Attribution of Colonoscopy Risk Does Not FIT! Reply
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Citation

Version: Not Applicable (or Unknown)
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Downloaded from: https://hdl.handle.net/1887/3492256

Note: To cite this publication please use the final published version (if applicable).
avoidance of colonoscopy complications when the FIT screening is negative.

Diagnostic and therapeutic colonoscopy remains the worldwide standard, yet its use as the primary CRC screening modality is primarily limited to the United States. Besides the population-based socioeconomic benefits, using noninvasive CRC screening methods and reserving colonoscopy for diagnosis and therapy can substantially reduce the burden of morbidity and mortality. Further refinements and advances in noninvasive CRC screening, such as blood tests under development that identify DNA from cancer and polyps, will lead to ever-greater compliance with safe, accurate, cost-effective screening. The earlier identification of polyps and cancers, with reallocation of limited colonoscopy resources to diagnosis, therapy, and prevention, will advance the effort to address this major public health concern.

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References

Conflicts of interest
The authors disclose no conflicts.

Most recent article
https://doi.org/10.1016/j.cgh.2021.07.042

Reply. In a recent publication on colonoscopy-related mortality in a fecal immunochemical test (FIT)-based colorectal cancer screening program we estimated the occurrence of fatal adverse events caused by colonoscopy as follow-up of a positive FIT result. In response to our findings, Weiss and colleagues stated that the complications by follow-up colonoscopy after positive FIT should not be
attributed to FIT screening, because other less invasive follow-up alternatives are available.

Although technically complications related to colonoscopy or other follow-up alternatives are not caused by the FIT itself, we strongly believe that screening should not be seen as the primary screening test but also include its consequential events. When comparing screening strategies, we aim to include the harms and benefits of the entire screening process. We attribute the estimated 33% colorectal cancer–related mortality reduction to FIT screening, yet this can only be accomplished through the follow-up colonoscopy.\(^2\) Simply doing the FIT does not result in any benefit. When possible, an “intention-to-treat” approach is preferred to realistically estimate the beneficial effects and risks of a certain screening strategy. This also accounts for providing information to potential screening participants. We firmly believe that invitees for a FIT-based screening program should be informed at time of invitation on the potential risks of the follow-up diagnostic test when the FIT turns out positive.

The authors argue that other diagnostic tests than colonoscopy could be considered for follow-up after a positive FIT. Yet, we would like to contest this view. Currently most colorectal cancer screening programs, if not all, use colonoscopy as primary screening test or to evaluate a positive screening (eg, stool-based screening or sigmoidoscopy screening).\(^3\) In the Netherlands, FIT-positive participants are invited for a precolonoscopy intake to estimate their eligibility for undergoing colonoscopy. Between 2014 and 2016, 93% of the FIT-positive participants were advised to undergo colonoscopy based on this intake, and 2% to undergo computed tomography colonography,\(^4\) which is often the only alternative diagnostic test in population-based screening programs. Although Liedenbaum et al\(^5\) showed that computed tomography colonography after a positive FIT could have similar accuracy for detecting lesions >10 mm as colonoscopy (93% vs 97%), it was less sensitive for lesions between 6 and 9 mm (78% vs 97%). Also, because of the high prevalence of adenomas or colorectal cancer in the FIT-positive population (70%), most (72%) of the individuals that underwent computed tomography colonography still needed colonoscopy for further follow-up.\(^5\) This shows the dominant role of colonoscopy as evaluation of a positive FIT result and demonstrates the limited use of other methods in screening programs. Nevertheless, whenever these alternatives become more popular in the future, the impact by such development on the harms of screening should not be overlooked when comparing screening strategies.

Weiss and colleagues propose risk stratification to offer individuals with a high risk for colonoscopy complications a less-invasive alternative as triage instrument. We agree that this could lower the rate of colonoscopy complications and thus prevent fatal adverse events. However, these high-risk individuals would constitute a very small proportion of the presumptively healthy screening population with a positive FIT result and even then, the larger part still undergoes colonoscopy when the triage instrument confirms the increased risk for colorectal neoplasia. This makes that the impact of selective triaging on the colonoscopy-related mortality after positive FIT is in our opinion negligible and should not be a reason to separate the risk for colonoscopy complications from FIT screening.

Because colonoscopy is such an integral part of FIT screening and crucial for achieving the intended colorectal cancer mortality reduction, we consider its (low) risk for complications inseparable of the FIT. Nevertheless, we strongly agree with Weiss and colleagues that FIT screening compares favorably with other colorectal cancer screening approaches and that its benefits vastly outweigh the potential harms.

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**Conflicts of interest**

The authors disclose no conflicts.

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**Most current article**

https://doi.org/10.1016/j.cgh.2021.09.012

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**Perinatal Risk Factors for Pediatric Nonalcoholic Fatty Liver Disease: Impact of Inborn Errors of Metabolism**

**Dear Editor:**

We read with great interest the systematic review on perinatal risk factors for pediatric nonalcoholic fatty liver disease by Querter et al.\(^1\) Nonalcoholic fatty liver disease is a leading cause of chronic liver disease in children,\(^2\) and attempts to identify potential risk factors are important. The authors found that maternal body mass