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

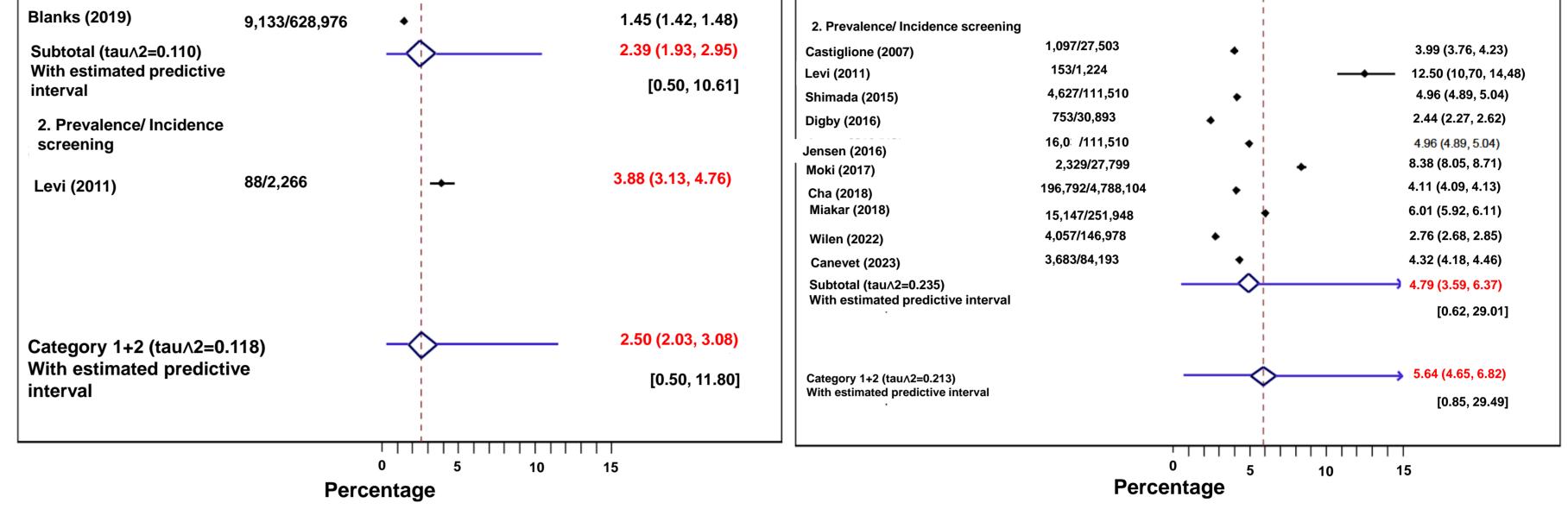
[1.46, 25.33]

