A systematic review and meta-analysis **EPH71** of interval cancer of stool testing for colorectal cancer screening Chisato Hamashima (Teikyo University, Japan) Teruhiko Terasawa, Koichiro Abe, Toshihiro Tadano, Keika Hoshi, Takafumi Katayama, Seiju Sasaki, Satoyo Hosono

### Background

- **Colorectal cancer (CRC) is a heavy burden** worldwide, and CRC screening has been implemented nationally in developed countries.
- The guaiac fecal occult blood test (gFOBT) has been the primary screening modality for CRC screening, but it has recently been replaced with fecal immunochemical testing **(FIT)**.

## Figure 1. Comparison of Positive rates

#### % Screening Positive by gFOBT

Author (published year)	n/N		ES (95%CI)  )	Author (published year)	n/N	
				1. Prevalence screening	10.17 101	
1. Prevalence screening				Launoy (2005)	434/7,421	+
Kwantor (1099)	340/9,040	•	3.76 (3.38, 4.17)	Chen (2011)	2,031/46,355	◆
Kwenter (1988)		•		Shin (2013)	129,139/1,809,139	
Hardcastle (1996)	960/44,838	•	2.14 (2.01, 2.28)	Parente (2013)	2,406/38,807	•
Bouvier (1999)	2,020/71,307	•	2.83 (2.71, 2.96)	McNamara (2014)	514/5,063	1
	, ,	l.	2.65 (2.71, 2.96)	Chiang (2014)	36,227/956,005	♦
Paimela (2010)	806/37,514	◆	2.15 (2.71, 2.30)	Stegman (2015)	232/2,871	1
Moss (2012)	651/30,480	♦	2.14 (1.98, 2.30)	Zorzi (2020)	7,031/123,347	4
	,			Toe-Zoutendijek (2020)	25,331/398,505	•
Paszat (2016)	13,127/307,456	•	4.27 (4.20, 4.37)	Toe-Zoutendijek (2020)	15,611/127,411	
Blom (2017)	593/25,049	◆¦	2.15 (1.98, 2.34)	Subtotal (tau∧2=0.131)		<
Blom (2017)	694/38,097	•	1.82 (1.69, 1.96)	With estimated predictive interv	<i>v</i> al	

#### % Screening Positive by FIT

ES (95%CI)

5.85 (5.33, 6.41)

4.38(4.20, 4.57)

7.14 (7.10, 7.18)

6.20 (5.96, 6.44)

10.15 (9.33, 11.02)

3.79 (3.75, 3.83)

8.12 (7.14, 9.18)

5.70 (5.57, 5.83)

6.36 (6.28, 6.43)

12.25 (12.07, 12.43)

62 (5.36. 8.16

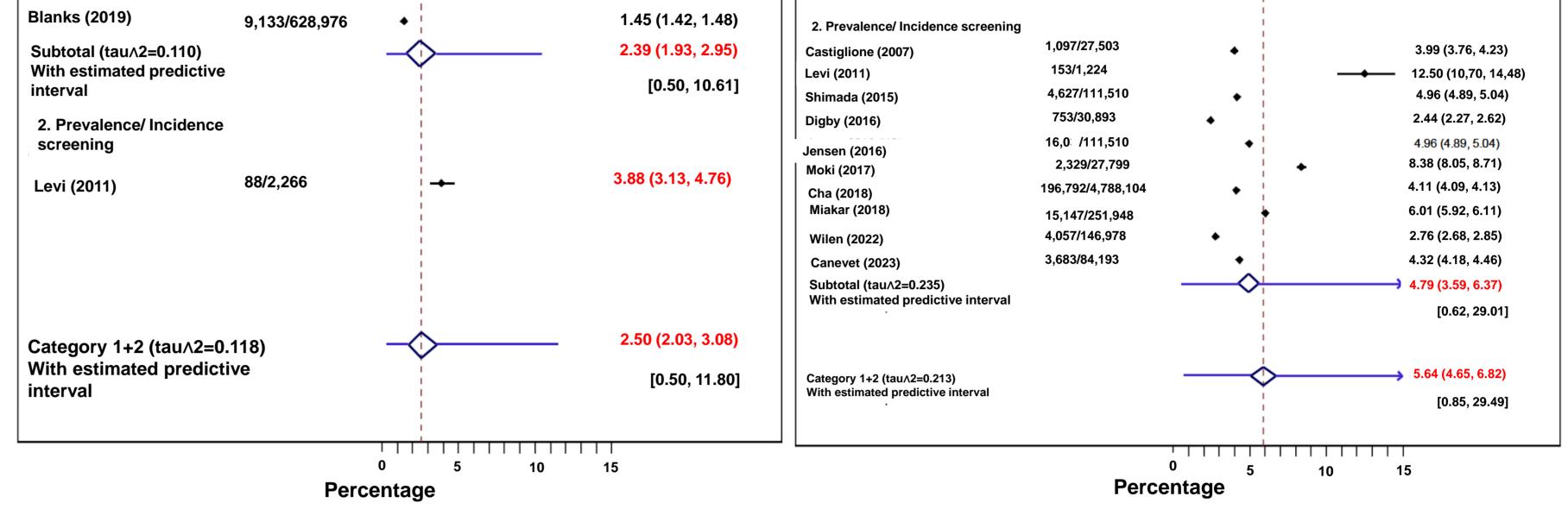
[1.46, 25.33]

