

## Rethinking ELSI in Birth Cohort Studies: Insights from Global Discourse and Local Practice

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**Objective & Methods :** This study aims to clarify current international discourse on Ethical, Legal, and Social Implications (ELSI) in birth cohort studies and to contextualize these findings within ongoing research practice. A scoping review of Japanese and English publications indexed in Web of Science and PubMed up to August 2023 was conducted. To gain practice-based insights, we conducted semi-structured interviews with 21 research staff from the Japan Environment and Children's Study across three prefectures between 2023 and 2025. Reflexive thematic analysis was applied to the interview data to identify key ethical challenges and practical responses encountered in everyday research settings.

**Results :** The scoping review identified 3,399 relevant publications, of which 62 met the inclusion criteria. These studies addressed a broad range of ELSI topics, including informed assent, parental consent, data governance, and efforts to ensure participant diversity and inclusion. Several publications also discussed the implementation of participant engagement approaches. The interview analysis revealed both ongoing efforts and limitations in maintaining participant inclusion over a decade, as research protocols and regulatory demands evolved. When asked about incorporating participants' views into the study, interviewees described difficulties in capturing the voices of less engaged participants, as well as concerns about the overrepresentation of voices from highly engaged individuals. Some reflected on situations in which those facing the greatest difficulties, despite their central importance to the cohort study, became invisible due to barriers to participating in follow-up surveys.

**Discussion :** As international data sharing expands, birth cohort studies must develop governance models that not only meet regulatory requirements but also respond to the evolving capacities and rights of child participants through ongoing dialogue with global stakeholders.

## Association between hypertension and progressive liver fibrosis among individuals with MASLD

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**Background :** Metabolic dysfunction-associated steatotic liver disease (MASLD) is a type of steatotic liver disease (SLD) defined by low alcohol consumption and meeting at least one of five cardiometabolic criteria (obesity, hypertension (HT), glucose metabolism disorder, hypertriglyceridemia, low HDL cholesterol) accounting for approximately 80% of SLD. Liver fibrosis (LF), one of the relevant health outcomes of MASLD, leads not only to liver diseases but also to cardiovascular diseases. There are limited studies examining risk factors other than diabetes mellitus (DM) for LF. This study aimed to examine the association between HT and LF.

**Methods :** This cross-sectional study utilized the data of health check-up examinees in fiscal year 2020, obtained from the Seirei Health Care Division. Individuals aged 40–69 years were included and then participants with missing values for any items required to calculate for Fatty Liver Index (FLI) and FIB4-Index. SLD was defined as  $FLI \geq 30$  and progressive LF as  $FIB4\text{-Index} \geq 1.3$ . Obesity and HT were defined in accordance with the MASLD cardiometabolic criteria, and DM was defined as fasting plasma glucose  $\geq 126$  mg/dL or glycated hemoglobin (HbA1c)  $\geq 6.5\%$  or current treatment for DM. Binomial logistic regression analysis was performed to evaluate the association between progressive LF and HT, adjusted for sex, age categorized by 10 years, obesity, and DM.

**Results :** A total of 19,906 participants (75.8% male; 94.1% with obesity) were analyzed. Across all age categories and either obesity status, the proportion of progressive LF was higher in the HT+ group and increased with age. The adjusted odds ratio (OR) for HT was 1.300 (95% confidence interval (95% CI): 1.190-1.421). Stratified analyses showed significant associations in both obese (OR: 1.27 (95% CI: 1.16–1.39)) and non-obese participants (1.84 (1.33–2.55)).

**Conclusions :** Among individuals aged 40–69 years with MASLD, HT was associated with LF, independent of obesity status.

## Trends and Regional Variation in Mortality from Ischemic Heart Disease in Korea and Japan, 1999-2023

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**Background :** Despite overall declines in cardiovascular mortality, ischemic heart disease (IHD) remains a leading cause of death in Korea and Japan.

**Objective :** To examine long-term trends and regional variation in IHD mortality within Korea and Japan from 1999 to 2023.

**Methods :** National mortality data from 1999 to 2023 were obtained using ICD-10 codes I20–I25. Age-standardized mortality rates (ASMRs) were calculated using the direct method with the 2015 Japanese population as the standard. Regional variation was assessed across 250 districts in Korea and 47 prefectures in Japan using standard deviation (SD) for absolute disparities and coefficient of variation (CV) for relative disparities.

