

The Impact of Short-Term Exposure to Ambient Air Pollution on Outpatient Visits for Cardiovascular Diseases: A Time-Series Analysis in Liuzhou, China

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Article

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Posted Date: October 5th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10049391/v1>

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Additional Declarations: No competing interests reported.

Title:

The Impact of Short-Term Exposure to Ambient Air Pollution on Outpatient Visits for Cardiovascular Diseases: A Time-Series Analysis in Liuzhou, China

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Acknowledgements

We extend our sincere gratitude to all the researchers and participants for their invaluable support for this study. We would also like to thank all the staff of the Liuzhou Center for Disease Control and Prevention, Guangxi, China, for providing us with a good research environment.

Funding

This work was supported by Scientific research Project of the Health Commission of Guangxi (grant Z-B20241388). The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the funding agencies.

Authors' Contributions

YL - data collection, primary data analysis, and writing

SY and DH - data collection, analysis, revisions, and writing

JL, JY, TW- conception and design

LZ- supervision, revisions, and final review

YL, SY and DH have made equal contributions to this article and are all recognized as co-first authors.

Data sharing statement

The data used in this study are stored at the Institute of Environmental Hygiene and School Health Prevention and Control, Liuzhou Center for Disease Control and Prevention. The data are managed in strict accordance with the data security and confidentiality requirements imposed by the Liuzhou Center for Disease Control and Prevention and are not publicly available. Access to the data may be granted to institutions that meet the criteria and have a reasonable research purpose. Formal requests must first be submitted to the Institute of Environmental Hygiene and School Health Prevention and Control (contact via lzcacsphj@163.com). Upon preliminary review, the request will be forwarded to the Liuzhou Center for Disease Control and Prevention for final approval.

Competing Interests

The authors have declared that no competing interests exist.

Abstract

Rapid industrialization worsened air pollution in Liuzhou, increasing cardiovascular disease (CVD) risks. We investigated short-term associations between six pollutants (PM_{2.5}, PM₁₀, SO₂, NO₂, CO, O₃) and daily CVD outpatient visits (2,986,820 from 2014–2024) and evaluated the impact of 2018 policies targeting polluting chemical enterprises. Using a distributed lag nonlinear model within a generalized additive Poisson regression, we quantified percent changes per interquartile range increase, adjusting for meteorology and temporal trends, with pre/post-2018 comparisons. NO₂ (lag5: RR=1.447, 95%CI: 1.413–1.483), PM₁₀ (lag1: RR=1.095, 1.079–1.112), and PM_{2.5} (lag1: RR=1.036, 1.021–1.051) significantly increased visits. After 2018, PM_{2.5}, PM₁₀, SO₂, NO₂, and CO declined ($p<0.01$); associations for SO₂, CO, PM_{2.5}, and PM₁₀ weakened. NO₂ effects were stronger in females and cold seasons, persisting in two-pollutant models. No significant links for SO₂, CO, or O₃ in single-pollutant models. Short-term NO₂, PM₁₀, and PM_{2.5} independently boosted CVD outpatient demand. The 2018 policies reduced key pollutants and their health impacts, supporting ongoing air quality strategies.

Keywords: Ambient air pollution, Cardiovascular diseases, Time series research, Environmental governance, Outpatient visit volume

Introduction

Liuzhou is located in the northern part of the Guangxi Zhuang Autonomous Region, China, and serves as the region's secondary central city. In recent years, key economic indicators such as gross domestic product (GDP) and total fiscal revenue have ranked second in Guangxi, trailing only Nanning. As a major industrial hub in Guangxi, Liuzhou hosts industries including automobile manufacturing, metallurgy, and chemical engineering. Pollutant emissions are predominantly industrial, compounded by vehicle exhaust and fugitive dust, resulting in a complex pollution profile characterized by multiple pollutants such as PM_{2.5}, O₃, and NO₂.

Situated in a subtropical monsoon climate zone, Liuzhou experiences hot and humid summers that facilitate haze formation, thereby increasing the risk of circulatory system diseases. In winter, reduced precipitation and dry conditions, coupled with poor atmospheric dispersion, allow PM_{2.5}, O₃, and other pollutants to accumulate near the ground, leading to persistent pollution episodes and heightened population exposure. Furthermore, Liuzhou is a basin city underlain by karst topography, encircled by mountains with a closed terrain. This geographical setting, combined with a pronounced urban heat island effect, impedes the dispersion of locally emitted industrial fumes and vehicle exhaust, resulting in significant pollutant interactions and synergistic effects.

In response to these environmental challenges, the Guangxi Autonomous Region government issued the *Three-Year Campaign Plan for Air Pollution Control in Guangxi (2018–2020)* in 2018, aiming to effectively manage environmental pollution across the region. The Liuzhou Municipal Government actively responded and facilitated the implementation of relevant measures.

Cardiovascular diseases (CVD) are among the leading causes of death globally, with mortality rates continuing to rise in recent years [1]. The global number of CVD deaths is projected to increase from 20.5 million in 2025 to 35.6 million in 2050 [2]. In China, the number of CVD patients has reached 330 million [3]. The high prevalence, along with associated disability and mortality, imposes a substantial burden on patients and their families and poses a serious threat to public health.

Rapid urban expansion has intensified population exposure to ambient air pollutants, establishing air pollution as one of the most severe environmental health threats worldwide. As the largest developing country, China faces increasingly pressing air pollution challenges amid its rapid socioeconomic development [4]. Ambient air pollution has been identified as the second-largest risk factor for non-communicable diseases [5] and is ranked by the World Health Organization as the fourth leading risk factor for human health, following hypertension, smoking, and hyperglycemia [6–7]. Studies have demonstrated that harmful particulate matter

and gaseous pollutants not only directly impair the respiratory system but also trigger cardiovascular diseases—such as heart disease and hypertension—through multiple biological mechanisms [8]. Both short-term and long-term exposure to ambient air pollution are significantly associated with elevated CVD risk [9–10]. Cardiovascular diseases account for more than one-third of global deaths, surpassing any other cause. Worldwide, ambient particulate matter pollution is responsible for an estimated 4.1 million premature deaths annually [11]. According to the *Summary of the China Cardiovascular Health and Disease Report 2024*, the prevalence and mortality of CVD in China continue to rise, driven by an aging population and a large pool of high-risk individuals. China has the highest number of CVD deaths globally, and CVD remains the leading cause of death among both urban and rural residents. In 2021, CVD accounted for 48.98% of deaths in rural areas and 47.35% in urban areas, meaning that approximately 2 out of every 5 deaths were attributable to CVD [12]. This situation not only severely compromises patients' quality of life but also imposes a heavy economic burden on the healthcare system.

In health effect assessments of air pollution, outpatient visit volume has emerged as a key indicator of acute health damage due to its high sensitivity (capable of detecting exposure responses within 24 hours) and strong timeliness (reflecting trends 2–3 weeks earlier than mortality data). Compared with lagging health endpoints such as hospitalization and death, outpatient data can more accurately capture early biological responses within 24 to 72 hours following pollutant exposure [13]. Moreover, hospitalized patients are generally in more severe condition and represent only a small fraction of the total patient population (as only a subset of outpatient or emergency patients are eventually admitted). Therefore, outpatient visit data offer greater representativeness and timeliness for studying the health impacts of ambient air pollutants and are frequently prioritized as analysis indicators [14].

Although the association between ambient air pollution and CVD outpatient visits has been widely examined [15–17], findings across different regions are not entirely consistent. This inconsistency may stem from regional variations in pollutant sources, chemical composition, meteorological conditions, and population characteristics, which in turn lead to geographically specific health effects. Consequently, conducting research in populations with distinct regional features remains essential for a deeper understanding of exposure–health relationships under specific environmental conditions.

