



Real-World Evidence of Total Colonoscopy for Colorectal Cancer Screening Based on Test Performance RCTs

Chisato Hamashima (Teikyo University, Japan) and Teruhiko Terasawa (Fujita University, Japan)
Satoyo Hosono, Takafumi Katayama, Koichiro Abe, Keika Hoshi, Toshihiro Tadano, Seiju Sasaki

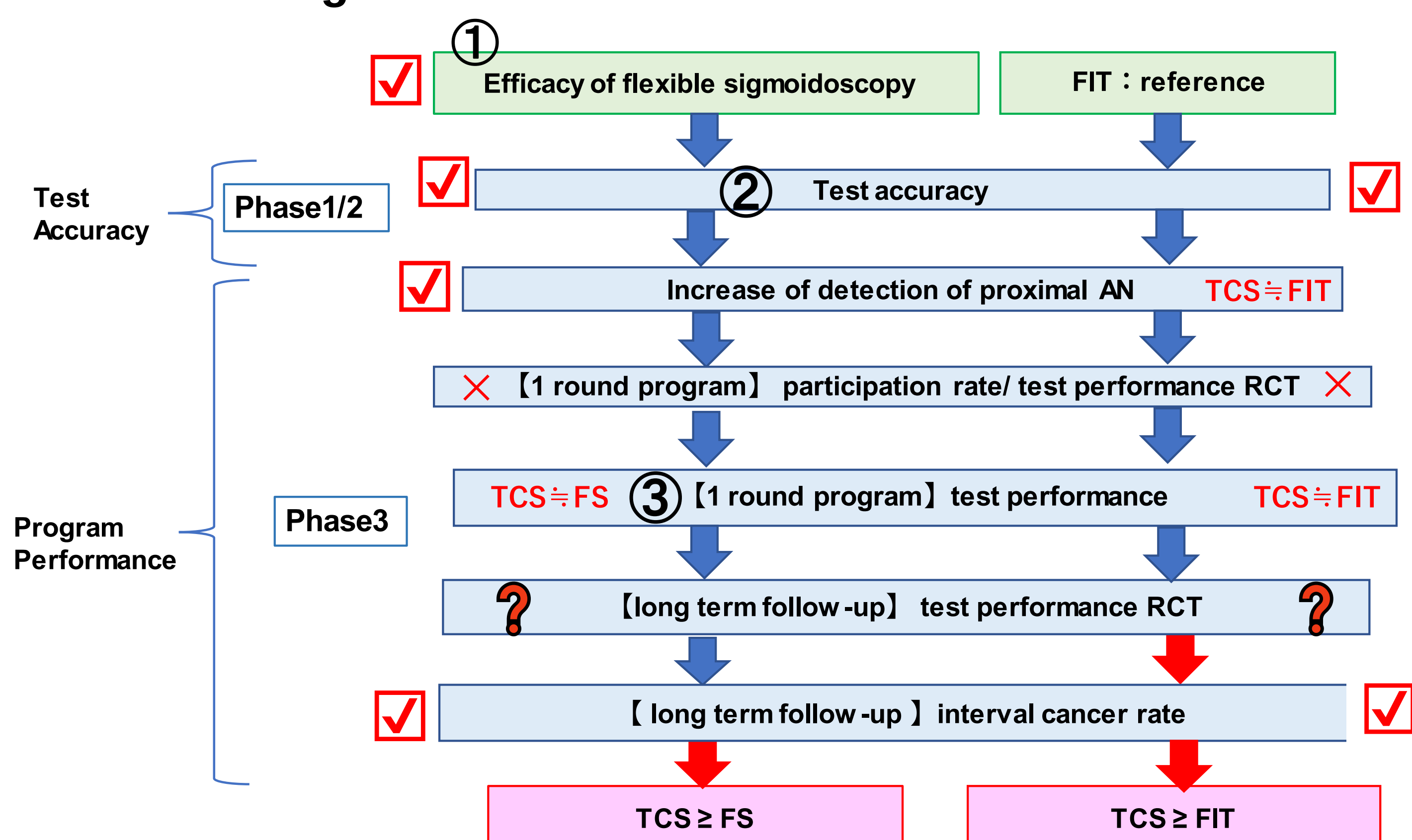
Background

- Total colonoscopy (TCS) has been anticipated as a new method for colorectal cancer screening.
- Although randomized control studies (RCTs) are ongoing, there has yet to be a conclusive result.
- We evaluated the effectiveness of TCS screening following the stepwise approach developed by the World Endoscopic Evaluation (WEO).

