Female reproductive and hormonal factors with gallbladder cancer risk in Asia: A pooled analysis of the Asia Cohort Consortium

Aesun Shin

Seoul National University College of Medicine, Seoul, Korea

September 25, 2024

Disclosure: Nothing to disclosure

WCE
WORLD CONGRESS OF EPIDEMIOLOGY 2024

Female reproductive and hormonal factors with gallbladder cancer risk in Asia: A pooled analysis of the Asia Cohort Consortium

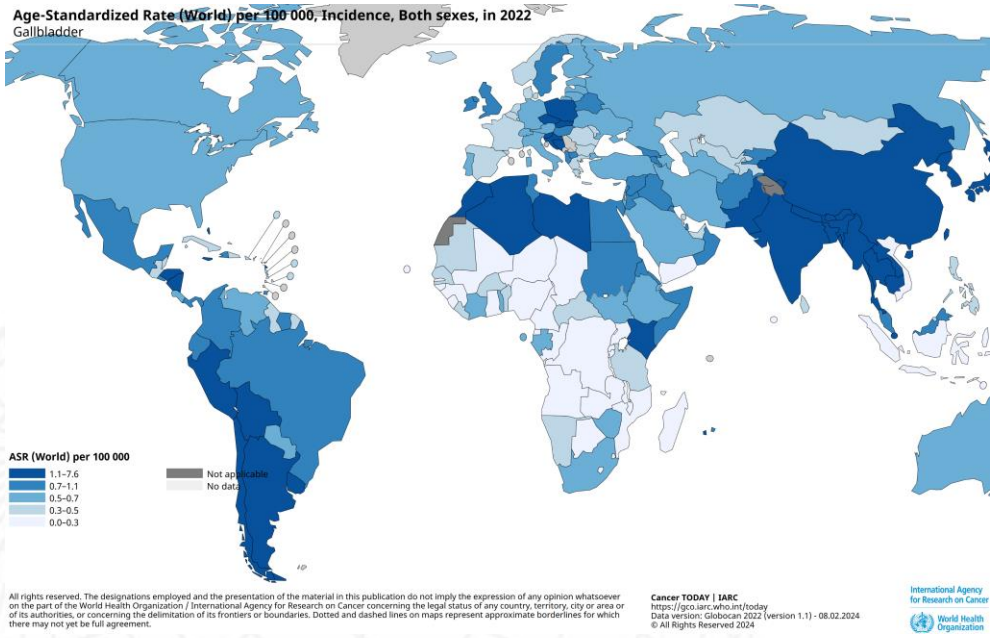
Aesun Shin, M.D., Ph.D.
Department of Preventive Medicine
Cancer Research Institute
Interdisciplinary Program in Cancer Biology
Integrated Major in Innovative Medical Science
BK4 Smart Healthcare
Division of Clinical Epidemiology, MRCC
Seoul National University College of Medicine
https://snucm.elsevierpure.com/en/persons/y-shin-9

