ICSN ICSN2023

Evaluation of Population-based Cancer Screening from Universal to Precision Strategy with a Digital Twin Design Approach

On behalf of Taiwan Screening Team

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Chao-Chung Wu (Director of General, HPA, Minister of Health)

2023-06-21

HPA

Director-General, Dr. Chao-Chun Wu

Evaluation of Universal Population-based Stool-based Screening

Pros and Cons	Evidence-based Support Low----------High +	+ +	+++
Benefits	**Mortality reduction (+++)**		**Incidence (++)**
Possible Harms	**Negligible Overdiagnosis of CRC (++)**		**Overdetection of Adenoma (Not well-studied)**

Evaluation of Universal Population-based Stool-based Screening

Evidence-based Support

Low----------High

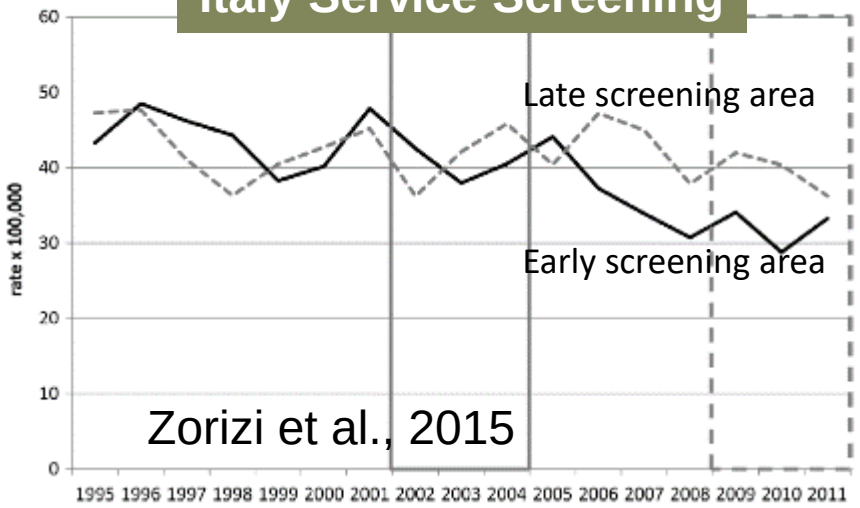
\+ + + + + +

Pros and Cons		
Benefit	Mortality reduction (+++)	Incidence (+)
Harm	Negligible Overdiagnosis of CRC (++)	Overdiagnosis of Adenoma (Not well-studied)

	Mortality Reduction
Minnesota Trial	33% (13%-50%)
Denmark Trial	18% (1%-32%)
Hardcastle Trial	15% (2%-26%)

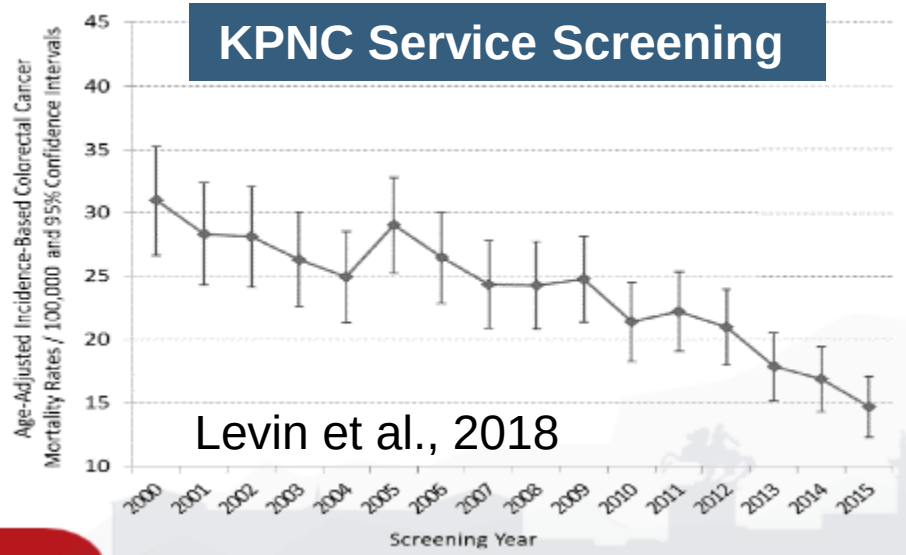
Universal Population-based FIT CRC Screening