## What is Interval Cancer?

- Interval cancer rate is a critical factor in evaluating the effectiveness of cancer screening programs.
- Interval cancer is diagnosed between the last negative screening and the next scheduled screening.

## **Methods**

- The interval CRC rate between gFOBT and FIT was compared based on a systematic review and meta-analysis.
- A literature search was conducted in the Ovid-**MEDLINE**, Embase, and Ichushi-Web databases for citations related to CRC screening based on stool tests, covering primarily the period from inception to April 2024.
- **Population-based screening for asymptomatic** individuals aged 40 years and above was also



# Figure 2. Comparison of CRC detection rates

%	Detection	of CRC by	gFOBT	
Author (published year)	n/N		ES (95% CI)	
1. Prevalence screening				
Kwenter (1988)	16/9,040	-	0.18 (0.10, 0.29)	
Hardcastle (1996)	104/44,838	-	0.23 (0.19, 0.28)	
Bouvier (1999)	152/71,307	+	0.21 (0.18, 0.25)	
Paimela (2010)	66/71,307	<b>–</b>	0.18 (0.14, 0.22)	
Moss (2012)	70/30,480	<b></b>	0.23 (0.18, 0.29)	
Paszal (2016)	76/307,456	•	0.25 (0.23, 0.27)	
	26/25 040		0.40 (0.07, 0.45)	

#### % Detection of CRC by FIT

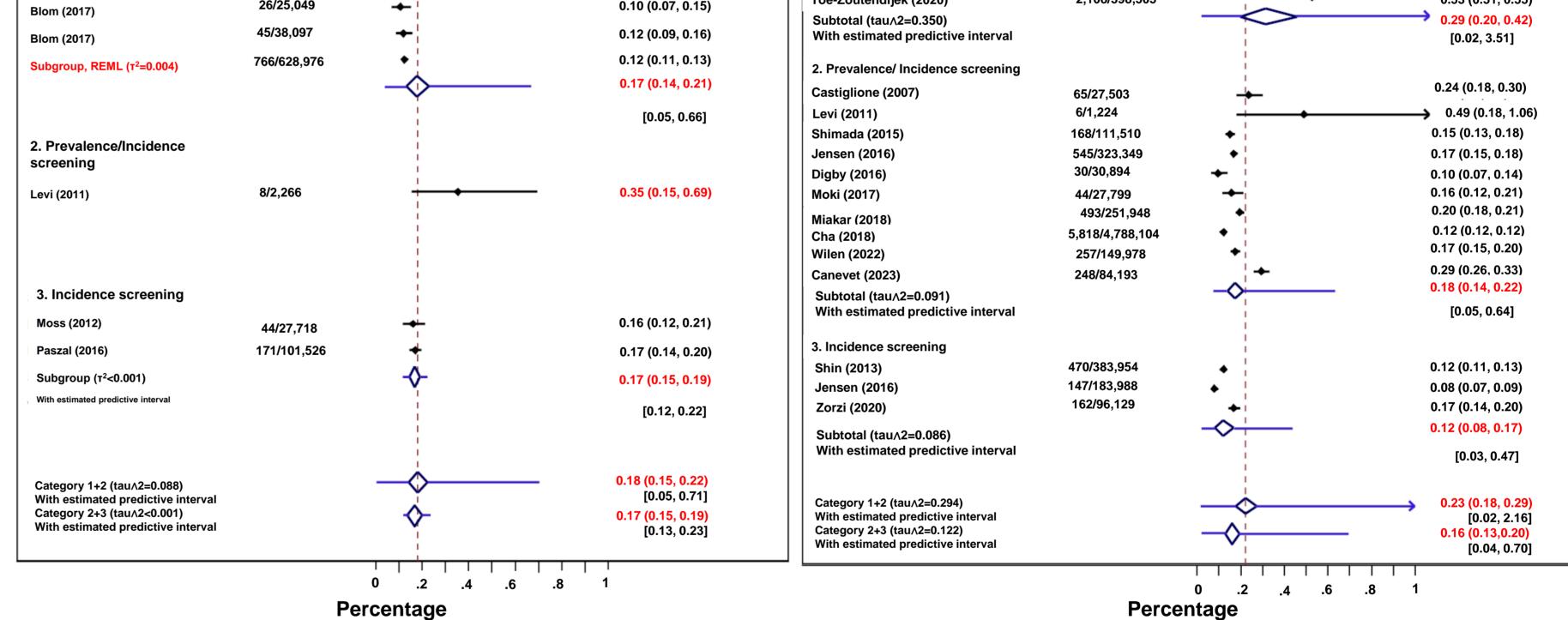
Author (published year)	n/N		ES (95%CI)		
1. Prevelence screening		1			
Launoy (2005)	22/7,421		0.24 (0.20, 0.30)		
Chen (2011)	52/46,355	+	0.11(0.08, 0.15)		
Parente (2013)	95/38.807	<del></del>	0.30 (0.19, 0.45)		
Shin (2013)	2,491/809,139	◆	0.14 (0.13, 0.14)		
Chiang (2014)	1,721/956,005	♦	0.18 (0.17, 0.19)		
McNamara (2014)	17/5,063	<u> </u>	0.34 (0.20, 0.54)		
Stegman (2015)	12/2,871	•	0.42 (0.22, 0.73)		
Toe-Zoutendijek (2020)	1,102/127,411		0.86 (0.81, 0.92)		
Zorzi (2020)	412/123,347	+	0.33 (0.30, 0.37)		
Toe-Zoutendijek (2020)	2,108/398,505	•	0.53 (0.51, 0.55)		

