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Time to Diagnostic Testing After a Positive Colorectal Cancer Screening Test

Chyke A. Doubeni, MD, MPH, Douglas A. Corley, MD, PhD, and Theodore R. Levin, MD

Department of Family Medicine and Community Health, University of Pennsylvania Perelman School of Medicine, Philadelphia (Doubeni); Division of Research, Kaiser Permanente Northern California, Oakland (Corley, Levin).

To the Editor Prompt evaluation of abnormal findings is a central tenet of clinical care, but it is often unclear what “prompt” means in minimizing harms from delayed diagnosis in cancer screening. Is it days, weeks, or months? That is the lens through which to evaluate the biological and clinical implications of our recent study.¹ We wish to clarify 2 points in the accompanying Editorial by Drs Rutter and Inadomi²: (1) the appropriate timing of colonoscopy and (2) potential methodological flaws that could bias the findings.

The effectiveness of the fecal immunochemical test (FIT) hinges on completing diagnostic testing when there is a positive result. Our study found trends of increasing risk of colorectal cancer after month 6 compared with more immediate follow-up, which is biologically plausible and indicates potential disease progression with increasing time to colonoscopy. Therefore follow-up should be done as soon as feasible after the result date.

Rutter and Inadomi² stated that an inability to adjust for colonoscopy indication may have biased the results; we wish to allay those concerns. The study accounted for the presence of symptoms, anemia, and other important factors at the time of FIT screening. There is general consensus on classifying colonoscopies done for a positive FIT result as “definitely diagnostic” (indication).³ Symptoms such as changes in bowel habits are common in the general population and not strongly associated with colorectal cancer risk.³ The Editorial suggested that patients having colonoscopy farther from the positive result date are more likely to have symptoms. Disease progression may result in symptoms; if correlated with receipt of colonoscopy, symptomatic patients would be expected to receive it sooner, especially with the added motivation of a positive FIT result, potentially biasing the results toward the null. In addition, although the Editorial raised a concern about loss to follow-up

Corresponding Author: Chyke A. Doubeni, MD, Department of Family Medicine and Community Health, University of Pennsylvania Perelman School of Medicine, 51 N 39th St, PPMC/Andrew Mutch Bldg, Floor 7, Philadelphia, PA 19104 (chyke.doubeni@uphs.upenn.edu).

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in the cohort, that occurred in only a few patients within 2 years of screening; 83% received colonoscopy within 12 months, and all patients had follow-up for cancer diagnosis. Prior work suggests that longer follow-up (>1–2 years) is unlikely to change our findings.⁴

Clinical programs should aim for completion of follow-up testing well before there is a measurable increase in risk. We therefore reemphasize performing follow-up colonoscopy, if clinically appropriate, in a timely manner, such as within 1 to 3 months—there are no harms in receiving it early, but multimonth delays incur increasing risk of less curable cancer.

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