Italy Service Screening



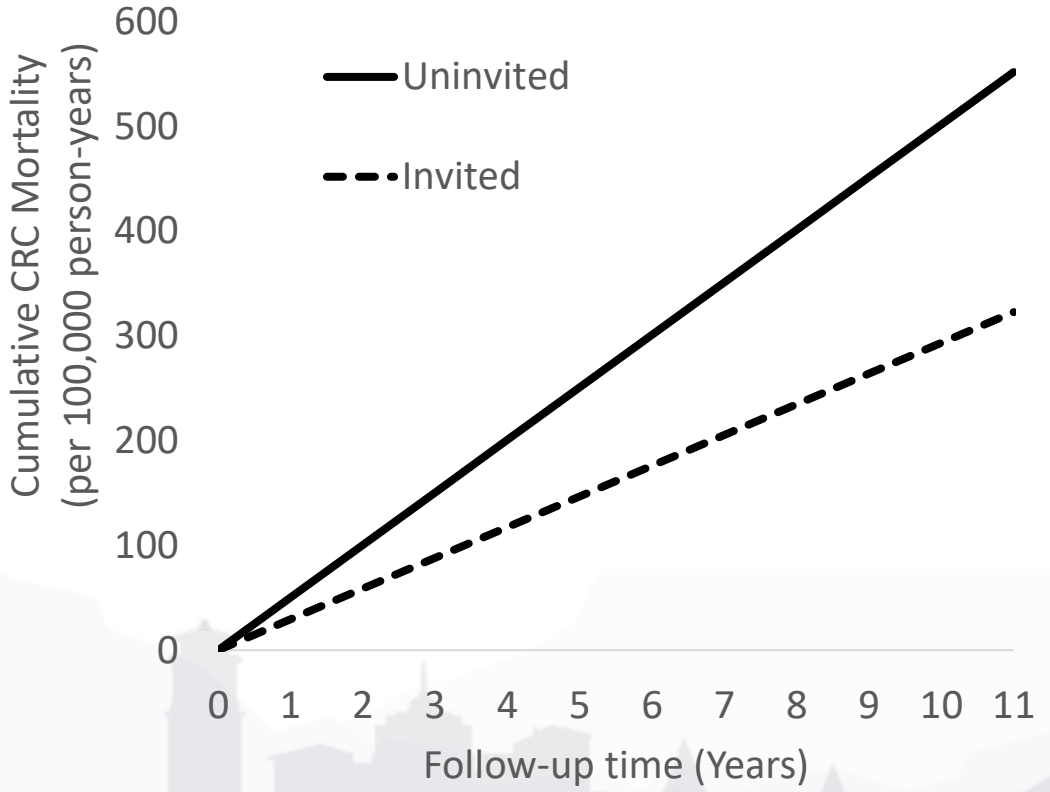
Mortality Reduction 22%

KPNC Service Screening



Mortality Reduction 52%

Taiwanese nationwide biennial FIT screening for colorectal cancer



Mortality reduction by 40%

Overdetection of Colorectal Cancer

Pros and Cons		
Benefit	Mortality reduction (+++)	Incidence (+)
Harm	Negligible Overdiagnosis of CRC (++)	Overdiagnosis of Adenoma (Not well-studied)

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Assessing overdiagnosis of fecal immunological test screening for colorectal cancer with a digital twin approach

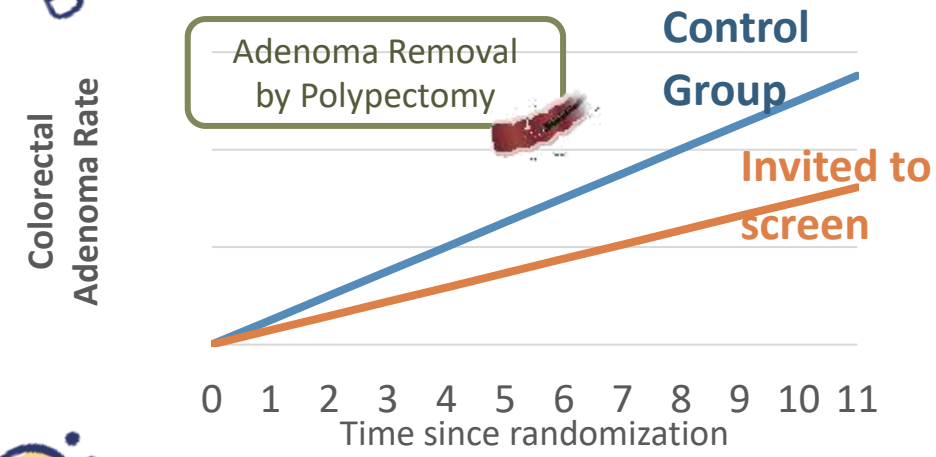
Ting-Yu Lin[1,7], Sherry Yueh-Hsia Chiu[2,3,7], Ling-Chun Liao[4], Sam Li-Sheng Chen[5], Han-Mo Chiu[6,8]✉ and Tony Hsiu-Hsi Chen[1,8]✉

Taiwan Service Screening

The percentage of overdiagnosis of colorectal cancer is 10%

Challenges for Evaluating CRC Incidence Reduction and Overdiagnosis of Colorectal Adenoma?

