Initial Screening Tests for Colorectal Cancer and Subsequent Adherence to Colonoscopy: An Ecological Study

Yihui Yang[1], Junjie Huang[2], Weimiao Wu[1], Foong-Ming Moy[3], Songsong Tan[1], Jiongxing Fu[1], Tao Ying[1], Mellissa Withers[4], Dandan Mao[1], Sikun Chen[1], Zhisheng Huang[2], Wanghong Xu[1*]

[1]School of Public Health, Fudan University, Shanghai, China, 200032; [2]J.C. School of Public Health and Primary Care, Faculty of Medicine, The Chinese University of Hong Kong, Sha Tin, Hong Kong, 999077; [3]Julius Centre University of Malaya, Department of Social and Preventive Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Wilayah Persekutuan, Malaysia, 50603; [4]Keck School of Medicine, University of Southern California, Los Angeles, CA, USA, 900064.

Abstract: **Objectives:** To analyze correlations between performance of initial screening tests for colorectal cancer (CRC) and adherence to colonoscopy in ecological perspective. **Methods:** Relevant studies published in English up to December 31, 2018 were searched in the PubMed, Embase and other databases. Sensitivity, specificity, or positive predictive value (PPV) of initial screening tests and adherence to colonoscopy were extracted. Crude incidence of CRC for each study population were obtained from cancer statistics data. Spearman correlation coefficients were calculated between performance of initial screening tests and adherence to colonoscopy. Joinpoint regression and sharp discontinuity regression were applied to identify "joinpoint" or "discontinuity point" in adherence to colonoscopy across incidence of CRC, which were used as cut-off points for further stratified analysis. **Results:** In 112 articles identified, the median (IQR) of adherence to colonoscopy was 82.5% (75.6%~91.0%), and significantly correlated with PPV of initial screening tests (r=0.200, *p*=0.006) and incidence of CRC in populations (r=0.274, *p*=0002). The joinpoint of adherence to colonoscopy was found at the incidence of 105/100,000 while the "discontinuity point" was at incidence of 102.4/100,000. In low incidence countries/areas, adherence to colonoscopy was significantly correlated with specificity and PPV of initial screening tests, whereas no significant correlations were observed in countries/areas with high incidence of CRC. When using FIT as an initial screening method, similar results were observed. **Conclusions:** The ecological study shows correlations of adherence to colonoscopy with specificity and PPV of initial screening tests, particularly among populations with low CRC incidence. Our results suggest that specificity of initial screening tests may play a role in compliance to colonoscopy.

Background

Colorectal cancer (CRC), the third most common cancer globally, can be early detected through mass screening. Guaiac fecal occult blood test (gFOBT) or fecal immunochemical test (FIT), with or without a questionnaire-based risk assessment (RA), has been the most frequently used initial screening method for CRC. Due to poor subsequent adherence to colonoscopy examinations, the effectiveness of the screening has been greatly compromised. Most previous studies have focused on potential influential factors for adherence to colonoscopy at individual levels within populations. The more important impact of performance of initial screening tests on compliance to colonoscopy, however, remains unclear.

Objective

To evaluate relationship between performance of initial screening tests and compliance to colonoscopy across populations, and thus provide implications for improving uptake of colonoscopy in ecological perspective.

Methods

Data sources and search strategy: We searched the PubMed, Ovid-Embase, Web of Science Core Collection, Cochrane Library for studies published in English up to December 31, 2018 with the terms of *colorect*, colon*, cancer*, carcinom*, early diagnosis, screen, occult blood, fecal, accuracy, sensitivity, specificity, predictive value, adherence, compliance, colonoscop*,* etc. We also manually searched reference lists of identified studies.

Study selection and extraction: All studies met the following five criteria were included in the analysis: 1) screening CRC in average-risk populations; 2) applying initial screening tests and subsequent colonoscopy; 3) reporting (or providing data to calculate) compliance to colonoscopy; 4) reporting (or providing data to calculate) sensitivity or specificity or PPV of the initial screening tests. Two investigators independently screened the literature, reviewed full texts and extracted data from selected studies. Any disagreements were resolved by discussion with a third investigator. Crude incidence of CRC in all study population were obtained from cancer statistics data.

Statistical analysis: All data analyses were performed using R 3.6.0 and Joinpoint Regression Program version 4.7.0.0. Spearman correlation analysis was used to evaluate the relationship of adherence to colonoscopy with crude incidence of CRC, sensitivity, specificity and PPV of initial CRC screening tests across populations. Joinpoint and discontinuity regression analysis were used to identify "joinpoint" and "discontinuity point" in adherence to colonoscopy across incidence of CRC by study populations. The identified "change points" were then used as cut-off points for further stratified analysis in all studies and in studies using a single FIT as the initial screening method.