Liuzhou's unique climate and industrial structure make it a representative case for studying the health effects of air pollution. Analyzing the characteristics of air pollution in Liuzhou, exploring its health impacts and associated risks, and assessing whether targeted policy interventions have altered the effect of ambient air pollutants on cardiovascular disease outcomes is not only an urgent necessity for improving the health of local residents but also provides a reference model and governance experience for air quality management in similar

cities nationwide. Furthermore, such research supports the development of regionally tailored strategies for air pollution control and health prevention, offering both scientific value and social benefits.

Methods

Environmental Governance Policies

Liuzhou City, situated in the northern part of the Guangxi Zhuang Autonomous Region, is a key industrial center and regional transportation hub. Covering an area of approximately 18,600 km², the city has a permanent resident population of about 4.16 million. In 2018, the Guangxi Zhuang Autonomous Region Government promulgated the *Three-Year Action Plan for Air Pollution Control in Guangxi (2018–2020)*, which set quantifiable targets: by 2020, the annual mean concentration of fine particulate matter (PM_{2.5}) in the 12 prefecture-level cities failing to meet national air quality standards was required to decrease by 15% relative to the 2015 baseline; concurrently, the proportion of prefecture-level cities achieving Grade II or higher air quality (as defined by the Chinese Ambient Air Quality Standards, GB 3095–2012) was to reach 91.5%. In response, the Liuzhou Municipal Government implemented targeted interventions—including the phased relocation and technological upgrading of major chemical enterprises with high emissions—thereby achieving measurable progress in regional air pollution control. Building on this policy milestone, the present study adopts January 1, 2019 as the designated intervention time point to assess temporal differences in ambient air pollutant concentrations and associated health outcomes before and after implementation.

Ambient Air Pollution and Meteorological Data

Daily ambient air quality monitoring data from January 1, 2014 to December 31, 2024 were obtained from the Liuzhou Municipal Ecological Environment Monitoring Center. The dataset includes daily mean concentrations of nitrogen dioxide (NO₂), sulfur dioxide (SO₂), carbon monoxide (CO), PM_{2.5}, and PM₁₀, as well as the maximum 8-hour rolling average concentration of ozone (O₃). Concentrations of CO are reported in milligrams per cubic meter (mg/m³), whereas all other pollutants are expressed in micrograms per cubic meter (μg/m³). Liuzhou operates six fixed-site air quality monitoring stations, each continuously measuring the aforementioned pollutants. For analytical purposes, the city-level daily exposure metric was derived as the arithmetic mean of pollutant concentrations across all six stations. Concurrently, daily meteorological variables—including mean temperature (°C) and relative humidity (%)—were collected to support confounder adjustment in subsequent modeling.

Outpatient Visit Data

This study compiled de-identified daily outpatient records from four large tertiary comprehensive hospitals in Liuzhou City over the same 2014–2024 period. Each record contains the date of visit, ICD-10-coded diagnosis, patient age, sex, and no personally identifiable information. During data preprocessing, entries with missing diagnostic codes or demographic variables were excluded; duplicate visits by the same patient on the same day were consolidated into a single record. A dedicated analytical database was constructed to examine associations between ambient air pollution exposure and outpatient utilization.

Specifically, outpatient cases were classified according to the following cardiovascular and cerebrovascular conditions: hypertension (ICD-10: I10–I15), coronary heart disease (ICD-10: I20–I25), heart failure (ICD-10: I50), and stroke (ICD-10: I60–I61, I63–I64).

Ethical approval

The incidence data utilized in this study were obtained from the recorded incidence data of major tertiary grade A general hospitals within the urban area of Liuzhou and received approval from the Ethics Review Committee of the Liuzhou Center for Disease Control and Prevention (LZCDC-2025-0006). As this dataset comprises solely case statistics and does not include personal or privacy-related information of the patients, The Ethics Review Committee of the Liuzhou Center for Disease Control and Prevention determined that this research waiver of informed consent according to the following Chinese law: Notice by the National Health Commission, the Ministry of Education, the Ministry of Science and Technology, and the National Administration of Traditional Chinese Medicine of Issuing the Measures for Ethical Review of Life Science and Medical Research Involving Human Being (No. 4 of the National Health Commission, 2023).

Descriptive Statistical Analysis

Continuous variables were assessed for normality using the Shapiro–Wilk test. Normally distributed variables are summarized as mean $\pm$ standard deviation (SD), and group comparisons between pre-intervention (2014–2018) and post-intervention (2019–2024) periods were conducted using two-sample independent t-tests. Non-normally distributed variables are presented as median (interquartile range, IQR), and differences between periods were evaluated using the Wilcoxon rank-sum test (Mann–Whitney U test). All statistical analyses were performed using R version 4.3.1, with significance set at $\alpha = 0.05$ (two-tailed).

Analysis of the Exposure–Response Lag Effect

Spearman’s rank correlation coefficient was employed to assess the monotonic associations between ambient air pollutants and meteorological variables. Given the well-documented temporal lag and non-linear exposure–response relationships between air pollution and cardiovascular morbidity, a distributed lag non-linear model (DLNM) was applied to quantify the lagged and non-linear effects of air pollutant exposure on daily outpatient visits for cardiovascular diseases [18]. As the daily count of such outpatient visits approximates a Poisson distribution, a generalized additive model (GAM) with a Poisson link function—integrated with the DLNM framework—was used to estimate the short-term, lagged associations between each air pollutant and visit counts. Model specifications, including functional forms and degrees of freedom for smooth terms, are detailed in the Supplementary Materials.

$$\begin{aligned}
\text{Log}(E[Y_t]) &= \alpha + \text{cb}(\text{Airpollutants}, \text{lag}, \text{df}) \\
&+ \text{ns}(\text{Temperature}, \text{df} = 3) \\
&+ \text{ns}(\text{Relativehumidity}, \text{df} = 3) \\
&+ \text{ns}(\text{Calendartime}, \text{df} = 7 \text{ per year}) \\
&+ \text{DOW}
\end{aligned}$$

Among these, $E[Y_t]$ denotes the expected daily count of outpatient visits on day t . The cross-basis function (cb) is specified using natural cubic splines (NCS), with three degrees of freedom (df) allocated to both the exposure concentration and lag dimensions; the R function ns() implements this NCS specification. Natural cubic splines are likewise employed to flexibly adjust for potential confounding by calendar time, ambient temperature, relative humidity, and day of the week (DOW).

This study estimates the association between ambient air pollutants and outpatient visits for cardiovascular diseases in terms of the relative risk (RR) and its corresponding 95% confidence interval (CI), defined as the percent change in the expected outpatient visit count associated with an interquartile range (IQR) increase in pollutant concentration. A single-pollutant model framework is adopted to isolate the independent effect of each ambient air pollutant. To characterize the temporal dynamics of the exposure–response relationship, a maximum lag of 7 days is considered; both distributed lag structures (i.e., lag-specific effects at lags 0–7) and cumulative lag effects (lag 0–7) are evaluated. Furthermore, to assess potential temporal heterogeneity in pollutant effects, we conduct a stratified analysis by calendar period—comparing estimates from the pre-2018 and post-2018 periods—to examine whether the magnitude or shape of the associations has changed over time.