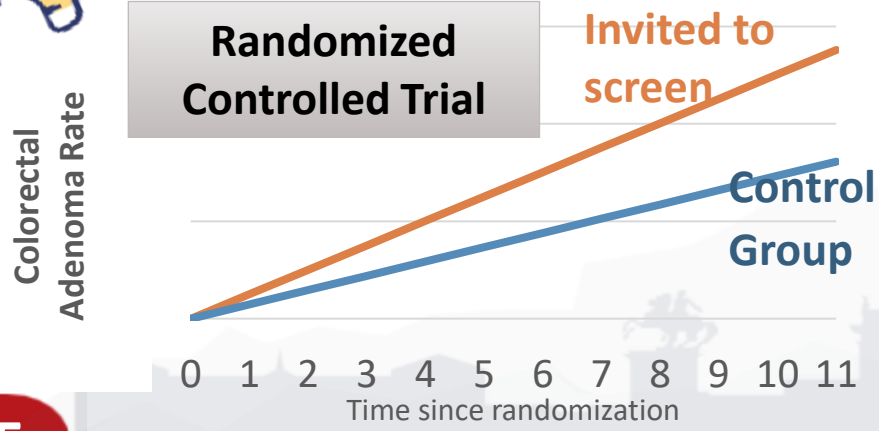
1 Incidence Reduction



A mixture of progressive and over-detected adenoma

2 Overdetection of Adenoma

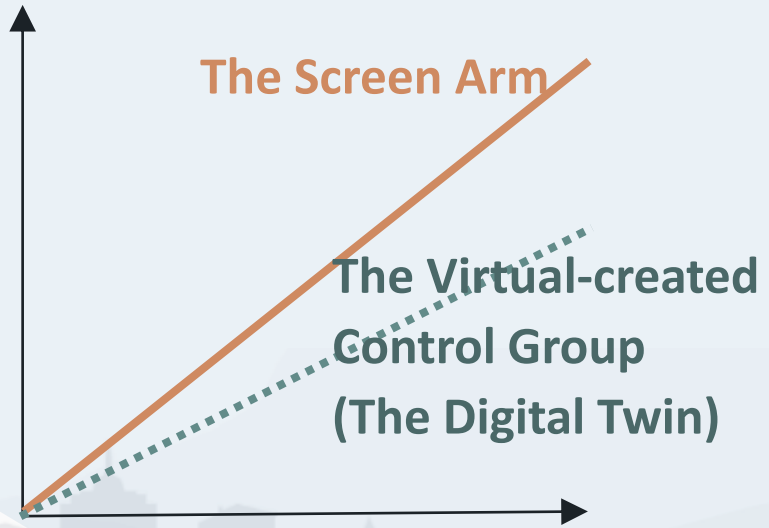
Randomized Controlled Trial



Control group is difficult to estimate colorectal adenoma rate

Solution

Digital Twin Design



Subsidiary Issues of Universal Screening

Good example

- **Inter-screening Interval**

Annual	↓ FN ↑ FP
Biennial	
Triennial	↑ FN ↓ FP

Risk-spectrum

Percentile of Risk Score
95-100
90-95
80-90
70-80
60-70
50-60 (Average Risk)
40-50
30-40
20-30
10-20
5-10
0-5

False Negative (FN)

High-Risk Group

Interval Cancer

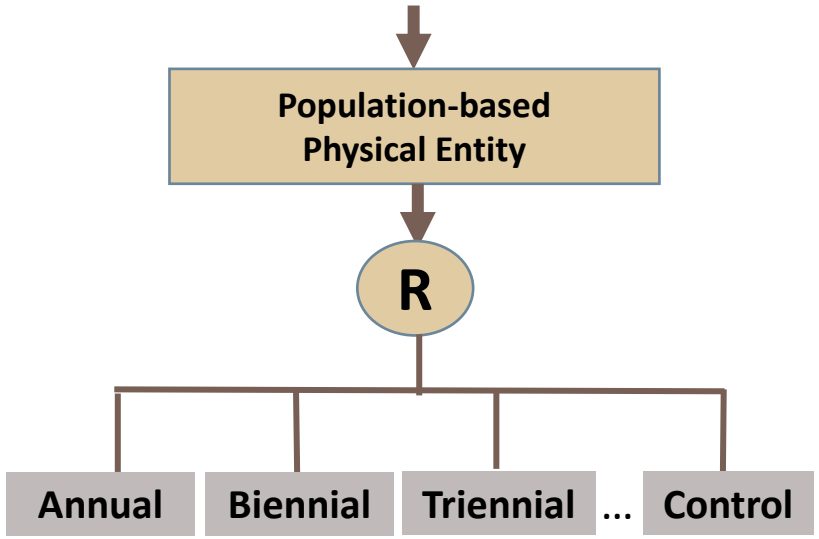
Overdetection

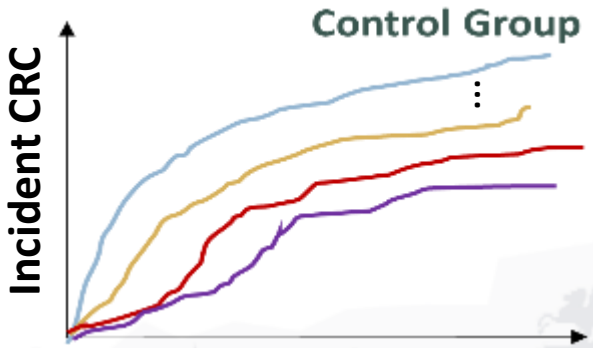
Low-Risk Group

False Positive (FP)