**Results :** IHD mortality declined markedly in both countries. In Korea, ASMR increased from 66.8 per 100,000 in 1999 to 95.7 in 2006, then decreased to 40.1 in 2023. In Japan, the ASMR steadily declined from 100.4 in 1999 to 48.5 in 2023. In Korea, SD rose from 33.8 to 42.4 (1999–2005) before falling to 19.6 in 2023, suggesting a reduction in absolute regional differences—likely due to declining overall mortality rather than regional convergence. CV declined modestly from 0.52 to 0.43 but fluctuated without sustained improvement. In Japan, SD remained low (13.0 to 14.1), yet CV doubled from 0.14 to 0.32, indicating widening relative disparities.

**Conclusion :** Despite substantial reductions in IHD mortality in both Korea and Japan, regional variations persist with differing patterns. In Korea, absolute regional differences decreased, but this appears to be largely driven by overall mortality decline rather than meaningful convergence across regions. In Japan, absolute differences remained low, but relative disparities increased over time. Sustained regional monitoring and targeted actions may support more balanced reductions in IHD mortality.

## Did the Launch of ChatGPT Affect Retraction Trends? Evidence from an Interrupted Time Series Study.

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**Introduction :** The recent proliferation of generative AI, such as ChatGPT, has raised concerns about research integrity. While the potential for AI-generated content to undermine scientific literature is discussed, its quantitative impact on retractions remains unclear. This study aims to evaluate this impact while accounting for other significant events.

**Methods :** I conducted an interrupted time series analysis using the Retraction Watch Database, focusing on biomedical papers. The analysis included papers published from January 2012 to July 2023 and that had been retracted by the time of data extraction (August 28, 2025). The intervention was the public release of ChatGPT (cutoff: March 1, 2023, with a 3-month lag). I modeled the monthly rate of retractions for "Computer-Aided Content" using a negative binomial regression, adjusting for the effects of the COVID-19 pandemic and Hindawi's mass retraction in October 2022. Sensitivity analyses used 0- and 6-month lags.

**Results :** After adjusting for the COVID-19 pandemic and Hindawi's mass retraction, the release of ChatGPT was associated with a significant acceleration in the trend of retractions for computer-aided content. The post-intervention trend increased by 69% per month (Incidence Rate Ratio [IRR]: 1.69, 95% Confidence Interval [CI]: 1.35-2.11). The immediate change in retraction level was not statistically significant (IRR: 2.30, 95% CI: 0.88-6.03). Sensitivity analyses yielded similar conclusions.

**Discussion :** The findings suggest that the release of ChatGPT is associated with an accelerated increase in retractions for computer-aided content, even after accounting for the effects of the COVID-19 pandemic and publisher-specific mass retraction events. While the pandemic was linked to a general rise and publisher crackdowns to a temporary fall, the post-ChatGPT era shows a distinct and significant upward trend. Continuous monitoring and updated research integrity policies are essential in the age of generative AI.

## Ethical and Methodological Considerations for Introducing Interventions in Trial-Ready Cohorts

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**Background :** Observational and interventional studies overlap and diverge in design, ethics, and social impact. The interest in preventive interventions among otherwise healthy individuals have been raising. However, methodological frameworks and ELSI (Ethical, Legal and Social Issues) research remain limited. This study focuses on the interface between observational and interventional studies to examine the significance, implications, and ELSI/RRI (Responsible Research and Innovation) issues of introducing interventions.

**Method :** A narrative review on trial-ready cohorts, especially virtual randomized controlled trials (vRCTs), was conducted to clarify disciplinary differences. Semi-structured interviews were also carried out with birth cohort investigators, exploring feasibility, requirements, challenges, and countermeasures for interventional studies in observational settings.

**Results :** Review of 7 vRCT studies showed advantages—low cost, speed, ethical feasibility, scalability—and limitations, including restricted causal inference, selection bias, missing data, and data quality. Interviews with 5 cohort investigators and one pediatric researcher revealed mixed views. Cohort investigators noted that feedback itself may act as an intervention. While some saw early action on developmental delay or depressive tendencies as a benefit, hesitation remained toward interventional research within cohorts. Still, cohorts were recognized as efficient infrastructures. The pediatric researcher argued that withholding treatment could disadvantage participants, and that effective therapies should be actively shared and tested.

**Discussion & Conclusion :** vRCTs offer promise in resource-limited settings but lack accuracy, serving more as complements to real RCTs. Trial-ready cohorts merit further consideration. Future work will design workflows for introducing interventional or secondary studies into observational research and mechanisms to feed data back into primary studies.