Methods

- We performed a systematic review of select studies during each phase by using of MEDLINE and Cochrane Library.
- First, we compared test accuracy for detecting advanced neoplasia (AN)/colorectal cancer (CRC) between fecal immunochemical testing (FIT), flexible sigmoidoscopy (FS), and TCS.
- Test performance indicators were compared based on single-round RCTs and performed a meta-analysis based on intention-to-treat (ITT) and per-protocol analysis.

Figure 1. A flow chart of stepwise evaluation for colorectal cancer screening



② Step2: Comparison of sensitivity for advanced adenoma

- One study compared sensitivity between FIT, FS, CTC, and TCS which were performed simultaneously.
- The sensitivity for the AN detection was consistently higher in TCS than others, even if the AN size was changed.

(Graser A, et al. Gut 2009)

Procedure	Reference standard	Sensitivity (95%CI)		
		>5mm adenoma	>9mm adenoma	Advanced Neoplasia
Colonoscopy	CTC	0.97 (0.89-1.00)	1.00 (0.86-1.00)	1.00 (0.88-1.00)
Sigmoidoscopy	Colonoscopy	0.67 (0.52-0.81)	0.68 (0.47-0.85)	0.83 (0.65-0.94)
FIT	Colonoscopy	0.40 (0.25-0.57)	0.33 (0.15-0.57)	0.32 (0.15-0.54)

Discussion

- Comparison of test accuracy is the first step for assessment of new technique. However, the sample is not representative of target population and prevalence differs.
- The success of cancer screening programs depends on participation rate.
- Although high sensitivity was confirmed in TCS screening, test performance as a screening program was insufficient because of the low participant rates.
- The difference of participations rates in TCS screening has been observed between the US and other countries.

What is step-wise comparative approach?

- The World Endoscopic Organization(WEO) approach is to assess test accuracy and program performance for each new technique.
- Reference standard technology (like guaiac fecal occult blood testing) should be evaluated by RCTs.
- Adoption of this method should be limited to a biologically identical method (like fecal immunochemical testing).