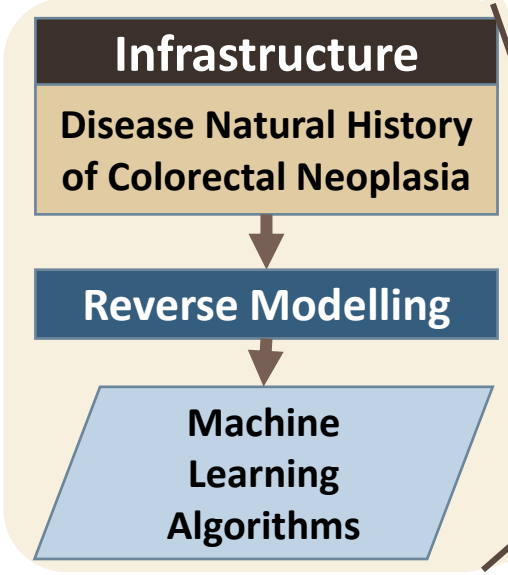
RCT vs Digital Twin Design for Impacts of Inter-screening Interval on Incident CRC

RCT Design

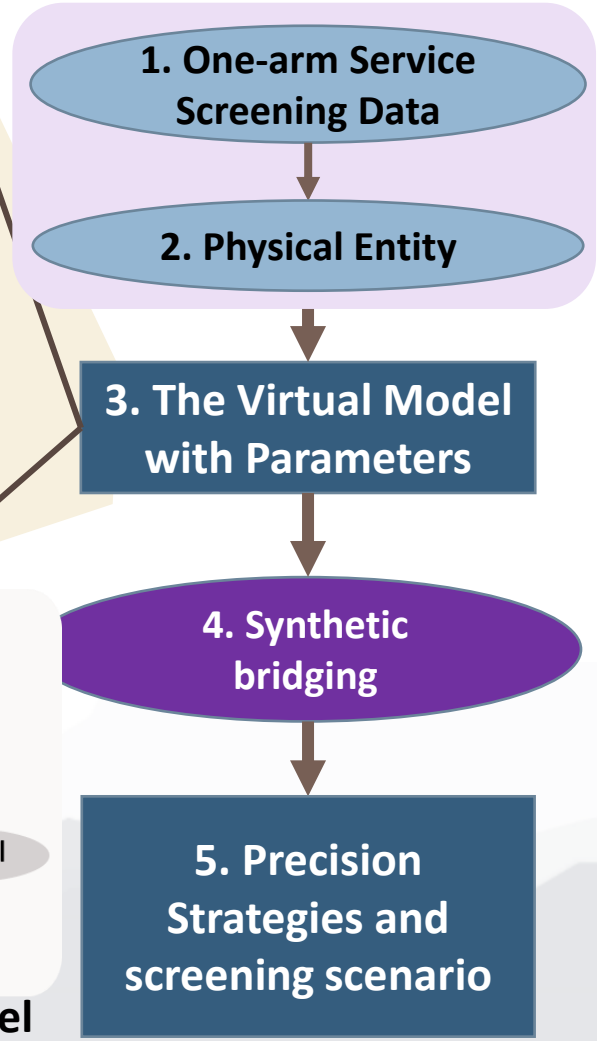


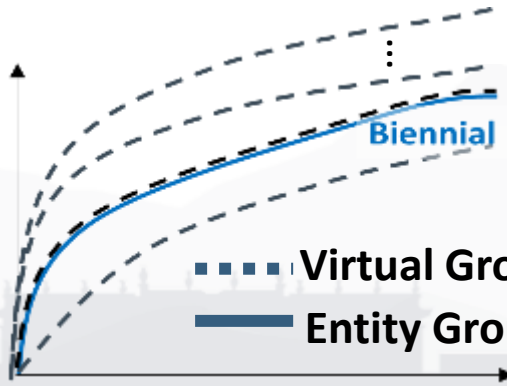


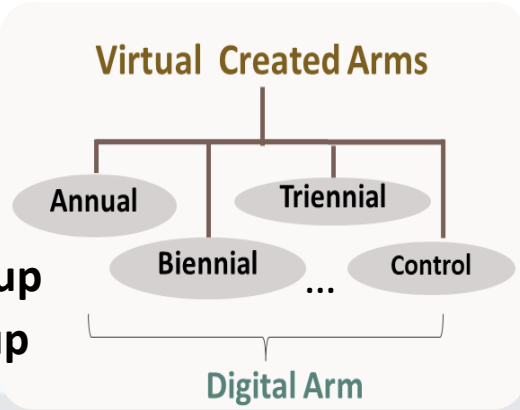
Digital Twin Design for FIT service screening