## 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

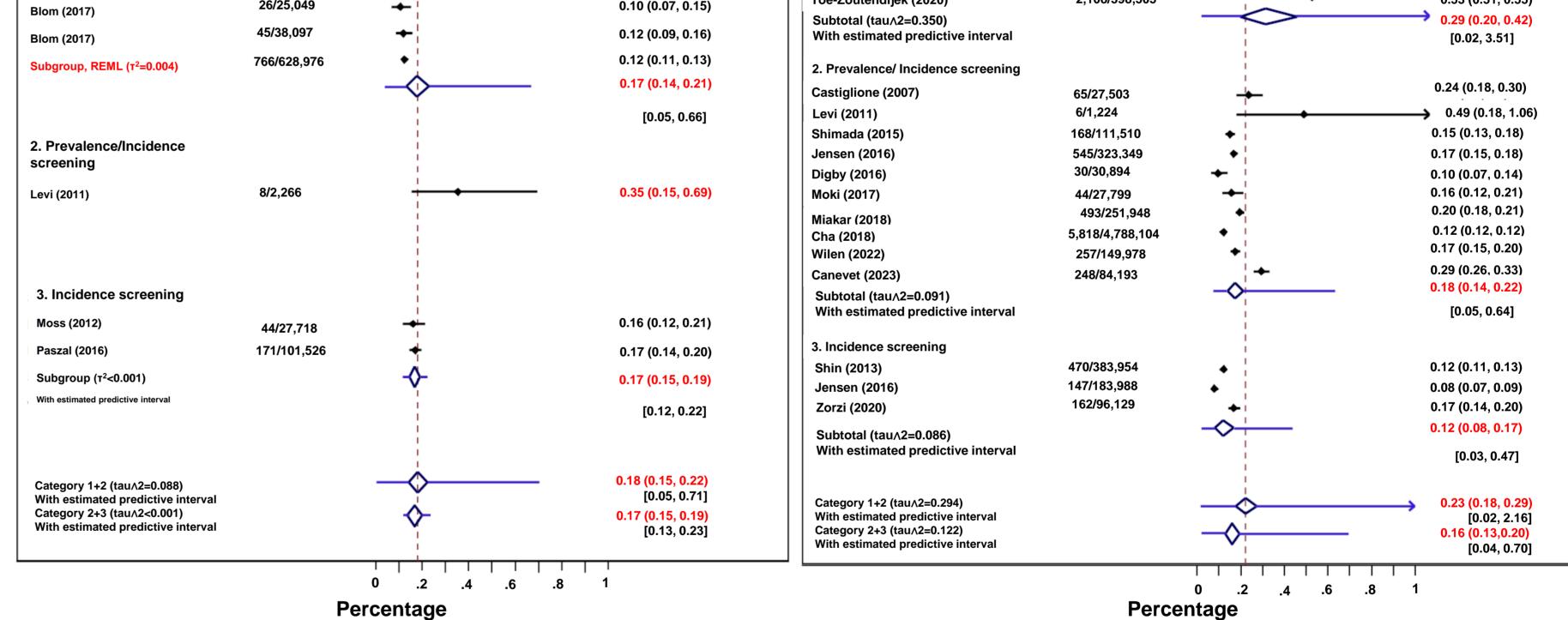
| Author (published year) | n/N           |             | ES (95%CI)        |  |  |
|-------------------------|---------------|-------------|-------------------|--|--|
| 1. Prevelence screening |               | 1           |                   |  |  |
| Launoy (2005)           | 22/7,421      |             | 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<br>n/P-Ys | Interval cancer<br>rate<br>n/100,000      | Author (published year)                            | Events<br>n/P-Ys  | Interval cancer<br>rate<br>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)<br>Chen (2011)                       | 4/13,974<br>16/44,324                                   | 28.6 (10.7, 76.3)<br>36.1 (22.1, 58.9)                      |
| Hard   | castle (1996)            | -+-           | 73/87,756        | 83.2 (66.1-104.6)                         | Crotta (2011)<br>Shin (2013)                       | → 3/3,176<br>↓ 1,608/1,680,000                          | 94.5 (30.5, 292.9)<br>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<br>1/9.098                                     | 11.0 (5.5, 22.0)<br>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)<br>Buron (2019)                     | <b>5/5,276 31/85,048</b>                                | 94.8 (39.4, 227.7)<br>36.5 (25.6, 51.8)                     |
|        | at (2016)                | •             | 481/588,658      | 81.7 (74.7, 89.3)                         | Toes-Zoutendijk (2020)<br>Zorzi (2020)             | <ul> <li>▲ 418/746,348</li> <li>▲ 51/232.600</li> </ul> | 56.0 (50.9, 61.6)<br>21.9 (16.7, 28.8)                      |
|        | n (2017)                 | _ <b>+</b> _  | 37/47,172        | 78.4 (56.8, 108.3)                        | Toes-Zoutendijk (2020)<br>Plantener (2023)         | 126/223,600<br>83/242.488                               | 56.4 (47.3. 67.1)<br>34.2 (27.6. 42.4)                      |
| Blon   | n <b>(2017)</b>          | -+            | 63/72,814        | 86.5 (67.6, 110.8)                        | Dedling (2023)<br>Subgroup, REML (tau∧2=0.069)     | <b>*</b> 829/2,321,804                                  | 35.4 (33.4, 38.2)<br>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<br>∆2=0.004) | $\rightarrow$ |                  | <b>71.7 (63.3, 81.8)</b><br>[38.0, 135.4] | Castigone (2007)<br>Shimada (2015)<br>Digby (2016) | 16/44.815<br>24/106,883<br>31/60,280                    | 35.7 (21.9, 58.3)<br>22.5 (15.1, 33.5)<br>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)

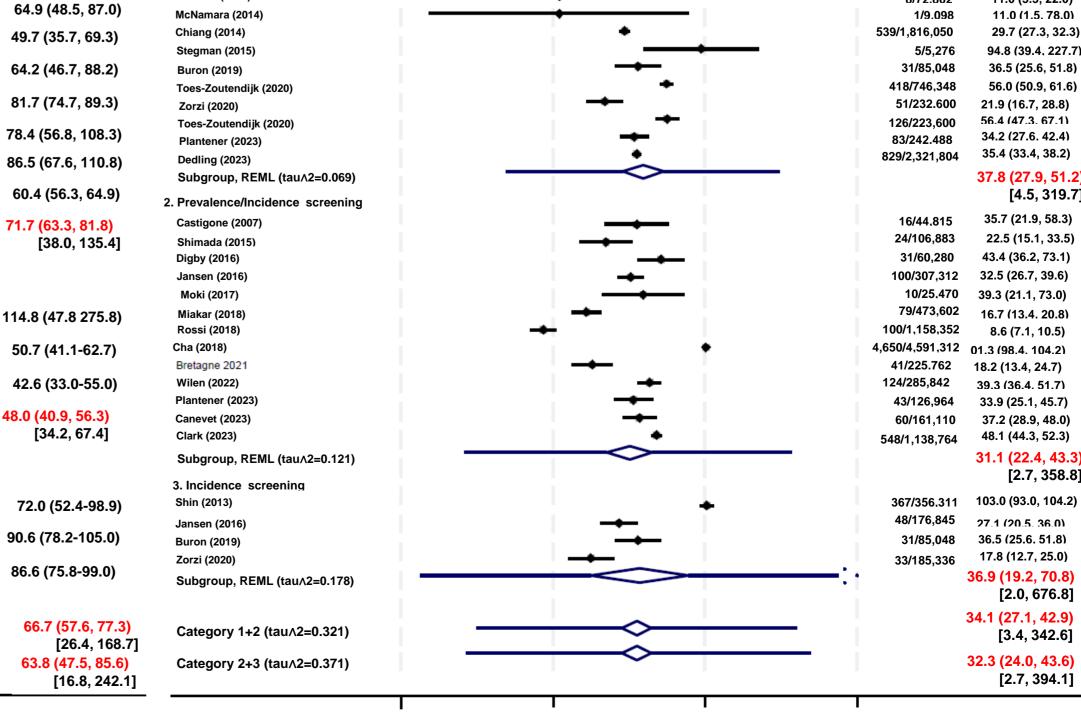
5/4,356 59/138.544 Subgroup, REML

10

38/52,809 177/195.360

1000

100



10

100

1000