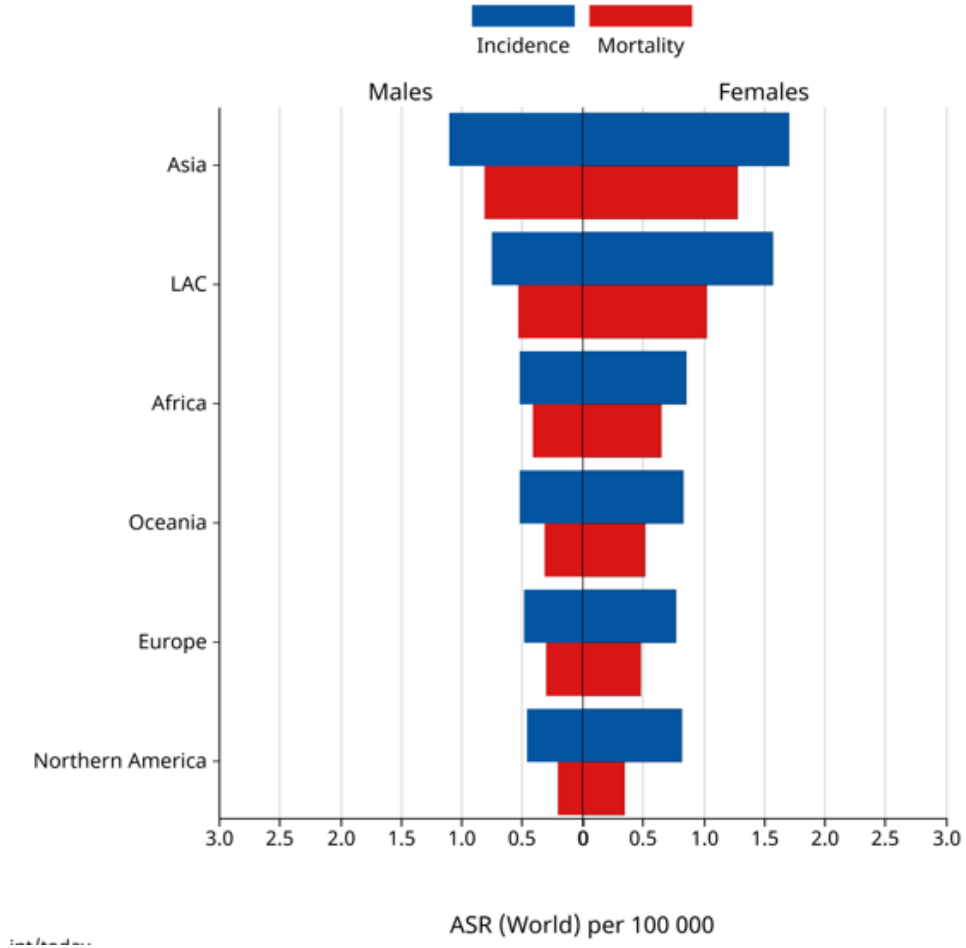
World Congress of Epidemiology
2024.9.24-27
Cape Town, SA

SNU MEDICINE
Seoul National University College of Medicine

Background

- **Gallbladder cancer (GBC)**
- The 6th most common malignancy of the gastrointestinal tract
- More than 70% cases and deaths occur in Asia
- Poor prognosis with 5-year survival rates 10-30%
- Female dominance





ASR (/100,000) incidence and mortality, males and females in 2022, Globocan 2022

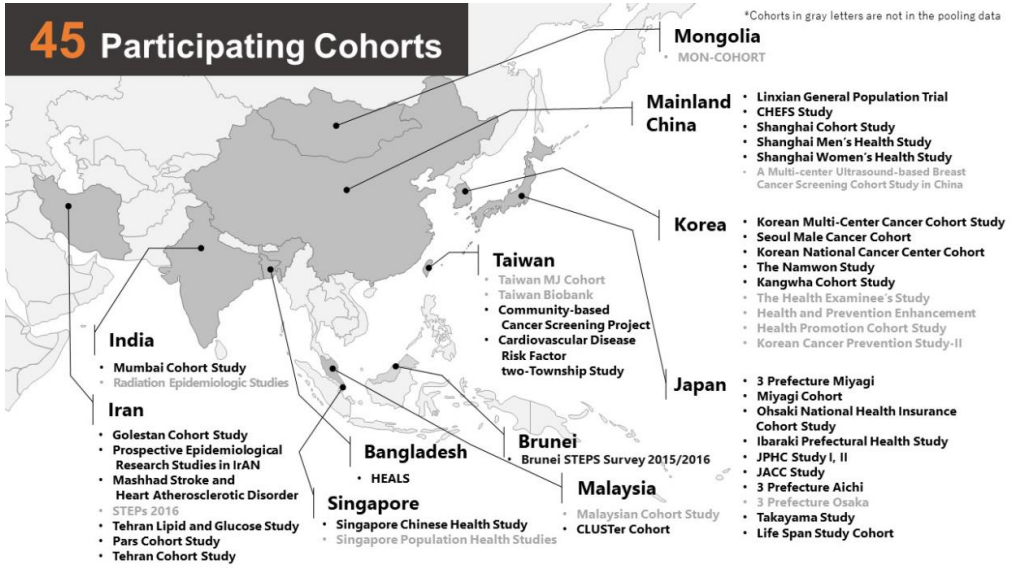
SNU MEDICINE
Seoul National University College of Medicine