5-D Model



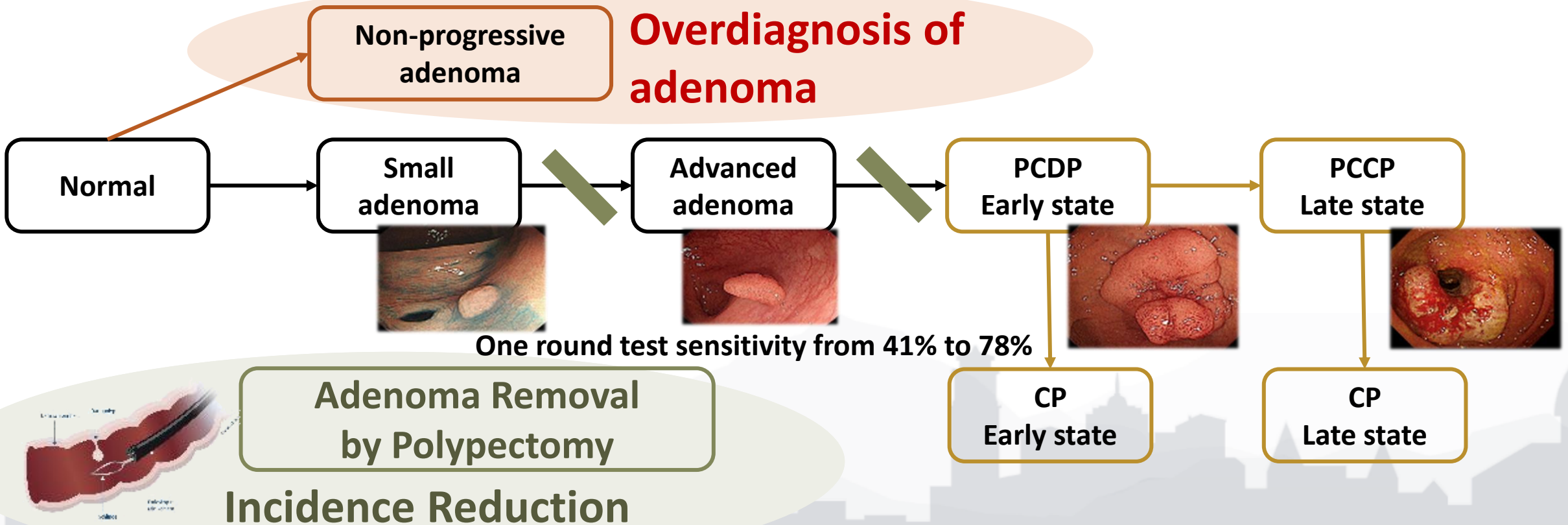




Inter-screening Interval by f-Hb level

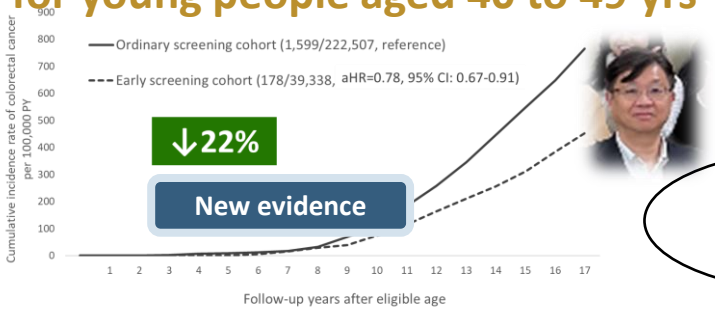
Infrastructure of Natural History Model for Deciphering Incidence Reduction and Overdiagnosis

- Data source: Taiwan Nationwide CRC screening (n=5,417,699)
- Period: 2004-2018 cohort (follow-up until 2021 to ascertain 144,028 adenoma and 32,158 CRCs)



Impacts of Inter-screening Interval on Incidence of CRC and Overdetection of adenoma

Reducing Colorectal Cancer Incidence with FIT Screening by 22% for young people aged 40 to 49 yrs