included. Screenings were divided into three types: prevalence screening, incidence screening, and combined screening.

Interval CRC rates per 100,000 person-years following negative results were calculated for each round of CRC screening and compared between gFOBT and FIT.

### **Results**

- Of 7,971 articles, 35 studies remained and were included in the meta-analysis. There were 11 studies on gFOBT and 27 studies on FIT. Twenty-nine studies were reported from Western countries, and 6 were from Asia.
- Although the CRC detection rate of FIT was twice as high as in gFOBT, the positive rate was also higher in FIT than in gFOBT (Figur 1&2).
- The incidence rates of interval CRC following gFOBT were 66.7 (95%CI:57.6-77.3) for prevalence screening and 63.8



## Figure 3. Comparison of Interval Cancer rates

e	Interval Cancer by gFOBT			Interval Cancer by FIT			
Autho	r (published year)		Events n/P-Ys	Interval cancer rate n/100,000	Author (published year)	Events n/P-Ys	Interval cancer rate n/100,000
1. Pre	valence screening		·		1. Prevalence screening		
Kwer	nter (1988)	<b>+</b>	16/14,790	108.2 (66.3, 176.6)	Launoy (2005) Chen (2011)	4/13,974 16/44,324	28.6 (10.7, 76.3) 36.1 (22.1, 58.9)
Hard	castle (1996)	-+-	73/87,756	83.2 (66.1-104.6)	Crotta (2011) Shin (2013)	→ 3/3,176 ↓ 1,608/1,680,000	94.5 (30.5, 292.9) 100.0 (95.3, 104.9)
Bouv	vier (1999)	<b>_</b>	45/69,287	64.9 (48.5, 87.0)	Parenta (2013)	8/72.802 1/9.098	11.0 (5.5, 22.0) 11.0 (1.5. 78.0)
Paim	ela (2010)	<b>—</b>	35/70,357	49.7 (35.7, 69.3)	Chiang (2014)	◆ 539/1,816,050	29.7 (27.3, 32.3)
Moss	s (2012)	<b>_</b>	38/59,235	64.2 (46.7, 88.2)	Stegman (2015) Buron (2019)	<b>5/5,276 31/85,048</b>	94.8 (39.4, 227.7) 36.5 (25.6, 51.8)
	at (2016)	•	481/588,658	81.7 (74.7, 89.3)	Toes-Zoutendijk (2020) Zorzi (2020)	<ul> <li>▲ 418/746,348</li> <li>▲ 51/232.600</li> </ul>	56.0 (50.9, 61.6) 21.9 (16.7, 28.8)
	n (2017)	_ <b>+</b> _	37/47,172	78.4 (56.8, 108.3)	Toes-Zoutendijk (2020) Plantener (2023)	126/223,600 83/242.488	56.4 (47.3. 67.1) 34.2 (27.6. 42.4)
Blon	n <b>(2017)</b>	-+	63/72,814	86.5 (67.6, 110.8)	Dedling (2023) Subgroup, REML (tau∧2=0.069)	<b>*</b> 829/2,321,804	35.4 (33.4, 38.2) 37.8 (27.9, 51.2)
Blan	ks (2019)	•	749/1,239,686	60.4 (56.3, 64.9)	2. Prevalence/Incidence screening		[4.5, 319.7]
-	Jroup, REML ∆2=0.004)	$\rightarrow$		<b>71.7 (63.3, 81.8)</b> [38.0, 135.4]	Castigone (2007) Shimada (2015) Digby (2016)	16/44.815 24/106,883 31/60,280	35.7 (21.9, 58.3) 22.5 (15.1, 33.5) 43.4 (36.2, 73.1)