Risk factors of GBC

- A history of gallstones
- Obesity
- Chronic infections such as *Salmonella typhi*, *Salmonella paratyphi*, and *Helicobacter pylori*
- Reproductive and hormonal factors
  - Gallbladder tissue expresses estrogen and progesterone receptors
  - Elevated estrogen increases cholesterol secretion, while progesterone reduces bile acid secretion and delays gallbladder emptying → supersaturation of bile and facilitating gallstone formation
  - The Biliary Track Cancers Pooling Project
    - An increasing number of live births
    - A later age at menarche among Asian women
    - Only four studies from three Asian countries were included

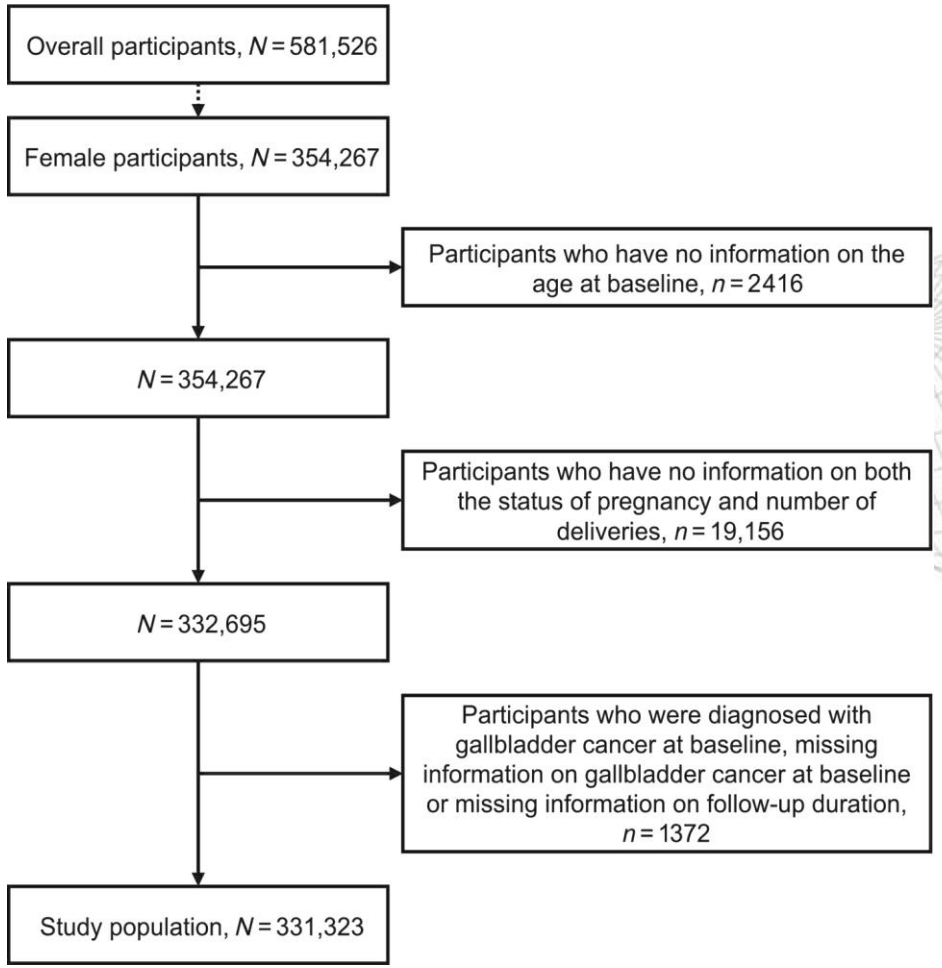
The Asia Cohort Consortium

- Rationale
  - Serving as a platform for cross-cohort collaborative projects
  - Acting as an incubator for new cohorts
- Established in 2004
- 37 publications and 40+ ongoing projects on mortality, cancer, diabetes, etc, as of September 2024