Results

Environmental air pollutants and general information of outpatient patients

Table 1 presents aggregated data from four large tertiary hospitals in Liuzhou City, covering daily outpatient visits for cardiovascular disease (CVD), concurrent ambient air pollutant concentrations, and meteorological parameters before and after 2018. The analysis encompasses 2,986,820 outpatient records, corresponding to a mean daily attendance of 827 patients. Median ambient concentrations were as follows: PM_{2.5}, 30.00 µg/m³; PM₁₀, 45.33 µg/m³; SO₂, 11.71 µg/m³; NO₂, 18.43 µg/m³; CO, 0.85 mg/m³; and 8-hour average O₃, 75.33 µg/m³. Male patients accounted for a higher proportion of visits than female patients, and individuals aged ≥65 years constituted a larger share than those aged ≤64 years (Supplementary Figure 1). With the exception of O₃, all other pollutants exhibited significantly higher median concentrations during the cold season compared with the warm season (Supplementary Figure 2). Median daily temperature and relative humidity were 22.2°C and 78.0%, respectively. Following 2018, outpatient volume declined marginally but without statistical significance; conversely, concentrations of the five major pollutants (excluding O₃) decreased substantially (all $P < 0.01$).

Inter-pollutant Correlations and Temperature Dependence

As illustrated in Supplementary Figure 3, PM_{2.5}, PM₁₀, SO₂, NO₂, and CO demonstrated moderate to strong positive inter-correlations (Spearman's $r = 0.42$ – 0.97), whereas O₃ showed weak or negligible correlations with the remaining pollutants ($r = 0.05$ – 0.21). The strongest correlation was observed between PM_{2.5} and PM₁₀ ($r = 0.97$); the weakest was between O₃ and SO₂ ($r = 0.05$). Furthermore, ambient temperature exhibited statistically significant negative correlations with all pollutants except O₃.

Single-Pollutant Associations with CVD Outpatient Visits

Figure 1 displays the relative risks (RRs) associated with an interquartile range (IQR) increase in each pollutant under single-pollutant models. NO₂ and PM₁₀ exerted the strongest acute effects on the exposure day (lag 0): RR = 1.103 (95% CI: 1.089–1.117) and RR = 1.052 (95% CI: 1.041–1.064), respectively. PM_{2.5} exhibited its peak effect at lag 1 day (RR = 1.028, 95% CI: 1.017–1.038). In contrast, short-term exposure to CO, SO₂, and O₃ was not significantly associated with CVD outpatient visits. Cumulative RRs across lag periods are shown in Figure 2. The maximal cumulative effect occurred at lag 7 for NO₂ (RR = 1.447, 95% CI: 1.413–1.483), while PM₁₀ and PM_{2.5} reached their highest cumulative RRs at lag 1 (RR = 1.095, 95% CI: 1.079–1.112; RR = 1.036, 95% CI: 1.021–1.051, respectively; Figure 3). No statistically significant cumulative associations were observed for CO, SO₂, or O₃.

Temporal Changes in Pollutant-Associated Risks (Pre- vs. Post-2018)

Figure 5 compares RRs associated with IQR increases in pollutant concentrations before and after 2018. Relative risks for PM₁₀, PM_{2.5}, SO₂, and CO declined post-2018. Specifically, the cumulative RR for PM₁₀ at lag 1 was 1.256 (95% CI: 1.228–1.284) during 2014–2018—significantly higher than the estimate for 2019–2024 ($P < 0.05$). For PM_{2.5}, the lag-1 cumulative RR was 1.084 (95% CI: 1.067–1.101) during 2014–2018, whereas no statistically significant association was detected during 2019–2024 (RR = 0.994, 95% CI: 0.980–1.008). Notably, the highest cumulative RRs for CO (lag 0: RR = 1.033, 95% CI: 1.015–1.050) and SO₂ (lag 1: RR = 1.078, 95% CI: 1.056–1.100) were both observed during 2014–2018; all corresponding estimates for 2019–2024 were below unity.

Stratified Analyses by Age, Sex, and Season

Supplementary Figures 8–10 present stratified risk estimates for the six pollutants. Age-stratified analysis revealed that PM₁₀, PM_{2.5}, and CO exerted stronger effects among older adults (≥ 65 years) than younger individuals (≤ 64 years), whereas NO₂ exhibited greater impact among the younger group—all differences reaching statistical significance ($P < 0.05$). Sex-stratified analysis indicated a marginally elevated effect of SO₂ among females versus males, though this difference was non-significant; in contrast, the effect of NO₂ was significantly stronger among females ($P < 0.05$). Seasonal analysis demonstrated that, with the sole exception of SO₂ (which showed greater effect in the warm season), NO₂, PM₁₀, PM_{2.5}, and CO all exhibited significantly stronger associations during the cold season (all $P < 0.01$).

Two-Pollutant Model Adjustments

In two-pollutant models, the estimated effect of NO₂ remained robust and largely unchanged upon co-adjustment for other pollutants. When NO₂ was included as a covariate, the associations of SO₂, CO, PM_{2.5}, and PM₁₀ with CVD outpatient visits attenuated, whereas the association with O₃ strengthened. Estimates for PM_{2.5} and PM₁₀ remained highly consistent across model specifications, and evidence of statistical interaction between these two particulate metrics was observed (Supplementary Figure 11).

Discussion

Cardiovascular diseases (CVDs) represent the leading cause of mortality worldwide, accounting for approximately one-third of all global deaths—surpassing any other single etiological factor. According to the *2024 Report on Cardiovascular Health and Diseases in China*, China bears the highest national burden of CVD-related mortality globally. Within China, CVDs remain the top cause of death among both urban and rural residents. Data from 2021 indicate that CVDs accounted for 48.98% and 47.35% of all-cause deaths in rural and urban populations, respectively—equivalent to nearly half of all fatalities [12]. This epidemiological burden not only compromises patients' quality of life but also imposes substantial strain on healthcare systems. Furthermore, robust epidemiological evidence identifies ambient air pollution as the predominant environmental determinant of adverse cardiovascular health outcomes, exceeding the attributable risk associated with chronic respiratory diseases and respiratory infections [19]. Against this backdrop, the present study investigates the short-term association between ambient air pollution exposure and outpatient visits for major cardiovascular conditions, with Liuzhou City—a representative industrial city in Guangxi Zhuang Autonomous Region—selected as the study site to generate empirically grounded insights applicable to comparable urban settings nationwide.

Given that hospital admissions predominantly reflect severe or acute clinical presentations and thus capture only a fraction of the total population-level disease burden, outpatient visit data offer a more sensitive and representative indicator of the broader public health impact of environmental exposures. Accordingly, this study integrates de-identified outpatient records for major cardiovascular diagnoses from four tertiary hospitals in Liuzhou between 2014 and 2024, and links them temporally with daily average concentrations of six regulated air pollutants (PM_{2.5}, PM₁₀, NO₂, SO₂, CO, and O₃) measured at six fixed-site monitoring stations across the city. The analysis focuses specifically on quantifying the acute, lagged associations between short-term (same-day and multi-day lag) pollutant exposure and same-day outpatient attendance for CVDs, while further examining how these associations evolved before and after the implementation of Guangxi's *Three-Year Campaign Plan for Air Pollution Control (2018–2020)*.