Reference group: No Screen

Eligible population

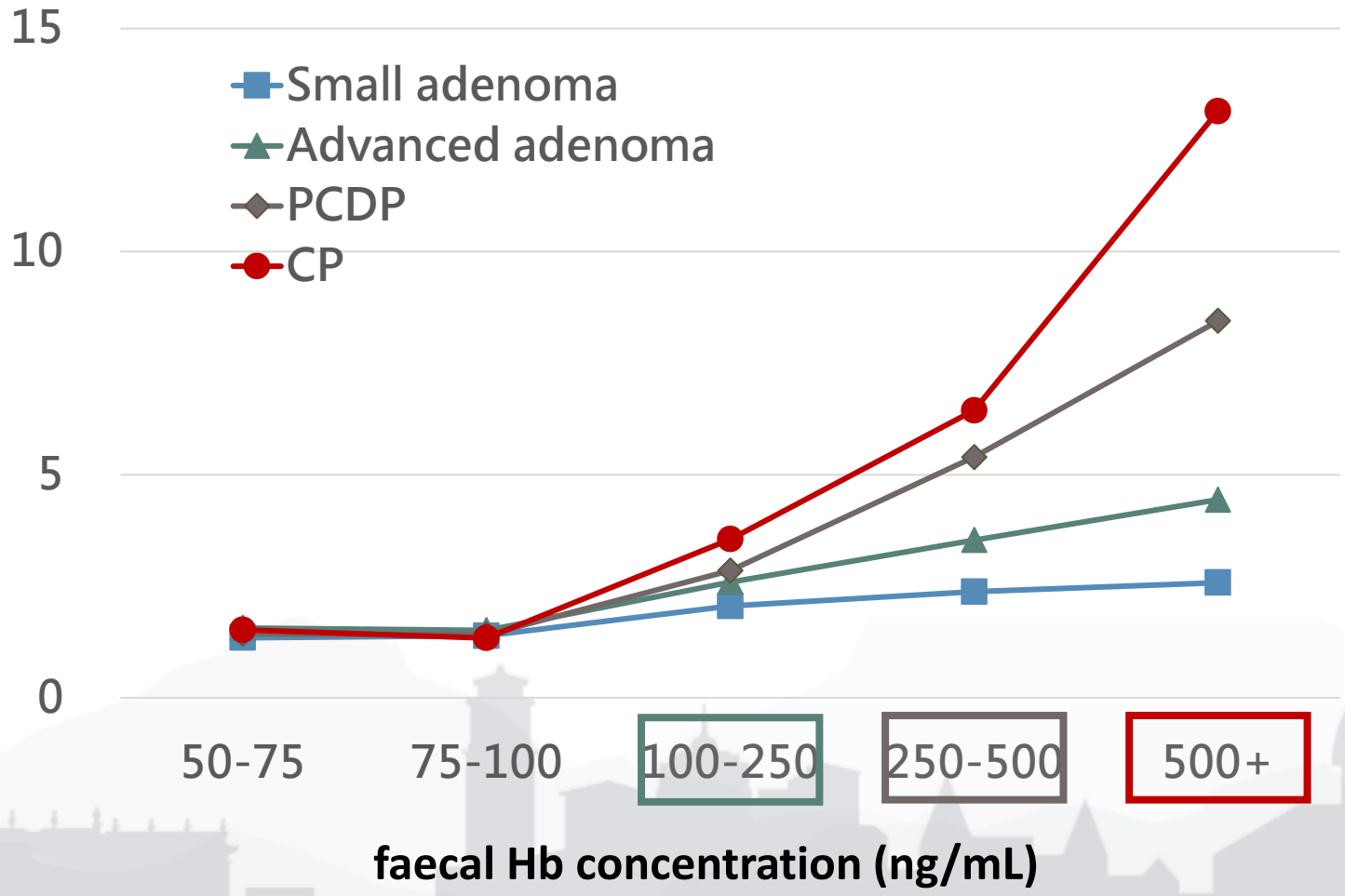
	Annual	Biennial	Triennial
Incidence Reduction	35%	33%	31%
Advance Cancer Reduction	44%	42%	39%
Overdiagnosis of Adenoma	46%	32%	25%

Taiwan Program

From Universal Population-based to Precision Colorectal Cancer Screening

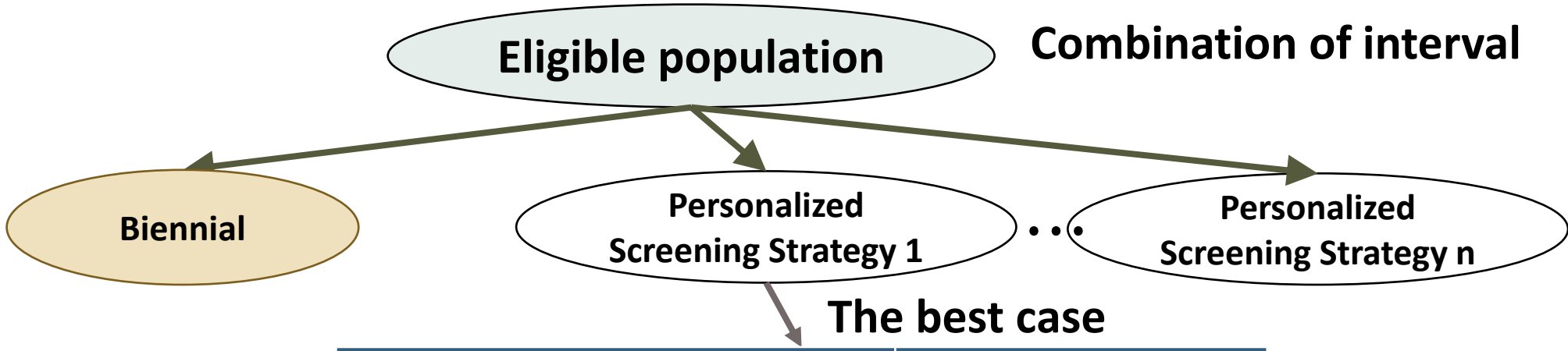
The fHb-based multistate risk model for precision colorectal cancer screening

