## Re: An Estimate of Severe Harms Due to Screening Colonoscopy: A Systematic Review

*To the Editor:* In the review of screening colonoscopy harms by Huffstetler et al.,[1] technical and methodological weaknesses undermine the study's results.

The authors dismiss meta-analysis in favor of reporting a "credible range" of harms, wherein they report the results of 2 observational studies which they judge to be the "most robust" sources. However, in Table 1, the authors have misclassified the NordICC trial results reported by Bretthauer 2016[2] as a "retrospective" study and then dismiss this study in their subsequent analysis. This disregards 12,574 colonoscopies reported from this large, multi-national, pragmatic randomized controlled trial (RCT) of screening colonoscopy. This RCT provides robust data for assessing harms. Bretthauer et al. report only 1 perforation and that "no deaths or other major complications related to the screening intervention occurred within 30 days after screening." This real-world perforation rate is nearly an order of magnitude lower than Huffstetler et al. report as the lower-bound of their credible range, yet they provide no basis for their implied assertion that the results from the NordICC trial are not credible.

In comparison, one of the studies which the authors classify as "most robust," Rabeneck 2008,[3] is a retrospective, observational study which uses administrative claims from all colonoscopies in 4 Canadian provinces from April 2002 through March 2003 and attempts to "approximate a screening colonoscopy cohort" via exclusion criteria. Use of this 20-year-old study ignores subsequent safety improvements in polypectomy techniques, such as mucosal lifting and cold snare polypectomy. For example, the Taiwan Cold Polypectomy Study (TCPS), a recent, large, multi-site RCT which 1:1 randomized 4270 patients with polyps to cold snare polypectomy (CSP) versus traditional hot snare polypectomy (HSP) showed CSP yielded a 74% reduction in any delayed bleeding and an 88% reduction in severe delayed bleeding. Notably, this clinical trial reported only 1 perforation, and it was successfully managed with endoscopic clipping and supportive care alone.[4] Indeed, CSP has been so effective at preventing perforations that many studies and reviews thereof have concluded that it virtually eliminates perforation risk,[5] and the first case report of a perforation associated with a dedicated cold snare device was published in 2021.[5] Thus, the risks associated with colonoscopy as practiced 2 decades ago do not accurately reflect the risks of modern colonoscopy. Prioritizing outdated, observational studies over a recent, multi-national RCT result warrants substantial justification.

Other large multi-site/multi-national RCT's of screening colonoscopy that warrant consideration are the COLONPREV trial (2009 to 2011, 1 perforation among 4953 screening colonoscopies)[6] and the SCREESCO trial (2014 to 2020, zero perforations among 10,679 screening colonoscopies).[7] Interestingly, combining the above mentioned TCPS outcome with the COLONPREV and SCREESCO outcomes yields only 2 perforations among 19,902 screening colonoscopies, a rate of 1.00 per 10,000 (ie, 1 per 9951), which is very similar to the NordICC trial outcome of 0.80 per 10,000 (ie, 1 per 12,574). The strength and consistency of such RCT results indicate that the lower-bound of Huffstetler et al.'s "credible range" is a substantial (approximately 500%) overestimate of the risk of harm associated with modern screening colonoscopy.

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