The results demonstrate statistically significant positive associations between short-term exposure to NO₂, PM_{2.5}, and PM₁₀ and increased risk of CVD outpatient visits. Specifically, per interquartile range (IQR) increase in daily mean concentration, the relative risk (RR) was 1.447 (95% CI: 1.413–1.483) for NO₂, 1.036 (95% CI: 1.021–1.051) for PM_{2.5}, and 1.095 (95% CI: 1.079–1.112) for PM₁₀. These findings align qualitatively with prior domestic and international evidence. For instance, a time-series study in Shijiazhuang reported 30.01%, 29.42%, and 14.98% increases in daily CVD outpatient visits at the 90th percentile versus the 10th percentile of PM₁₀,

PM_{2.5}, and NO₂ concentrations, respectively [15]. In Beijing, each 10 µg/m³ increment in PM_{2.5} was associated with an RR of 1.005 (95% CI: 1.001–1.009) for CVD emergency department visits after adjusting for temperature and relative humidity [20]. Similarly, in Shanghai, a 2-day lagged 10 µg/m³ increase in PM₁₀ and PM_{2.5} corresponded to 0.23% (95% CI: 0.12–0.34) and 0.74% (95% CI: 0.44–1.04) increases in coronary heart disease incidence, respectively [21]. A study in Hohhot found RRs of 1.0028 (95% CI: 1.0019–1.0037), 1.0091 (95% CI: 1.0053–1.0130), and 1.0142 (95% CI: 1.0052–1.0234) per 10 µg/m³ increment in PM_{2.5}, PM₁₀, and NO₂, respectively [22]. Likewise, research in Tangshan identified a positive association between ambient PM_{2.5} levels and daily CVD outpatient volume [23]. While effect directions are consistent across studies, quantitative heterogeneity in risk estimates likely reflects differences in exposure-response reference levels, population susceptibility, pollutant composition, and healthcare infrastructure. Comparable associations have been widely replicated in high-income and low- and middle-income countries alike [24–25].

No statistically significant associations were observed between short-term exposure to SO₂, CO, or O₃ and CVD outpatient visits in the overall population. Several contextual factors may account for these null findings, including variations in study design, geographic and climatic conditions, pollutant mixture profiles, baseline exposure levels, and demographic characteristics of the target population. Notably, subgroup analyses revealed that during the 2014–2018 period—when mean ambient CO and SO₂ concentrations in Liuzhou were 0.93 mg/m³ and 19.17 µg/m³, respectively—both pollutants exhibited statistically significant associations with CVD outpatient visits. In contrast, the overall cohort (2014–2024) reflected declining concentrations due to policy interventions, potentially attenuating detectable effects. Supporting this interpretation, studies conducted in cities with higher baseline exposures—such as Shijiazhuang (SO₂: 50.59 µg/m³; CO: 1.49 mg/m³) [17] and Yichang (CO: 1.07 mg/m³) [26]—reported significant CO- and SO₂-CVD associations. The above evidence suggests that the concentration level of pollutants might be one of the key factors determining whether their health effects can be detected or not. Consistent with findings from Hohhot [22], our analysis identified a modest protective association between O₃ and CVD outpatient visits—though this finding warrants cautious interpretation given the lack of biological plausibility and methodological challenges (e.g., strong negative correlations between O₃ and co-pollutants, seasonal confounding) [27–30]. The mechanistic and epidemiological relationship between short-term O₃ exposure and CVD outcomes thus remains unresolved and requires further rigorous investigation.

Stratified analyses revealed effect modification by age and sex. Elderly individuals (>65 years) exhibited significantly stronger associations between PM₁₀, PM_{2.5}, and CO exposure and CVD outpatient risk compared with younger adults—a pattern corroborated by findings from Shijiazhuang [22]. Women demonstrated heightened susceptibility to NO₂, consistent with evidence from Tianjin [31]. Potential explanations include sex-specific differences in

pulmonary deposition efficiency, hormonal regulation of vascular function, occupational and behavioral patterns (e.g., time-activity budgets, indoor/outdoor exposure ratios), and smoking prevalence. Moreover, seasonal variation modulated pollutant effects: the associations between NO₂, PM₁₀, PM_{2.5}, and CO and CVD outpatient visits were significantly stronger during cold seasons than warm seasons [32–33]. Plausible mechanisms include: (i) elevated pollutant concentrations due to enhanced emissions and reduced atmospheric dispersion; (ii) seasonal shifts in pollutant chemical composition (e.g., secondary organic aerosol formation); (iii) meteorological interactions (e.g., temperature, humidity, wind speed) altering toxicokinetics or physiological stress responses; and (iv) behavioral adaptations—such as increased indoor time and air conditioner use in summer—that reduce outdoor exposure.

In two-pollutant models adjusting for NO₂, the estimated associations between all other pollutants and CVD outpatient visits attenuated markedly—except for O₃, whose association strengthened. Conversely, when adjusting for other pollutants, the NO₂–CVD association remained robust (RR: 1.447; 95% CI: 1.413–1.483). As a key tracer of traffic-related air pollution, NO₂ has well-documented pathophysiological effects, including induction of oxidative stress, endothelial dysfunction, systemic inflammation, autonomic nervous system imbalance, and dyslipidemia—all contributing to accelerated atherosclerosis and acute cardiovascular events [34]. Its strong and persistent association with CVD outcomes, coupled with high collinearity among co-emitted pollutants, suggests that NO₂ may serve as both a direct toxicant and a proxy for complex traffic-related pollutant mixtures. Consequently, controlling NO₂ emissions may yield disproportionate cardiovascular benefits beyond those attributable to reductions in co-pollutants.

Ambient air pollution constitutes the largest environmental risk factor for global mortality and ranks fourth among all modifiable risk factors for premature death. Its causal role in CVD pathogenesis is increasingly well-established, rendering it a priority target for public health intervention. Projections from the Chinese Cardiovascular Disease Policy Model indicate that achieving the national secondary standard (35 µg/m³ annual mean) or WHO-recommended guideline level (5 µg/m³) for PM_{2.5} by 2030 would yield greater cardiovascular health gains than either a 25% reduction in population-level systolic blood pressure or a 30% decline in smoking prevalence [35]. Liuzhou exemplifies a rapidly industrializing city characterized by concentrated heavy industry—including automobile manufacturing, metallurgy, and chemical production—where industrial emissions dominate ambient pollution, compounded by vehicular exhaust and resuspended road dust. Its karst basin topography, surrounded by mountains and exhibiting a pronounced urban heat island effect, impedes atmospheric dispersion and fosters recurrent stagnation episodes, thereby amplifying population exposure. Following the launch of Guangxi's *Three-Year Campaign Plan* in 2018, Liuzhou implemented targeted measures—including relocation, retrofitting, and closure of high-emission enterprises—resulting in measurable improvements: post-2018, concentrations of PM_{2.5}, PM₁₀, SO₂, NO₂, and CO

declined significantly ($p < 0.01$), whereas O_3 increased modestly—consistent with photochemical dynamics under reduced NO_x titration. Crucially, the magnitude of the pollutant–CVD outpatient association weakened substantially for $PM_{2.5}$, PM_{10} , SO_2 , and CO after 2018. These convergent trends provide compelling quasi-experimental evidence that air quality governance in Liuzhou has yielded tangible cardiovascular health benefits—not merely environmental improvements. While this observational design precludes definitive causal inference, the temporal coherence, dose–response consistency, and policy-relevant specificity of findings strengthen their validity. Concurrent socioeconomic or demographic shifts cannot be entirely ruled out; however, the pollutant-specificity and timing of observed changes lend credence to policy attribution.

This study carries three principal public health implications. First, it reinforces ambient air pollution—as exemplified by NO_2 —as a potent, modifiable driver of outpatient demand for cardiovascular care, underscoring the preventive potential of stringent emission controls. Second, it provides empirical validation that structural interventions targeting industrial emissions can translate into measurable reductions in population-level cardiovascular morbidity, thereby strengthening the economic and health rationale for sustained investment in clean air policies. Third, integrating such evidence into regional air quality management frameworks can inform the development of targeted, equity-oriented strategies—particularly in rapidly industrializing regions where healthcare systems face mounting pressure from environment-attributable disease burdens.