The aim and methods

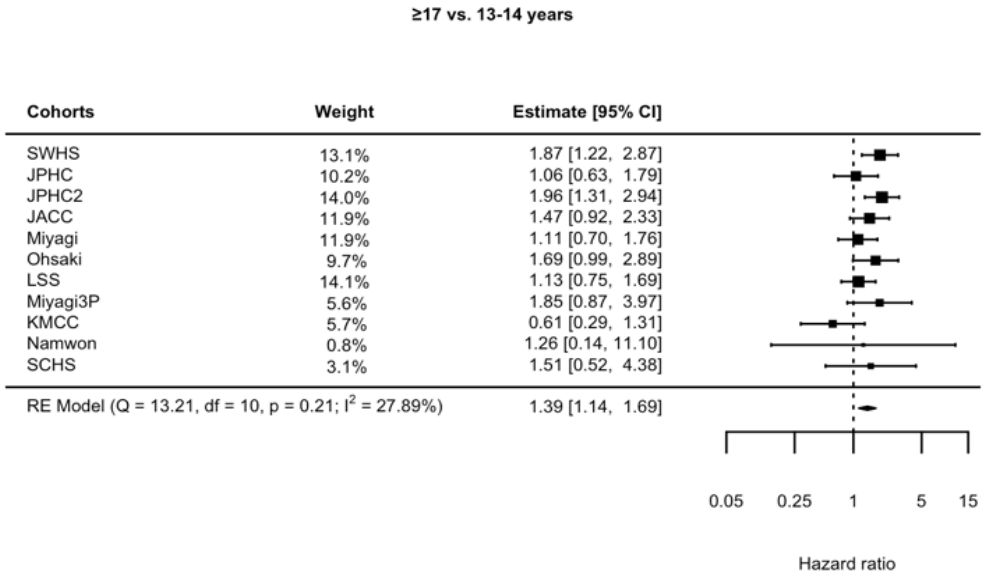
- The aim : To investigate the association between female reproductive factors and GBC risk, considering birth cohorts of Asian women
- Study design : The pooled analysis of data collected by the Asia Cohort Consortium
- 331,323 women from 12 cohorts from 4 countries (China, Japan, Korea, and Singapore)
- Cancer ascertainment: Linkage to local cancer registries (1173 GBC cases during mean of 16.5 years of follow-up)
- Analysis
  - Cox proportional hazards models to estimate the hazard ratios (HRs) and corresponding 95% confidence intervals (CIs)
  - Random effect models to pooling the cohort-specific HRs
  - Stratification by birth cohorts



Results

- No clear associations: parity, age at the first delivery or pregnancy, breastfeeding, age at menopause, OC use, HRT use
- Later age at menarche
  - 17 years vs. 13-14 years HR 1.39 (95% CI 1.14-1.69)
- Birth cohort born in 1940 or later
  - Age at menarche: Stronger association among birth cohort born in 1940 or later

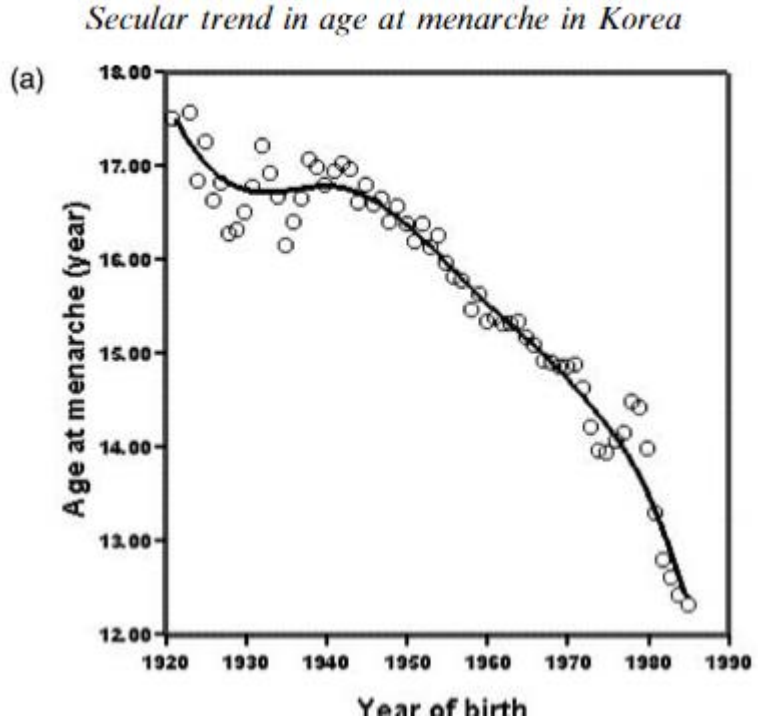
    HR 2.56 (95% CI 1.50-4.35)
  - Age at first delivery of 31 years or older HR 1.56 (95% CI 1.09-2.25) compared to women with an age at fist delivery of 20 years or younger



