose a test that they will complete.

8.0: Cologuard is intended for the qualitative detection of colorectal neoplasia associated DNA markers and for the presence of occult hemoglobin in human stool. A positive result may indicate the presence of colorectal cancer (CRC) or advanced adenoma (AA) and should be followed by diagnostic colonoscopy. Cologuard is indicated to screen adults of either sex, 45 years or older, who are at typical average risk for colorectal cancer. Cologuard is not a replacement for diagnostic colonoscopy or surveillance colonoscopy in high-risk individuals

Cologuard is not for high-risk individuals, including patients with a personal history of colorectal cancer and adenomas; have had a positive result from another colorectal cancer screening method within the last 6 months; have been diagnosed with a condition associated with high risk for colorectal cancer such as IBD, chronic ulcerative colitis, Crohn’s disease; or have a family history of colorectal cancer, or certain hereditary syndromes.

Positive Cologuard results should be referred to diagnostic colonoscopy. A negative Cologuard test result does not guarantee absence of cancer or advanced adenoma. Following a negative result, patients should continue participating in a screening program at an interval and with a method appropriate for the individual patient.

False positives and false negatives do occur. In a clinical study, 13% of patients without cancer received a positive result (false positive) and 8% of patients with cancer received a negative result (false negative). The clinical validation study was conducted in patients 50 years of age and older. Cologuard performance in patients ages 45 to 49 years was estimated by sub-group analysis of near-age groups.

Cologuard performance when used for repeat testing has not been evaluated or established. Rx only.

9.0. “Information provided is not treatment advice for any particular patient and results may vary. Not every person will have the same treatment, experience, outcome, or result. Exact Sciences Corporation does not recommend or endorse any particular course of treatment or medical choice.”

“There are potential risks associated with the Cologuard test and it may not be appropriate for all patients. For more information about the risks visit www.cologuard.com for more information about Cologuard.”

10. Dr. Limburg serves as Chief Medical Officer, Screening for Exact Sciences through a contracted services agreement with Mayo Clinic. Dr. Limburg and Mayo Clinic have contractual rights to receive royalties through this agreement.

**EXACT SCIENCES CORPORATION**

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   Footnote:

   \*Up-to-date defined as FOBT/FIT, sigmoidoscopy, colonoscopy, computed tomographic colonography (CTC), or sDNA test in the past 1, 5, 10, 5 and 3 years, respectively.

   † Source: National Health Interview Survey, 2018 [↑](#footnote-ref-4)
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    Footnote:

    \*Based on people diagnosed with CRC in stage I, stage IIa, or stage IIb between 2010 and 2016.

    † Localized: There is no sign that the cancer has spread outside of the colon or rectum. This includes AJCC stage I, IIa, and IIb cancers. Regional: The cancer has spread outside the colon or rectum to nearby structures or lymph nodes. This includes stage IIc and stage III cancers in the AJCC system. Distant: The cancer has spread to distant parts of the body such as the liver, lungs, or distant lymph nodes. This includes stage IV cancers25 [↑](#footnote-ref-25)
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    † **Source:** National Health Interview Survey, 2018.

    ‡ Cluster-randomized trial performed in 11 urban and rural federally qualified health centers across 2 health systems in metropolitan St. Louis and rural southeastern Missouri aimed at evaluation of self-identified barriers to CRC screening (n=483). Data were collected through surveys administered in person, by phone, of by mail. Previously screened and unscreened participants (aged ≥50 years) were asked about health insurance and access to care, what “What barriers/things got in the way of being screened?” CRC screening with fecal occult blood test/fecal immunochemical test (FOBT/FIT), sigmoidoscopy, and colonoscopy were assessed. [↑](#footnote-ref-31)
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    \***Study Design**: In a randomized study of racially and ethnically diverse adults aged 50 to 79 years at average risk for colorectal cancer (CRC) (N=997), healthcare providers presented patients with CRC screening recommendations by one of the following methods1: Fecal occult blood test (FOBT) (n=344), Colonoscopy (n=332), Choice of FOBT or colonoscopy (n=321), FOBT-only completion rate was not statistically different vs choice arm, *P=0.64*.

    †Excludes prior users of mt-sDNA. Screening history of Cologuard users: Exact Sciences patient survey conducted 4/1/20-3/31/21. N=3962 [↑](#footnote-ref-33)
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