Several limitations warrant acknowledgment. First, as with most time-series studies, individual-level exposure was approximated using area-wide (six-station) average pollutant concentrations, introducing non-differential exposure misclassification that may bias effect estimates toward the null. Second, administrative outpatient data lack granular covariates—including socioeconomic status, education, insurance type, comorbidities, and lifestyle factors—which may confound or modify observed associations. Third, genetic and epigenetic determinants of CVD susceptibility were not assessed; future gene–environment interaction studies are needed to refine risk stratification. Finally, while the quasi-experimental design enhances policy relevance, unmeasured time-varying confounders (e.g., concurrent healthcare reforms, macroeconomic shifts) could partially explain observed trends. Nevertheless, the convergence of environmental, epidemiological, and policy timelines strengthens confidence in the primary conclusions.

Conclusion

This time-series study demonstrates that short-term ambient exposure to nitrogen dioxide (NO₂), fine particulate matter (PM_{2.5}), and coarse particulate matter (PM₁₀) is significantly associated with an elevated risk of cardiovascular disease (CVD) among outpatients in Liuzhou, China. Notably, the implementation of stringent environmental governance policies following 2018 led to substantial reductions in ambient concentrations of PM_{2.5}, PM₁₀, sulfur dioxide (SO₂), NO₂, and carbon monoxide (CO), concurrently attenuating the adverse cardiovascular effects attributable to SO₂, CO, PM_{2.5}, and PM₁₀. These findings underscore the public health benefits of targeted industrial emission controls in mitigating air pollution–related CVD burden. While the results offer robust epidemiological support for evidence-informed policy formulation, residual confounding—particularly from unmeasured individual-level exposures—warrants further investigation using high-resolution personal exposure assessment methodologies.

Acknowledgements

We extend our sincere gratitude to all the researchers and participants for their invaluable support for this study. We would also like to thank all the staff of the Liuzhou Center for Disease Control and Prevention, Guangxi, China, for providing us with a good research environment.

Funding

This work was supported by Scientific research Project of the Health Commission of Guangxi (grant Z-B20241388). The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the funding agencies.

Authors' Contributions

YL - data collection, primary data analysis, and writing

SY and DH - data collection, analysis, revisions, and writing

JL, JY, TW- conception and design

LZ- supervision, revisions, and final review

YL, SY and DH have made equal contributions to this article and are all recognized as co-first authors.

Data sharing statement

The data used in this study are stored at the Institute of Environmental Hygiene and School Health Prevention and Control, Liuzhou Center for Disease Control and Prevention. The data are managed in strict accordance with the data security and confidentiality requirements imposed by the Liuzhou Center for Disease Control and Prevention and are not publicly available. Access to the data may be granted to institutions that meet the criteria and have a reasonable research purpose. Formal requests must first be submitted to the Institute of Environmental Hygiene and School Health Prevention and Control (contact via lzcdephj@163.com). Upon preliminary review, the request will be forwarded to the Liuzhou Center for Disease Control and Prevention for final approval.

Competing Interests

The authors have declared that no competing interests exist.

Table

Table 1 Comparison of daily CVD visits and contaminant concentrations before and after 2018

Variables	Overall(N=4013),Median (Q1,Q3)	2014- 2018(N=1821),Median (Q1,Q3)	2019- 2024(N=2192),Median (Q1,Q3)	P-value
Visits(n)	827 (403, 1027)	834 (398, 1042)	818.5 (407, 1020)	0.616
NO ₂ (μg/m ³)	18.43 (14, 25)	20.83 (16.6, 27.5)	16.29 (12.29, 22.5)	<0.001
PM _{2.5} (μg/m ³)	30 (18, 47.17)	37.17 (24.17, 59.67)	24.29 (15, 38.75)	<0.001
PM ₁₀ (μg/m ³)	45.33 (29.4, 70.5)	56 (36.67, 87)	37.29 (25.29, 58.29)	<0.001
SO ₂ (μg/m ³)	11.71 (7.67, 19.5)	19.17 (11.67, 27.5)	9 (6.71, 12.68)	<0.001
O ₃ (μg/m ³)	75.33 (55.67, 96.67)	71.67 (53, 91.83)	78.86 (58.14, 100.32)	<0.001
CO(mg/m ³)	0.85 (0.71, 1)	0.93 (0.8, 1.1)	0.79 (0.67, 0.91)	<0.001
Temperature(°C)	22.2 (14.9, 27.1)	23 (15.3, 27.5)	21.6 (14.6, 26.8)	<0.001
Relative humidity (%)	78 (68, 87)	75 (67, 83)	81 (70, 90)	<0.001

Figure

Figure 1: From 2014 to 2024, in Liuzhou City, Guangxi Province, China, for every increase of the quartile range of environmental air pollutants by a different lag period, the relative risk (RR) of visiting a hospital due to cardiovascular diseases

Figure 2: From 2014 to 2024, in Liuzhou City, Guangxi Province, China, for every increase of the quartile range of environmental air pollutants by a certain number of days, the cumulative relative risk (RR) of visiting a hospital due to cardiovascular diseases

Figure 3: Relative Risk of Visiting a Clinic for Cardiovascular Disease for Each Quartile Spacing Increase in Six Ambient Air Pollutants in Liuzhou City, China

Figure 4: Change in Relative Risk per IQR Increase in Ambient Air Pollutant Concentration in Liuzhou City before and after 2018

Supplementary Table

S Table 1. Descriptive statistics of cardiovascular disease outpatient attendances and environmental data in Liuzhou, China, 2014-2024

Supplementary Figure

Supplementary Figure 1 Daily Visits for Cardiovascular Diseases by Gender and Age in Liuzhou City, China, 2014-2024

Supplementary Figure 2 Cold and warm season concentration levels of different air pollutants in Liuzhou City, China, 2014-2024

Supplementary Figure 3 Spearman's correlation coefficients between daily air pollutant concentrations and weather conditions in Liuzhou City, China. RH: Relative humidity

Supplementary Figure 4 Relative risk of PM_{2.5} and PM₁₀ to cardiovascular disease outpatient visits at different stages of life

Supplementary Figure 5 Cumulative Relative risk of PM_{2.5} and PM₁₀ to cardiovascular disease outpatient visits at different stages of life

Supplementary Figure 6 Relative risk of CO and SO₂ to cardiovascular disease outpatient visits at different stages of life

Supplementary Figure 7 Cumulative Relative risk of CO and SO₂ to cardiovascular disease outpatient visits at different stages of life

Supplementary Figure 8 Relative Risk of Visiting the Doctor for Cardiovascular Disease for Each Quartile Spacing Increase in Six Air Pollutants, Categorized by Age

Supplementary Figure 9 Relative Risk of Visiting the Doctor for Cardiovascular Disease for Each Quartile Spacing Increase in Six Air Pollutants, Categorized by Gender

Supplementary Figure 10 Relative Risk of Visiting the Doctor for Cardiovascular Disease for Each Quartile Spacing Increase in Six Air Pollutants, Categorized by Season

