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Guaiac fecal occult blood test and colorectal cancer incidence

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May 28th, 2021

Dear Professor Fasiha Kanwal,

We are pleased that our manuscript, "Guaiac fecal occult blood test and colorectal cancer incidence" (CGH-D-21-01235), has been provisionally accepted for publication in Clinical Gastroenterology and Hepatology. We would like to thank the Editors and Reviewers for their review and have incorporated their suggested sentence into our manuscript, "We will work with the editorial office to publish an erratum, removing 'which has never been demonstrated for gFOBT' from the sentence in contention".

Yours sincerely,

Amanda J Cross, on behalf of all authors

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Dear Editors,

We thank Shaukat et al. for their comments¹ regarding our Editorial.² We would like to apologise for writing it has “never been demonstrated” that screening with the guaiac faecal occult blood test (gFOBT) reduces colorectal cancer (CRC) incidence,² because as noted by Shaukat et al.,¹ results from extended follow-up of the Minnesota trial showed that CRC incidence was reduced in the biennial and annual gFOBT screening arms, compared with the control arm.³ We will work with the editorial office to publish an erratum, removing “which has never been demonstrated for gFOBT” from the sentence in contention. ~~We would be happy to remove “which has never been demonstrated for gFOBT” from the sentence in contention.~~

Even though the Minnesota trial reported reductions in CRC incidence with gFOBT screening,³ when all relevant existing studies are examined, the evidence that gFOBT screening reduces CRC incidence is not convincing. Several other randomised controlled trials (RCTs) of gFOBT screening, performed across Europe, have found no effect of gFOBT on CRC incidence over 16-20 years’ follow-up.⁴⁻⁶ Moreover, a systematic review and meta-analysis synthesising data from the Minnesota trial and European trials reported that “gFOBT screening made little or no difference on colorectal cancer incidence compared with no-screening, neither annually nor biennially”.⁷

The referral rate to colonoscopy after gFOBT testing was substantially greater in the Minnesota trial (28% and 38% in biennial and annual screening arms, respectively)⁸ than in the European trials (~5%).⁴⁻⁶ This is likely because in the Minnesota trial, the majority of gFOBTs were rehydrated, which resulted in higher positivity rates.⁸ It is reasonable to assume that the high colonoscopy referral rate in the Minnesota trial drove the association between gFOBT screening and lower CRC incidence. We acknowledge that gFOBT screening is a two-step process and the gFOBT is “meant to risk-stratify individuals that would benefit from a colonoscopy”;¹ however, in the context of CRC incidence reduction, this would mean risk-stratifying individuals according to likelihood of harbouring premalignant polyps and existing data do not indicate that the gFOBT can perform such a function.⁹

There is hope for faecal immunochemical test (FIT)-based screening to have a greater impact on CRC incidence. As Shaukat et al. note,¹ Levin et al. reported reductions in CRC incidence following implementation of a FIT-based screening programme in a community-based population;¹⁰ however, this study was observational and more robust data are needed from RCTs of programmatic application of FIT screening at different FIT positivity thresholds.

Yours sincerely,

Professor Amanda J Cross & Emma C Robbins.

The authors have no conflicts of interest to declare.

References

- 1) Shaukat A, Church TR, Mandel JS. Guaiac Fecal Occult Blood Test and Reduction in Colorectal Cancer Incidence. *Clin Gastroenterol Hepatol*. 2021.
- 2) Robbins EC, Cross AJ. Guaiac Fecal Occult Blood Tests and Mortality: A 30-Year Follow-up of Two Pooled Trials. *Clin Gastroenterol Hepatol*. 2021;19(5):892-894
- 3) Mandel JS, Church TR, Bond JH, et al. The Effect of Fecal Occult-Blood Screening on the Incidence of Colorectal Cancer. *N Engl J of Med*. 2000;343(22):1603-1607.
- 4) Scholefield JH, Moss SM, Mangham CM, et al. Nottingham trial of faecal occult blood testing for colorectal cancer: a 20-year follow-up. *Gut*. 2012;61:1036-40.
- 5) Kronborg O, Jørgensen OD, Fenger C, et al. Randomized study of biennial screening with a faecal occult blood test: results after nine screening rounds. *Scand J Gastroenterol*. 2004;39:846-51.
- 6) Lindholm E, Brevinge H, Haglund E. Survival benefit in a randomized clinical trial of faecal occult blood screening for colorectal cancer. *Br J Surg*. 2008;95:1029-36.
- 7) Jodal HC, Helsing LM, Anderson JC, et al. Colorectal cancer screening with faecal testing, sigmoidoscopy or colonoscopy: a systematic review and network meta-analysis. *BMJ Open*. 2019;9:e032773.
- 8) Mandel JS, Bond JH, Church TR, et al. Reducing mortality from colorectal cancer by screening for fecal occult blood. Minnesota Colon Cancer Control Study. *N Engl J Med*. 1993;328(19):1365-71.
- 9) Allison JE, Fraser CG, Halloran SP, Young GP. Population screening for colorectal cancer means getting FIT: the past, present, and future of colorectal cancer screening using the fecal immunochemical test for hemoglobin (FIT). *Gut Liver*. 2014;8(2):117-30.

10) Levin TR, Corley DA, Jensen CD, et al. Effects of Organized Colorectal Cancer Screening on Cancer Incidence and Mortality in a Large Community-Based Population. *Gastroenterology*. 2018;155(5):1383-1391

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