Results

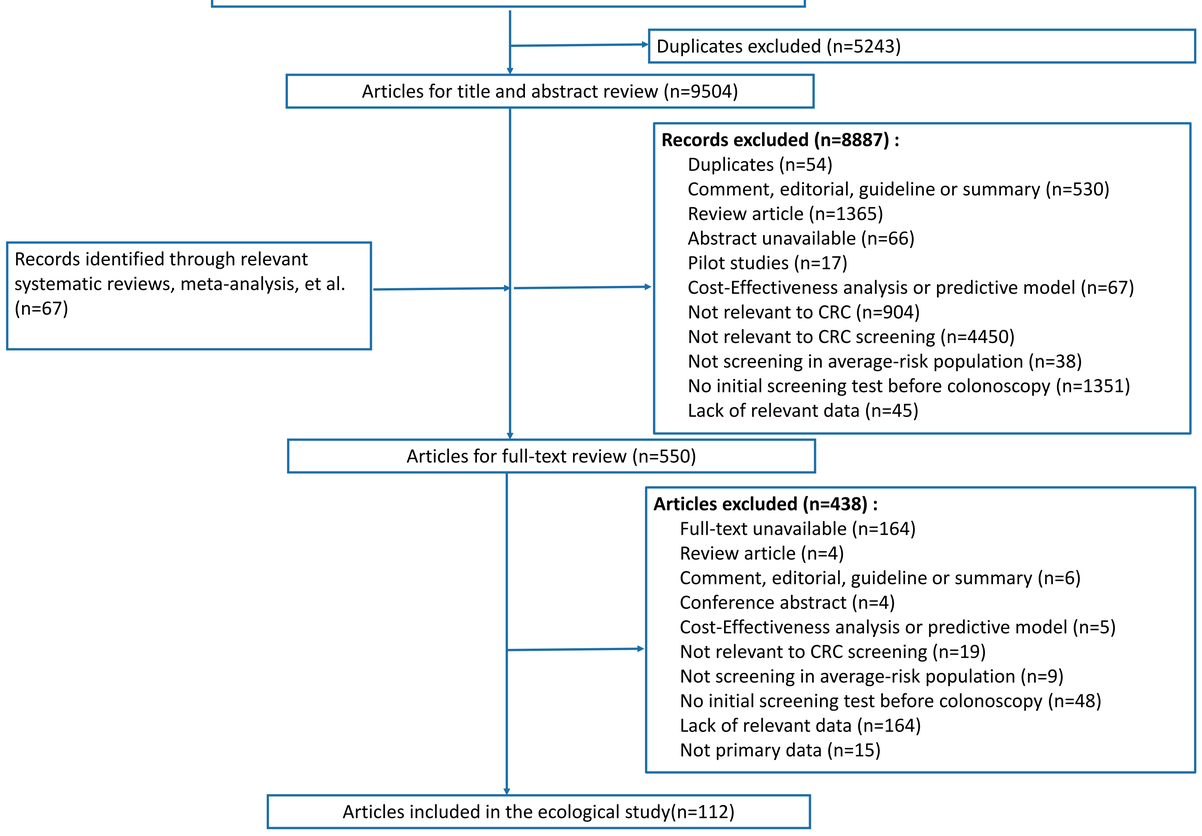


Figure 1 Flow chart of literature search and selection

Table 1 Overall crude incidence of CRC, performance of initial screening tests and adherence to colonoscopy

	Median	IQR
Crude incidence of CRC (1/100,000)	122.7	97.4~142.6
Sensitivity (%)	70.6	45.4~84.0
Specificity (%)	96.2	92.3~97.6
PPV (%)	5.6	3.4~7.9
Adherence to colonoscopy (%)	82.5	75.6~91.0

