

## Supplementary File

This supplementary file has been provided by the authors to give readers additional information about their work.

Supplement to: Chiu SYH, Chuang SL, LS Chen SLS, *et al.* **“Fecal Hemoglobin Concentration Influences Risk Prediction of Interval Cancers Resulting From Inadequate Colonoscopy Quality: Analysis of Taiwanese Nationwide Colorectal Cancer Screening Program”**

**Supplementary table 1** Severity of histology in association with FHbC of colorectal neoplasm that detected at index colonoscopy

<b>FHbC (µg Hb/g feces)</b>	<b>Subjects with non-advanced adenoma only, n</b>	<b>PPV for non-advanced adenoma only, % (95%CI)</b>	<b>Subjects with advanced adenoma, n</b>	<b>PPV for advanced adenoma, % (95%CI)</b>	<b>Subjects with CRC, n</b>	<b>PPV for CRC, % (95%CI)</b>
20-49	3,956	25.5 (23.9-27.1)	1,398	9.0 (7.4-10.6)	304	2.0 (0.4-3.5)
50-99	2,165	24.9 (22.8-27.0)	1,005	11.6 (9.5-13.7)	283	3.3 (1.2-5.4)
100-149	875	23.8 (20.6-27.1)	512	14.0 (10.7-17.2)	183	5.0 (1.8-8.2)
≥150	2,183	19.9 (18.1-21.8)	1,737	15.9 (14.0-17.7)	1,190	10.9 (9.0-12.7)
NA	578	-	229	-	807	-

FHbC: fecal hemoglobin concentration; PPV: positive predictive value

**Supplementary table 2** Staging details of interval cancers (IC) after colonoscopy and comparison with screening detected cancers in this study

<b>AJCC stage</b>	<b>IC, N (%)</b>	<b>Screening detected cancers<sup>*</sup>, N (%)</b>
0	9 (8.6)	239 (14.4)
I	22 (21.0)	595 (35.9)
II	36 (34.3)	339 (20.5)
III	24 (22.9)	384 (23.2)
IV	14 (13.2)	99 (6.0)
Total	105 (100)	1,656 (100)
NA	57	385

<sup>\*</sup>: Screening detected CRC confined to those who received complete colonoscopy as confirmatory exam in the first round of Taiwanese Nationwide Screening Program within the same time frame.

NA: not available due to missing at least one item required for AJCC VI TNM staging system

**Supplementary table 3** Anatomical distribution of ICs after colonoscopy and comparison with screening detected cancers in this study

<b>Location</b>	<b>IC, N (%)</b>	<b>Screening detected cancers<sup>*</sup>, N (%)</b>
<b>Proximal colon</b>	<b>57(39.0)</b>	<b>423 (31.3)</b>
Cecum	10 (6.8)	66 (4.9)
Ascending colon	35 (24.0)	202 (14.9)
Hepatic flexure	1 (0.7)	43 (3.2)
Transverse colon	11 (7.5)	112 (8.3)
<b>Distal colon</b>	<b>89 (61.0)</b>	<b>927 (68.7)</b>
Descending colon	5 (3.4)	132 (9.8)
Sigmoid colon	41 (28.1)	661 (49.0)
Rectum	43 (29.5)	134 (9.9)
<b>Total</b>	<b>146</b>	<b>1,350</b>
Not specified	16	691

\*: Screening detected CRC confined to those who received colonoscopy as the confirmatory exam in the first round of Taiwanese Nationwide Screening Program within the same time frame

The OR of proximally located IC in reference to screening detected cancer was 1.24 (95% CI = 1.00-1.55).

**Supplementary Table 4** The results of cross validation

Index colonoscopy findings	Derivation data set		Validation data set		Test result
	Total subjects, n	Colonoscopy IC, n	Total subjects, n	Colonoscopy IC, n	Predicted colonoscopy IC, n
Non-advanced adenoma	5,185	28	2,627	19	15.5
Advanced adenoma	2,730	19	1,295	6	7.8
Negative finding	12,064	59	6,068	31	29.7
Total	19,979	106	9,990	56	53.0

P=0.76 comparing the result of predicted number of colonoscopy IC estimated from the testing set and the actual colonoscopy IC in the validation set by Chi-square test.

**Supplementary table 5** Association of various risk factors and IC after colonoscopy in all subjects that received colonoscopy in Taiwanese Nationwide Screening program from 2004 to 2009

Risk factors	Whole cohort		Subjects with negative colonoscopy	
	Univariate analysis	Multivariate analysis	Univariate analysis	Multivariate analysis
	Crude RR (95%CI)	Adjusted RR (95%CI)	Crude RR (95%CI)	Adjusted RR (95%CI)
<b>Age</b>				
60–69 vs. 50–59 years	1.71 (1.33-2.19)	1.55 (1.19-2.01)	1.86 (1.33-2.59)	1.62 (1.14-2.30)
<b>Gender</b>				
Male vs. female	1.15 (0.90-1.46)	---	1.16 (0.83-1.61)	---
<b>Fecal hemoglobin concentration (<math>\mu\text{g Hb/g feces}</math>)</b>				
20-49	1.00	1.00	1.00	1.00
50-99	1.28 (0.89-1.84)	1.34 (0.92-1.97)	1.35 (0.85-2.15)	1.44 (0.88-2.37)
100-149	2.20 (1.46-3.30)	2.17 (1.40-3.35)	2.28 (1.34-3.86)	2.17 (1.21-3.92)
$\geq 150$	2.20 (1.62-2.99)	2.41(1.74-3.34)	1.96 (1.30-2.95)	2.33 (1.50-3.61)
<b>Adenoma detection rate</b>				
>30%	1.00	1.00	1.00	1.00

Risk factors	Whole cohort		Subjects with negative colonoscopy	
	Univariate analysis	Multivariate analysis	Univariate analysis	Multivariate analysis
	Crude RR (95%CI)	Adjusted RR (95%CI)	Crude RR (95%CI)	Adjusted RR (95%CI)
15%-30%	1.26 (0.87-1.82)	1.34 (0.90-2.01)	1.65 (0.91-2.99)	1.63 (0.85-3.13)
<15%	2.08 (1.25-3.46)	2.40 (1.40-4.14)	2.44 (1.16-5.10)	2.46 (1.11-5.44)
<b>Cecal intubation (incomplete vs. complete)</b>	1.70 (1.29-2.24)	1.76 (1.33-2.32)	1.48 (1.02-2.14)	1.44 (0.99-2.10)
<b>Index colonoscopic findings</b>				
No adenoma	1.00	1.00	-	-
Non-advanced adenoma only	1.54 (1.17-2.04)	1.73 (1.29-2.33)	-	-
Advanced adenoma	2.29 (1.59-3.30)	2.20 (1.51-3.21)	-	-

Ambient temperature and FIT kit brand were included in the analyses, and both univariate analyses revealed no significant impact of these factors.

RR: relative risk; Hb: hemoglobin

**Supplementary figure** The change of colonoscopy IC rate in relation to the calendar year of index colonoscopy in Taiwanese Nationwide screening program