The fHb-based risk profile(compared to faecal Hb concentration below 50 ng/mL) by multistate colorectal neoplasia



Personalized Screening Strategies by the f-Hb calibrated multistate risk model

Digital Twin Approach



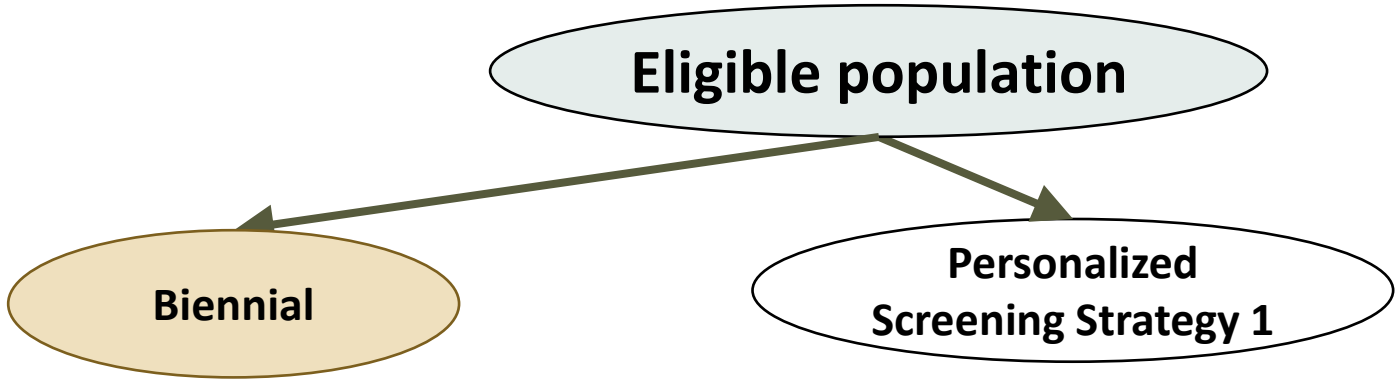
Low-Risk Group

High-Risk Group

faecal Hb concentration (ng/mL)	Inter-Screening Interval
0-50	6
50-75	3
75-100	3
100-250	2
250-500	1
500+	0.5

Personalized Screening Strategy of Reducing Over- detection of Adenoma and Unnecessary Screening Utilization

Digital Twin Approach



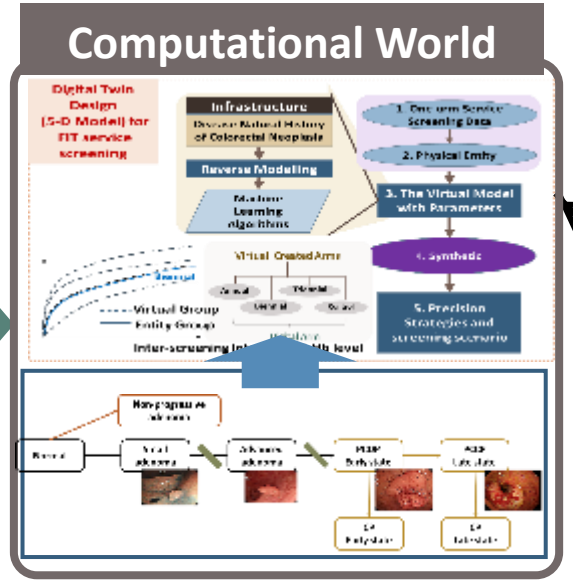
Overdiagnosis of Adenoma (Reduction)	**32%**	**12%** (20%)
Reduction of Screening Utilization	Reference group	FIT tests: 39% Colonoscopy: 35%