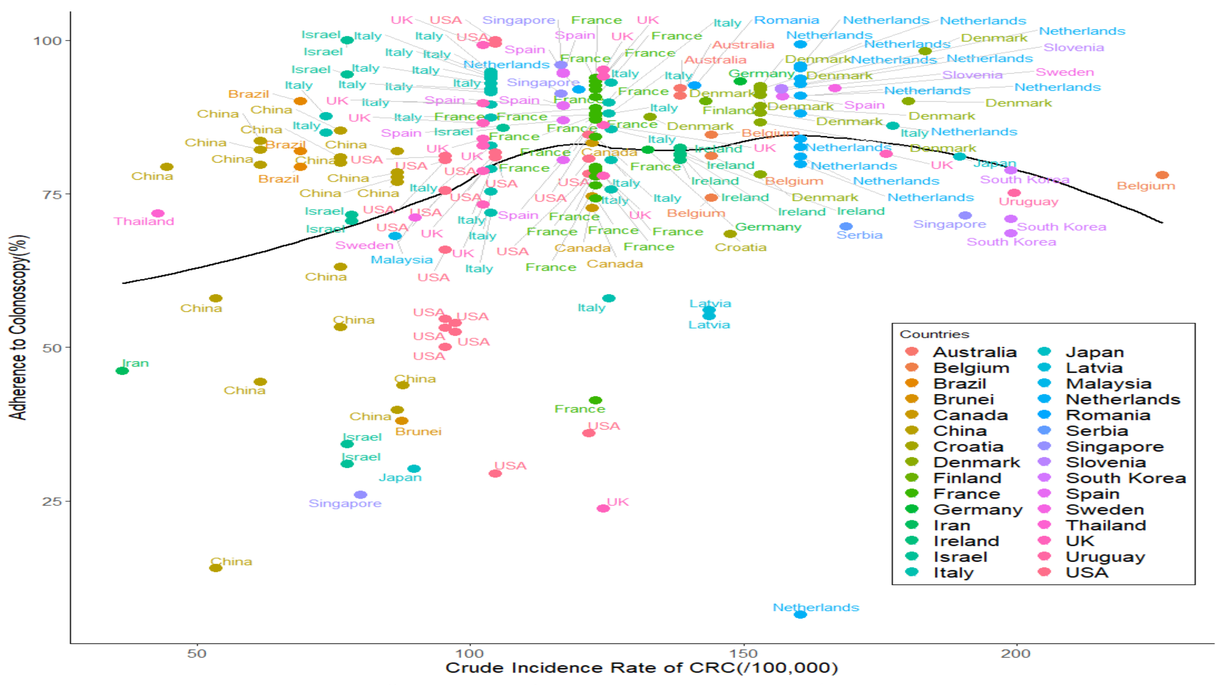


Figure 2 Adherence to colonoscopy across countries / areas.

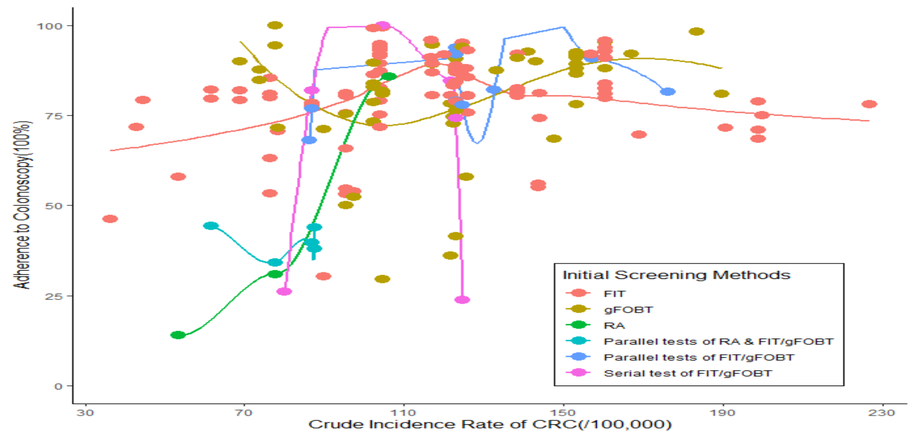
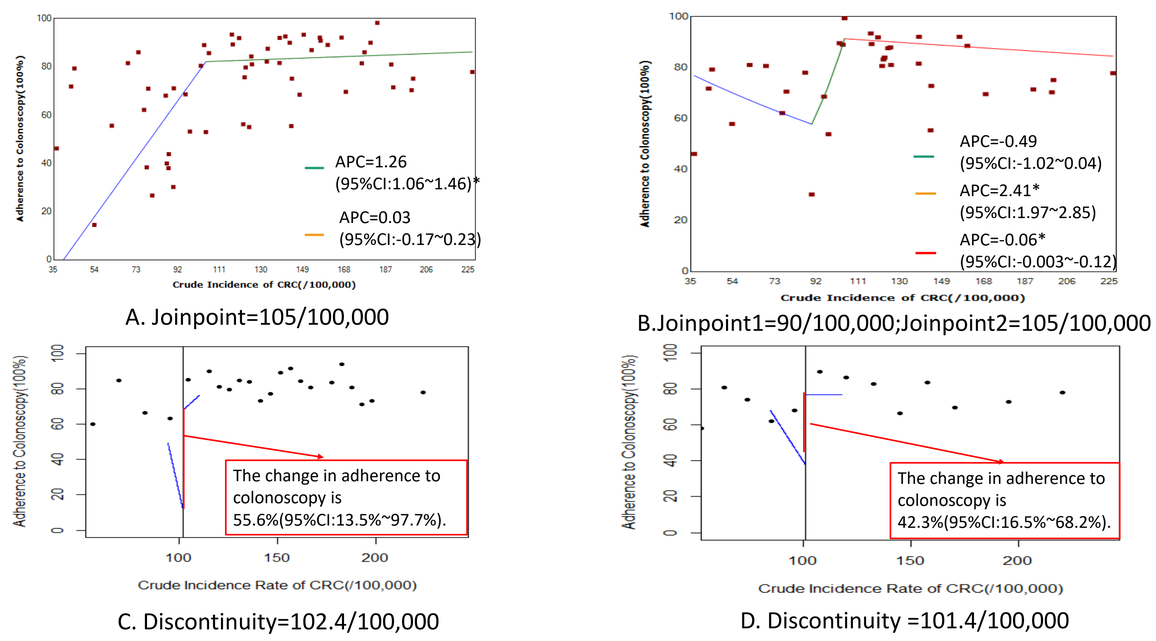


