

Supplemental Table 1: Study population acquisition.

Search Domain	Description
Lab	<b><i>Cologuard</i></b> Query restricted to 1/1/2014-12/31/2017
Order	<b><i>Cologuard</i></b> Query restricted to 1/1/2014-12/31/2017
CPT procedure codes	<b>81528</b> <b>G0464</b> Colorectal stool-based screening, DNA markers and fecal occult hemoglobin (Cologuard)
Diagnosis codes	<b>792.1</b> Positive Cologuard, Hemoccult positive stool, stool mucus, nonspecific abnormal findings in stool contents <b>R19.5</b> Positive Cologuard, Hemoccult positive stool, stool mucus, abnormal feces, other fecal abnormalities

Supplemental Table 2: Positive predictive value of mt-sDNA after screening colonoscopy by patient risk for colorectal cancer.

	Average Risk (N=743)	Increased Risk (N=107)	<i>P</i> -value
Any colorectal neoplasia, N (%)	464 (62)	71 (66)	0.46
Advanced colorectal neoplasia, N (%)	168 (23)	27 (25)	0.54
Right sided colorectal neoplasia, N (%)	375/736* (51)	67/107 (63)	0.03
Sessile serrated polyp, N (%)	186 (25)	15 (14)	0.01

\*missing location on 7 patients

Supplemental Table 3: Stage of colorectal cancer among those with positive mt-sDNA with history of prior screening colonoscopy.

Individual	Interval (years) since last screening colonoscopy	Stage
1	6-9	I
2	10	In situ
3	10	II
4	10	III
5	10	IV
6	11 or greater	I
7	11 or greater	II
8	11 or greater	II

Supplemental Table 4: Polyp characteristics at diagnostic colonoscopy among average risk patients with mt-sDNA use 0 to 9 years after prior colonoscopy.

Years since prior colonoscopy and indication for MT-sDNA	Advanced colorectal neoplasia* n (%)	1-2 Polyps <sup>†</sup> 5 to 10mm n (%)	≥3 Polyps <10mm n (%)	1-2 Polyps ≤5mm n (%)	CRC n (%)
0-5 Salvage	5/13 (38)	3/13 (23)	3/13 (23)	8/13 (62)	0/13 (0)
0-5 Screening	3/14 (21)	1/14 (7)	7/14 (50)	6/14 (43)	0/14(0)
6-9 Screening	12/53 (23)	11/53 (21)	12/53 (23)	30/53(57)	1/53 (4)
6-9 Salvage	2/16 (13)	6/16 (38)	5/16 (31)	5/16 (31)	0/16 (0)

\*Colorectal cancer (CRC) or adenoma/sessile serrated polyps ≥1cm or with high grade dysplasia or villous elements

†Polyp refers to tubular adenoma or sessile serrated adenoma

Supplemental Table 5: Rate of adequate colon preparation, cecal intubation and withdrawal time at colonoscopy prior to mt-sDNA use between 0-9 years as noted within baseline colonoscopy report

<b>Group</b>	<b>Bowel Preparation N (%)</b>	<b>Cecal intubation N (%)</b>	<b>Withdrawal Time N (%)</b>
<b>Average Risk Screen (%)</b> Reported Not Reported or Unknown	73 (68) 34 (32)	87 (81) 20 (19)	7 (7) 100 (93)
<b>Average Risk Salvage (%)</b> Reported Not reported or Unknown	39 (83) 8 (17)	46 (98) 1 (2)	5 (11) 42 (89)
<b>High Risk Surveillance (%)</b> Reported Not Reported or Unknown	42 (76) 13 (24)	52 (95) 3 (5)	6 (11) 49 (89)
<b>High Risk Salvage (%)</b> Reported Not Reported or Unknown	11 (85) 2 (15)	12 (100) 0 (0)	1 (8) 12 (92)