Perspective Digital Twin Design from Primary to Tertiary Prevention

ICSN International Cancer Screening Network

Physical World

Computational World



Virtual World

Primary Prevention

Chemoprevention

Microbiota supply

Environmental Change

Life Style and Behavior Modification

Prophylactic Surgery for FAP

Secondary Prevention

Endoscopic exam

f-HB guided Screening Strategy

Image Profiles

CTC

Molecular Biomarkers

Molecular or DNA-based biomarkers

Treatment and Therapy

Surgery/Mini invasive surgery

Radiotherapy

Immunotherapy

Adjuvant Chemotherapy and Target Therapy

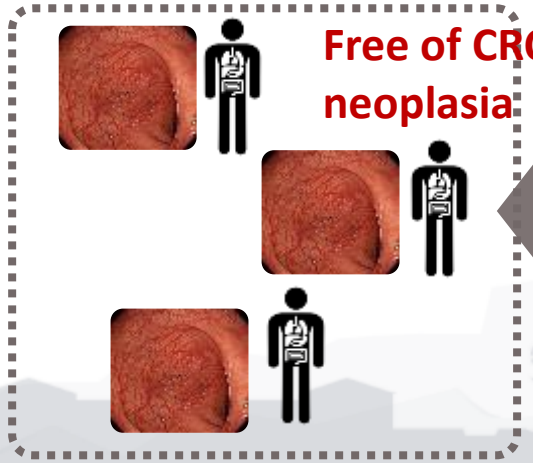
Precision Prevention

Life Style+ Micr

Chemoprevention

Annual FIT test

Molecular biomarkers + Endoscopic exam + Surgery+ Immunotherapy



Conclusions

- Precision FIT screening with f-Hb-calibrated model not only reduces incident CRCs but also avoids colorectal adenoma over-detection as well as unnecessary FIT tests and colonoscopies.
- The Digital Twin Approach provides an efficient means for evaluating precision population-based FIT CRCs.

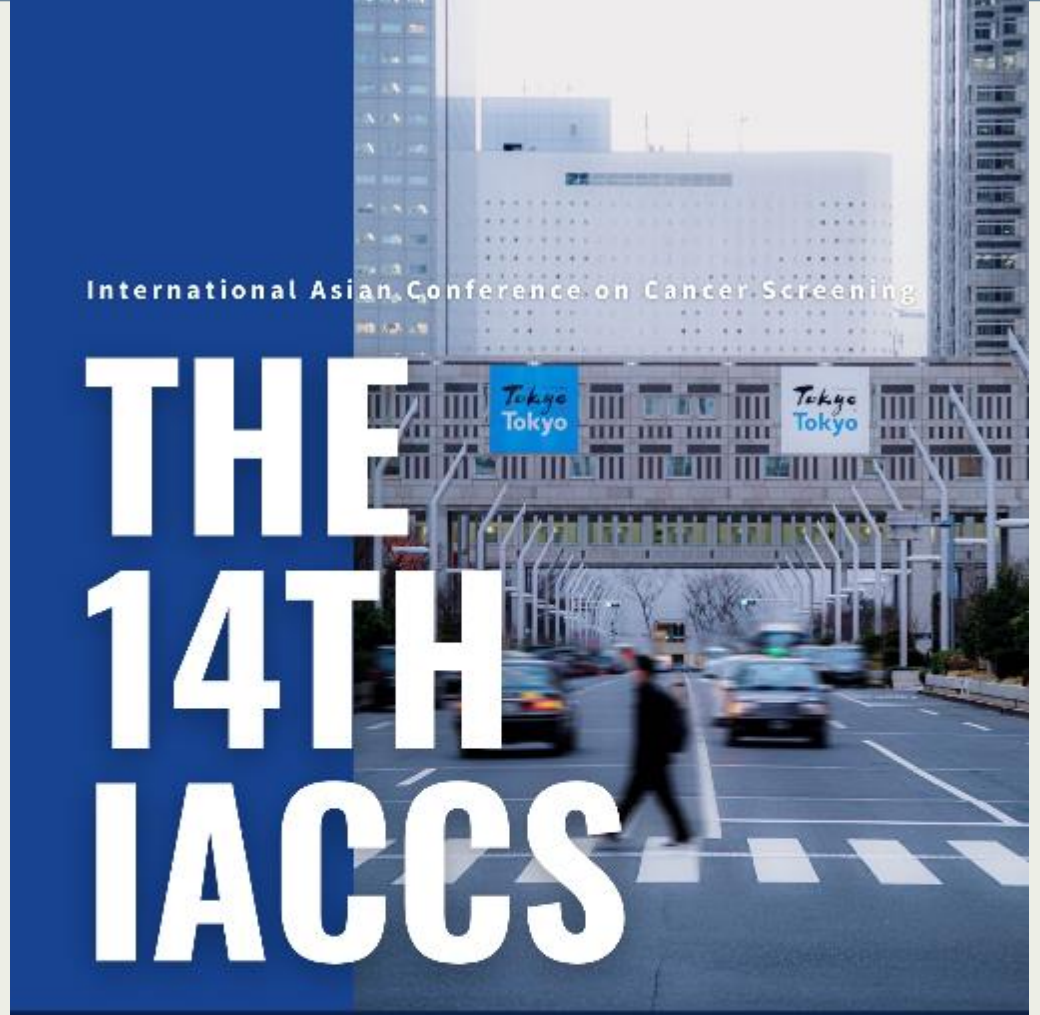
Thank You for Your Attention

Director-General, Dr. Chao-Chun Wu

Section Director, Li-Ju Lin

Taiwan Cancer Screening Evaluation Group

International Asia Conference on Cancer Screening, IACCS



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