



What Do ‘False-Positive’ Stool Tests Really Mean? Data from the New Hampshire Colonoscopy Registry

Lynn F Butterly^{1,2,4}, William Hisey^{2,4}, Christina M. Robinson^{2,4}, Paul J. Limburg³, Bonny Kneeder³, Joseph C Anderson^{1,5}

1. Geisel School of Medicine at Dartmouth, Hanover, NH, United States. 2. New Hampshire Colonoscopy Registry, Lebanon, NH, United States. 3. Exact Sciences, Madison, WI, United States. 4. Dartmouth Hitchcock Medical Center Lebanon NH. 5. White River Junction VAMC WRJ VT.



INTRODUCTION

Accurate understanding of the frequency of meaningful ‘true positive’ and ‘false positive’ mt-sDNA and FIT results is essential to optimizing the use of these important, common colorectal cancer (CRC) screening tests. We utilized the statewide, population-based New Hampshire Colonoscopy Registry (NHCR) to investigate colonoscopy outcomes using distinct definitions of a ‘positive’ colonoscopy, and present the corresponding false discovery rate and Positive predictive values (PPV).

METHODS

Data from Exact Sciences Laboratories and the NHCR identified patients with mt-sDNA+ tests followed by colonoscopy resulting from routine care (8/15-12/20). We calculated false discovery rates (FDR) (# positive stool tests with negative colonoscopy divided by all positive stool tests) and the corresponding PPVs for both mt-sDNA+ and FIT+ cohorts using the following definitions of positive colonoscopy:

- 1) Detection of colorectal advanced adenomatous Polyps and Cancer: DeeP-C Study: Exams with any CRC, adenomas >1 cm or with villous/tubulovillous histology or high grade dysplasia or any serrated polyp >1 cm were considered positive.
- 2) USMSTF <10 years: Exams with lesions requiring <10 year follow up per USMSTF guidelines were considered positive. This group includes the above DeeP-C findings in addition to 1 or more SSPs <1 cm (with/without dysplasia) or 1 or more tubular adenomas <1 cm.
- 3) Clinically Significant: Positive colonoscopies were considered to include findings from the categories above with the addition of clinically significant serrated polyps (CSSPs): all traditional serrated adenomas, all sessile serrated adenomas, all hyperplastic polyps > 1 cm, and 5-9 mm hyperplastic polyps which are located in the proximal colon. The major difference between Clinically Significant and USMSTF is the inclusion of proximal 5-9 mm HPs, which have been shown to have an increased risk for future neoplasia and may represent misdiagnosed SSPs.

RESULTS

When using the strictest definition of positive colonoscopy, DeeP-C, the FDR was 71.9% for mt-sDNA+ and 81.7% for FIT+. Using the USMSTF definition, the FDR decreased to 33.2% for mt-sDNA+ and 47.6% for FIT+. Finally, adding 5-9 mm proximal HPs to the USMSTF < 10 year definition resulted in the lowest FDRs: 32.2% for mt-sDNA+ and 47.1% for FIT+ results. These decreasing FDRs correspond to increasing PPVs of 28.1% for mt-sDNA+ and 18.3% for FIT+ (DeeP-C) to 67.8% for mt-sDNA+ and 52.9% for FIT+ (DeeP-C + USMSTF + CSSP, Table 1).

Table 1 False discovery rates and positive predictive value (PPV) according to different definitions of positive colonoscopy

False discovery rate (“negative” colonoscopy)				
	Mt-sDNA N=549		FIT N=410	
	#	%	#	%
DeeP-C*	395	71.9	335	81.7
DeeP C* + USMSTF** <10 yrs	182	33.2	195	47.6
DeeP C* + USMSTF** <10 yrs + CSSP	177	32.2	193	47.1
Positive Predictive Value (PPV)				
	#	%	#	%
DeeP-C*	154	28.1	75	18.3
DeeP C* + USMSTF** <10 yrs	367	66.8	215	52.4
DeeP C* + USMSTF** <10 yrs + CSSP	372	67.8	217	52.9

DISCUSSION

Our analysis demonstrates a substantial decrease in FDRs (and corresponding increases in PPV) when using a definition of positive colonoscopy that includes additional significant precancerous findings such as adenomas or SSPs. These data present a more comprehensive and clinically relevant understanding of false positive outcomes at colonoscopies following positive stool tests, and to our knowledge this is the first such assessment of these outcomes.