Figure 3 Compliance to colonoscopy by initial screening tests along with crude incidence of CRC



A. Joinpoint=105/100,000

B.Joinpoint1=90/100,000;Joinpoint2=105/100,000

C. Discontinuity=102.4/100,000

D. Discontinuity =101.4/100,000

Figure 4 Joinpoint and discontinuity regressions in all studies and in studies using a single FIT as initial screening method.

A: Joinpoint regression in all studies;
B: Joinpoint regression in studies using a single FIT as initial screening method;
C: Discontinuity regression in all studies;
D: Discontinuity regression in studies using a single FIT as initial screening method.
* p value < 0.05.

Table 2 Spearman's correlation coefficient between performance of initial screening tests and adherence to colonoscopy by crude incidence of CRC

	No. of records[a]	r with compliance to colonoscopy			
		Sensitivity	Specificity	PPV	Incidence
Overall	52,186	0.037	0.078	0.200***	0.274***
By crude CRC incidence (1/100,000)					
<105	27,76	0.209	0.296	0.283**	--
≥105	25,110	0.211	-0.141	0.077	--
<102.4	14,48	-0.042	0.622**	0.310**	--
≥102.4	38,138	0.134	-0.0852	0.006	--
By initial screening tests					
FIT	24,100	0.131	-0.239	-0.014	0.163
gFOBT	22,53	-0.159	0.440**	0.297**	0.266 *
Parallel tests of RA & FIT/gFOBT	1,5	/	/	-0.300	-0.100
Parallel tests of FIT/gFOBT	2,11	/	/	0.500	0.257
Serial test of FIT/gFOBT	2,6	/	/	-0.029	-0.257

* p value <0.10; **p value<0.05; ***p value <0.01.
/: No enough records on sensitivity or specificity to calculate coefficients.
[a] number of records for extracting sensitivity and specificity (the former) and PPV (the latter).

Table 3 Spearman's correlation coefficient (r) of performance of a single FIT with adherence to colonoscopy by crude incidence of CRC.

Crude CRC incidence (1/100000)	No. of records[a]	r with compliance to colonoscopy		
		Sensitivity	Specificity	PPV
Joinpoints				
[36.4,90)	6,17	-0.257	0.771*	0.253
[90,105)	10,26	0.491	-0.370	-0.076
[105,226.7]	8,57	0.214	-0.238	-0.104
Discontinuity regression				
<101.4	10,25	-0.309	0.758**	0.005
≥101.4	14,75	0.312	-0.323	-0.178

* p value <0.10; **p value<0.05; ***p value <0.01.
[a] number of records for extracting sensitivity and specificity (the former) and PPV (the latter).

Conclusions

This ecological study shows correlations of adherence to colonoscopy with crude incidence of CRC, and specificity and PPV of initial screening tests used, with varied correlation coefficients by screening strategies and by countries / areas. Our results suggest that to improve specificity of initial screening test may be the key to increase compliance to colonoscopy, particularly among populations with low CRC incidence.

References

1. Xiao, Q.L., et al., Colonoscopy compliance in high risk population identified by different screening modalities: colorectal cancer screening program in Pudong New Area of Shanghai. Chinese Journal of Cancer Prevention and Treatment, 2019. 26(02): p. 75-81.
2. Hassan, C., et al., Meta-analysis: adherence to colorectal cancer screening and the detection rate for advanced neoplasia, according to the type of screening test. Aliment Pharmacol Ther, 2012. 36(10): p. 929-40.