Supplementary Figure 11 Cumulative relative risk in two-pollutant models

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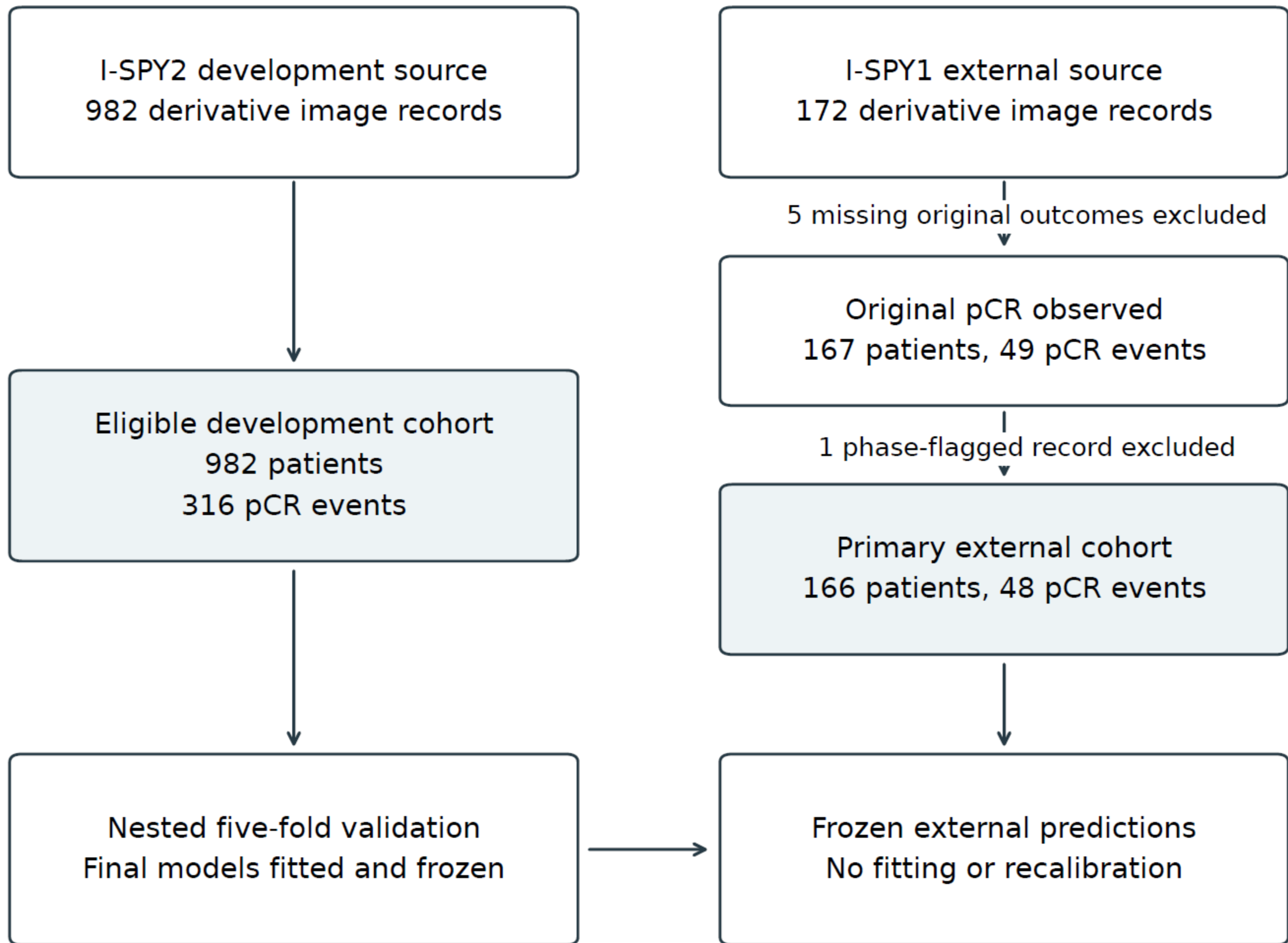