(95%CI: 47.5-85.6) for incidence screening. For FIT, the rates were 34.1 (95%CI: 27.1-42.9) for prevalence screening and 32.3 (95%CI: 24.0-43.6) for incidence screening. (Figure 3)

## Conclusion

- Although these studies could not be directly compared due to their varying contexts, including differences in devices and cut-off values for stool testing, interval **CRC** rates were lower in **FIT** than in **gFOBT**.
- This result also supports the superiority of test accuracy in FIT for CRC screening.

2. Prevalence/Incidence screening Levi (2011)

Bretagne (2021) Bretagne (2021)

(tau∧2<0.001) 3. Incidence screening Moss (2012)

Pazat (2016)

(tau/2<0.001)

Subgroup, REML

Category 1+2 (tau 12=0.044)

Category 2+3 (tau \2=0.081)

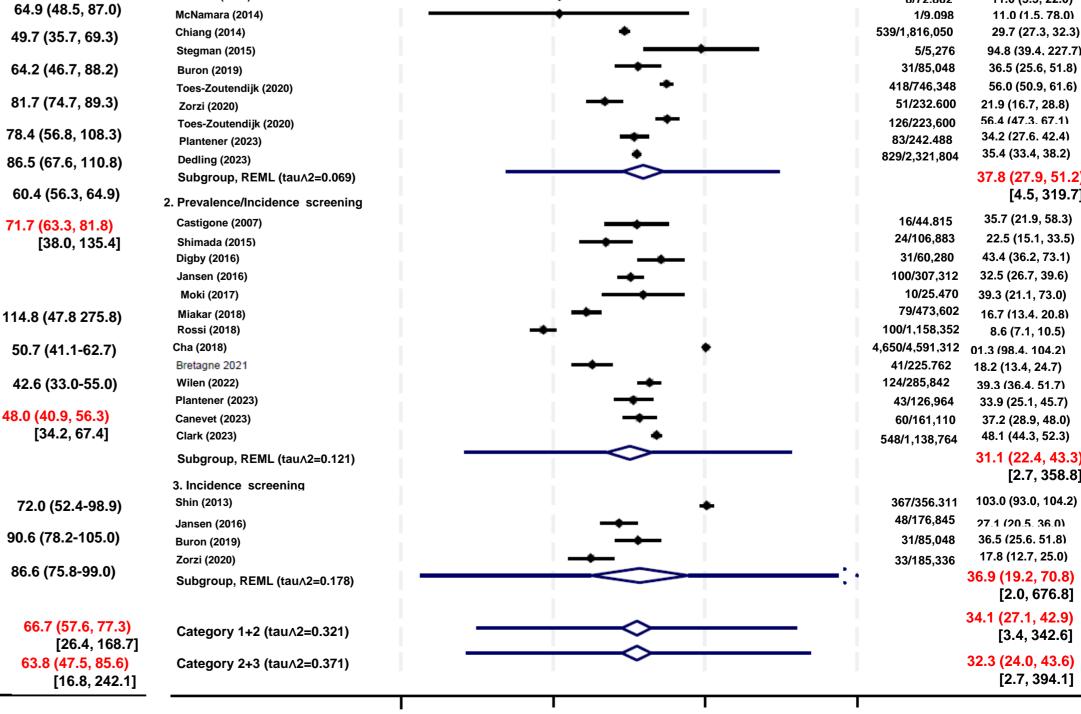
5/4,356 59/138.544 Subgroup, REML

10

38/52,809 177/195.360

1000

100



10

100

1000