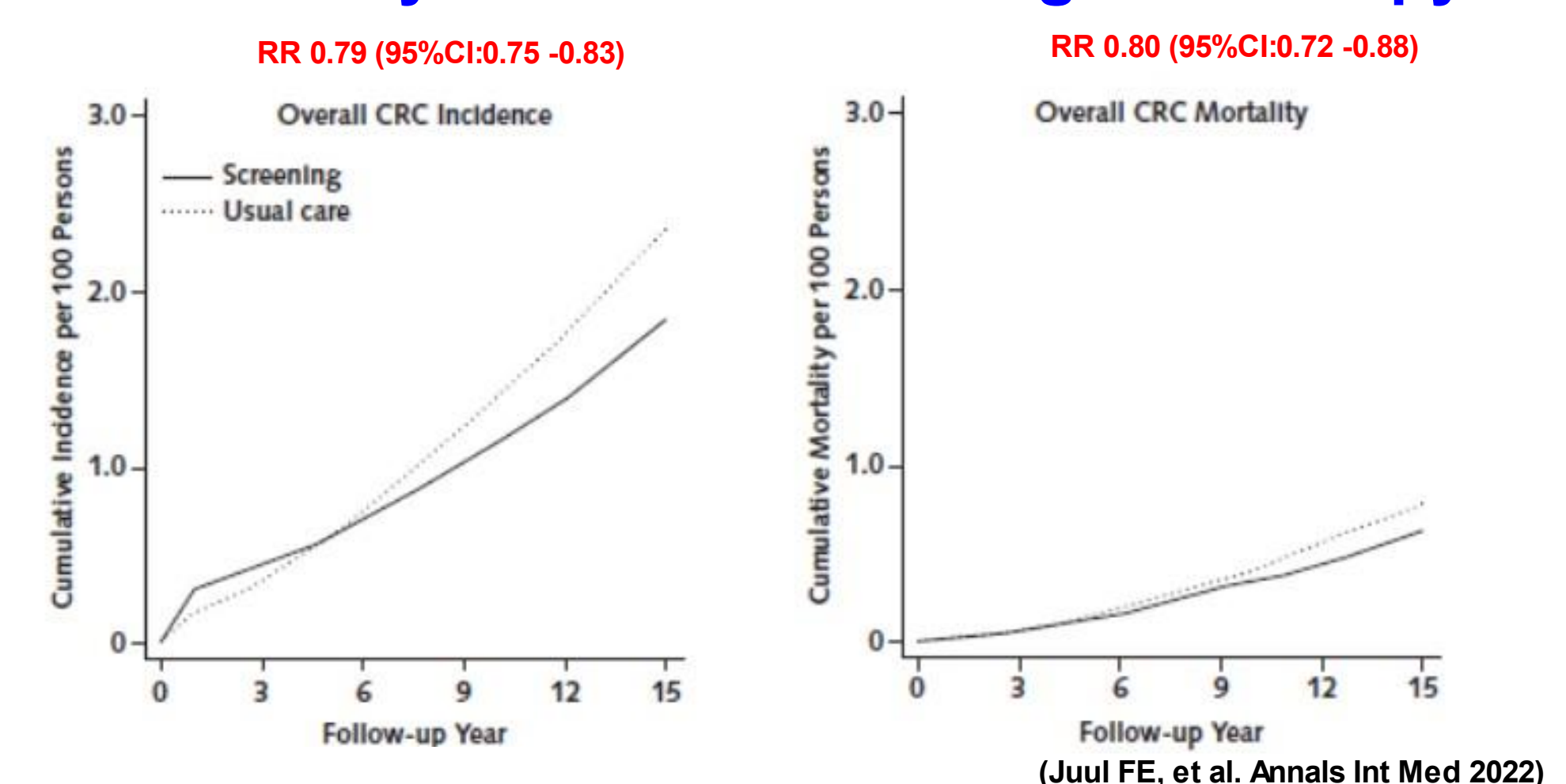
Table 1. Step-Wise Comparative approach (WEO) (Young GP, et al. Cancer 2016)

Process	Nature	Main aim
Phase 1	Prescreening: Retrospective estimation of ability to discriminate between cancer cases and controls without neoplasia	Test accuracy
Phase 2	Detection of lesions along the neoplastic continuum: prospective clinical studies	Test accuracy
Phase 3	Initial screening evaluation; single round of screening	Test performance (program)
Phase 4	Screening program evaluation over multiple rounds	Test performance (program)

① Step 1: Efficacy of sigmoidoscopy for CRC screening

- Efficacy of sigmoidoscopy was confirmed by 4 RCTs.
- Twenty percent mortality reduction from colorectal cancer was observed in the results of pooled analysis.
- To assess program performance of TCS screening, sigmoidoscopy can be used as reference for evaluation.

Pooled analysis of 4 RCTs for sigmoidoscopy



③ Step 3: Effectiveness of TCS for CRC screening

- One 14 RCTs of test performance as colorectal cancer screening were selected.
- In the ITT analysis, the TCS participation rate of the meta-analysis was lower than FIT. Although the AN detection rate was higher than FIT and FS. CRC detection was higher but not statistically significant.
- In the per-protocol analysis, AN and CRC detection rates were higher in TCS than others.

Meta-analysis: Program performance

Analysis	Indicators	Ref	TCS RR (95%CI)	Ref	TCS RR (95%CI)
	Participation rate	FS	0.83 (0.78-0.88)	FIT	0.49 (0.22-0.89)
Modified	AN detection rate	FS	1.15 (0.88-1.51)	FIT	2.25 (1.40-3.61)
ITT	CRC detection rate	FS	1.08 (0.49-2.37)	FIT	1.48 (0.66-3.43)
PP	AN detection rate	FS	1.45 (1.00-2.07)	FIT	4.14 (3.03-5.85)
	CRC detection rate	FS	1.30 (0.60-2.85)	FIT	2.57 (1.17-5.87)

Conclusion

- The test performance of RCT could predict the effectiveness of the screening program.
- Since efficacy/effectiveness of TCS is still unclear, we should wait the final results of ongoing RCTs to introduce the national programs.