SNU MEDICINE
Seoul National University College of Medicine

Discussion

- A later age at menarche and an increased risk of GBC, especially among the birth cohort born in 1940 and later
  - Associations were generally consistent across cohort
  - Consistent with a previous pooled analysis (the Biliary Track Cancers Pooling Project) and Korean National Health Insurance study
- Later birth cohorts
  - Experienced early menarche → Reflects nutritional status during childhood and puberty
  - A later age at first delivery or pregnancy and low parity → lower lifetime exposure to sex hormone



Conclusions

- Later age at menarche and at first delivery were associated with a higher risk of GBC.
- These associations varied by birth cohort.

Received: 9 October 2023 | Revised: 18 January 2024 | Accepted: 22 January 2024
DOI: 10.1002/ijc.34916

IJC INTERNATIONAL JOURNAL of CANCER | UICC

RESEARCH ARTICLE
Cancer Epidemiology

Association of female reproductive and hormonal factors with gallbladder cancer risk in Asia: A pooled analysis of the Asia Cohort Consortium

Aesun Shin[1,2,3,4] | Sooyoung Cho[1,4] | Sarah Krull Abe[5] |
Md Rashedul Islam[5,6] | Md Shafiur Rahman[5,7] | Eiko Saito[8] |
Sayada Zartasha Kazmi[1] | Ryoko Katagiri[9,10] | Melissa Merritt[11] |
Ji-Yeob Choi[12] | Xiao-Ou Shu[13] | Norie Sawada[9] | Akiko Tamakoshi[14] |
Woon-Puay Koh[15,16] | Ritsu Sakata[17] | Atsushi Hozawa[18] | Jeongseon Kim[19] |
Sue K. Park[1,2,3] | Sun-Seog Kweon[20] | Wanqing Wen[13] |
Shoichiro Tsugane[9,21] | Takashi Kimura[14] | Jian-Min Yuan[22,23] |
Seiki Kanemura[18] | Yumi Sugawara[18] | Min-Ho Shin[20] | Habibul Ahsan[24] |
Paolo Boffetta[25,26] | Kee Seng Chia[27] | Keitaro Matsuo[28,29] |
You-Lin Qiao[30] | Nathaniel Rothman[31] | Wei Zheng[13] |
Manami Inoue[5] | Daehee Kang[1,3]

Shin A et al. Int J Cancer. 2024;155(2):240-250.

SNU MEDICINE Seoul National University College of Medicine 125

Ackownledgements

ACC Executive Committee Members
Jeongseon Kim (NCC, Korea)
You-Lin Qiao (Chinese Academy of Medical Sciences & Peking Union Medical College, China)
Paolo Boffetta (Stony Brook University, USA)
Keitaro Matsuo (Aichi Cancer Center, Japan)
Manami Inoue (NCC, Japan)
Daehee Kang (Seoul National University, Korea)
Aesun Shin (Seoul National University, Korea)
Jung Eun Lee (Seoul National University, Korea)
Wei Zheng (Vanderbilt University, USA)
Nathaniel Rothman (NCI, USA)

Reproductive Factors Working Group Members

Ryoko Katagiri (NCC, Japan)
Melissa Merritt (University of Sydney, Australia)
Aesun Shin (Seoul National University, Korea)
Ji-Yeob Choi (Seoul National University, Korea)
Sarah Abe (NCC, Japan)
Md. Rashedul Islam (NCC, Japan)
Md. Shafiur Rahman (NCC, Japan)
Seow Wei Jie (National University of Singapore , Singapore)

Participating cohorts
Shanghai Cohort Study
Shanghai Women's Health Study
Japan Public Health Center-based prospective Study 1,2
Japan Collaborative Cohort Study
Miyagi Cohort Study
Ohsaki National Health Insurance Cohort Study
Life Span Study Cohort
Three Prefecture Cohort Study Miyagi
Korean Multi-center Cancer Cohort Study
Korean National Cancer Center Cohort
The Namwon Study

Seoul National University
Sooyoung Cho, PhD

SNU MEDICINE
Seoul National University College of Medicine

Thank You

SNU MEDICINE

Seoul National University College of Medicine