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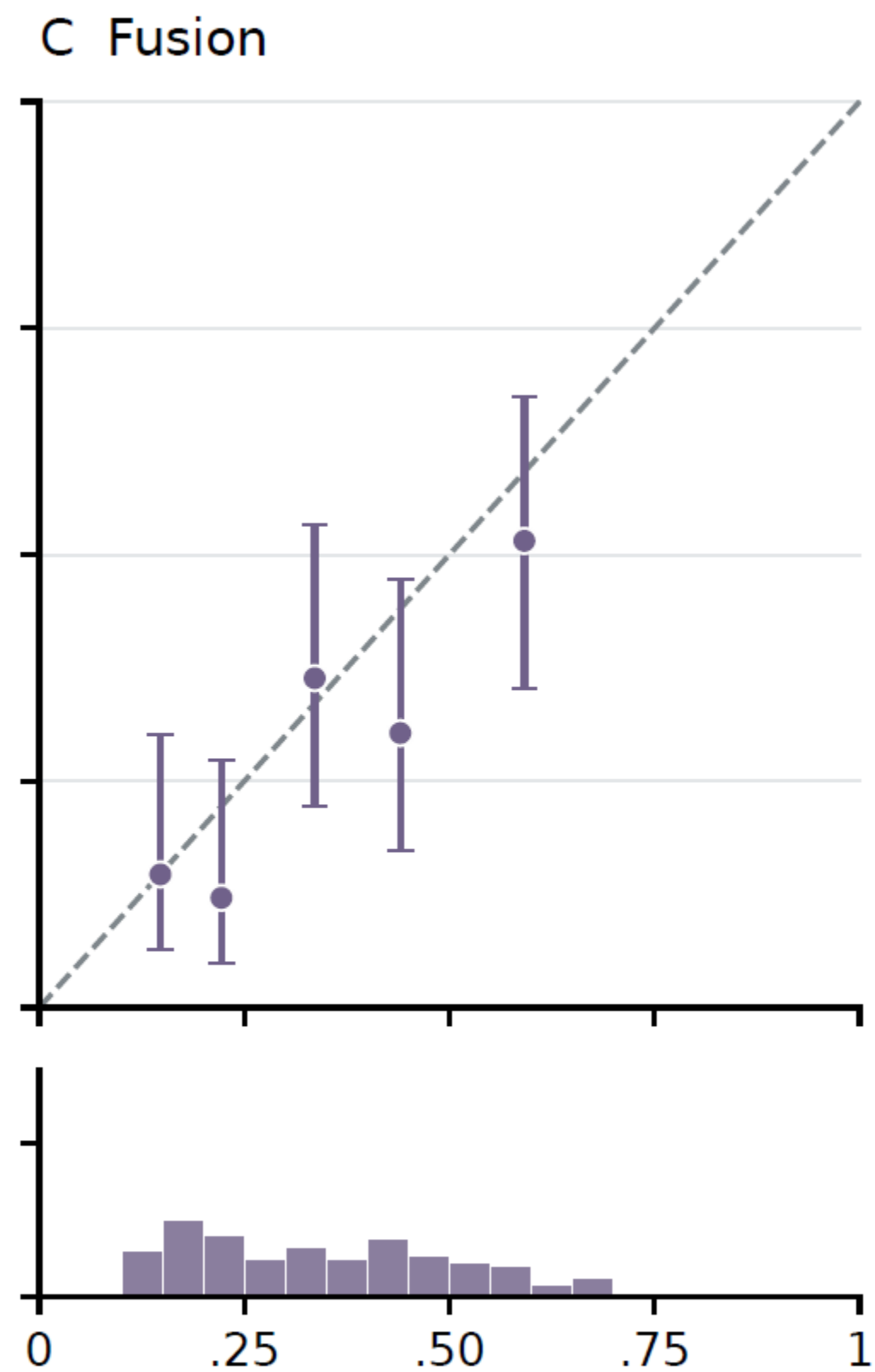
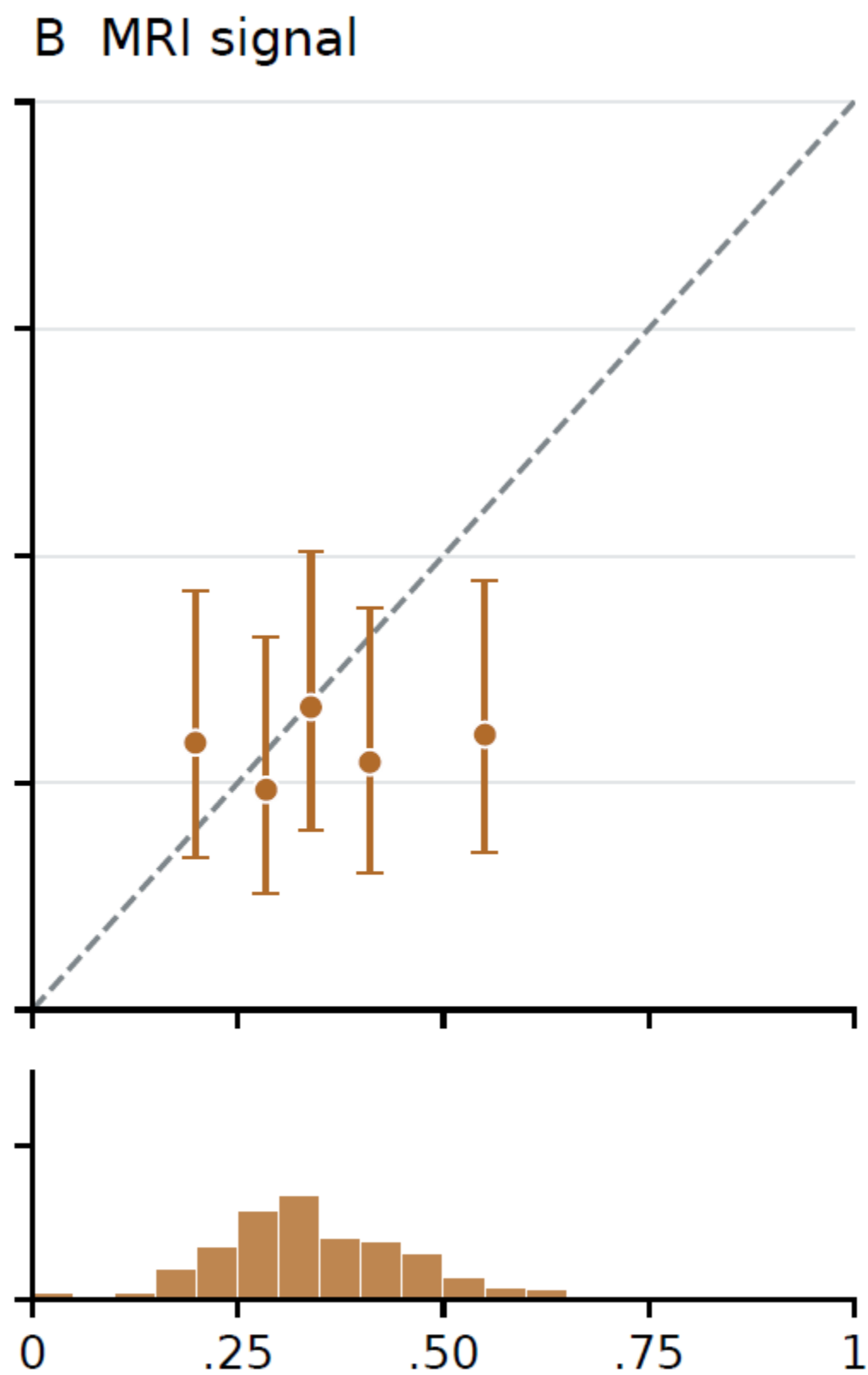
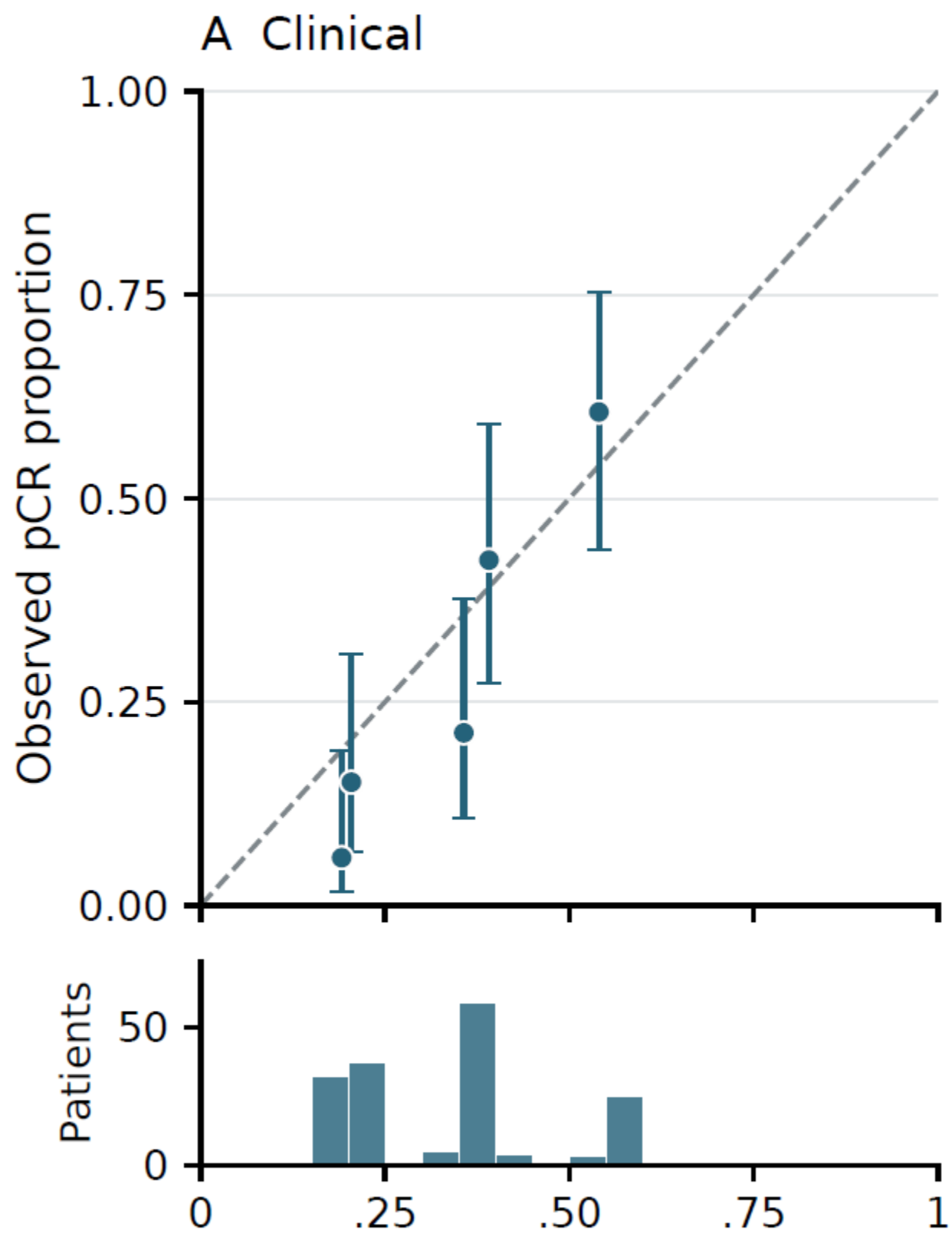
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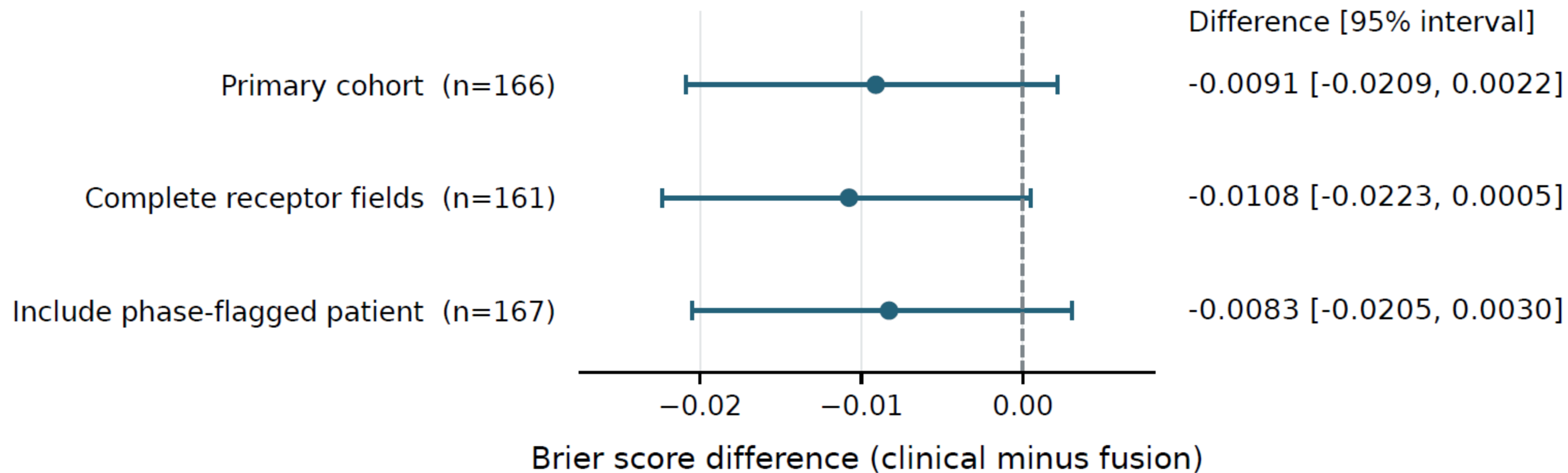
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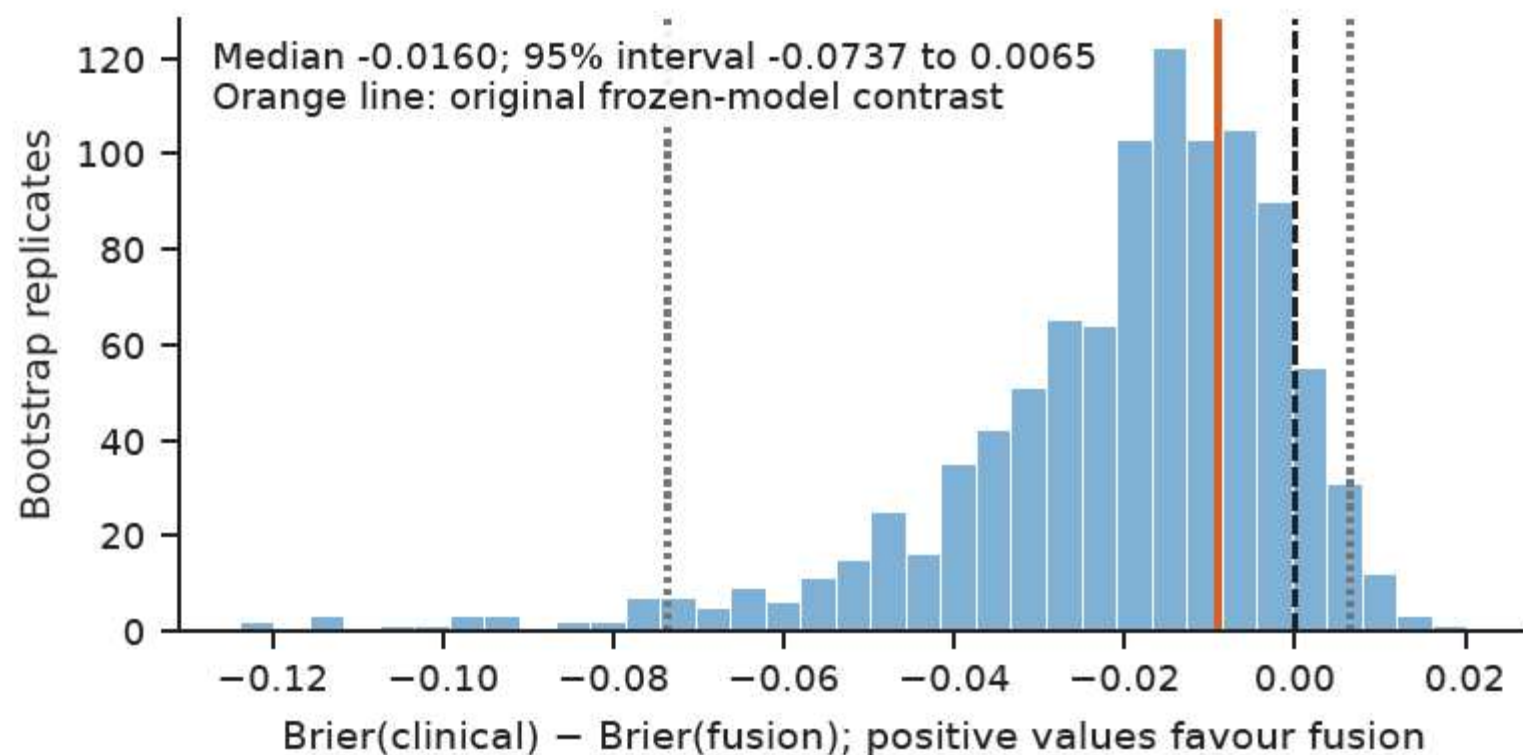
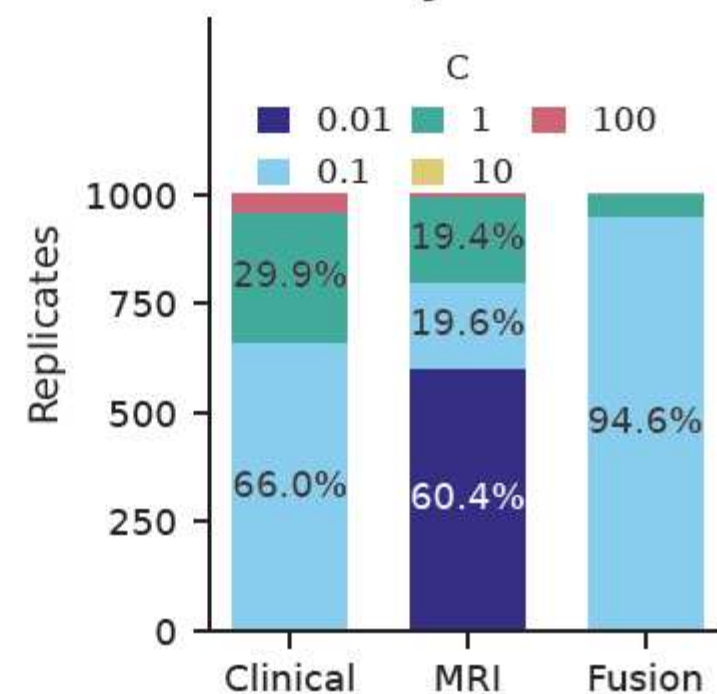
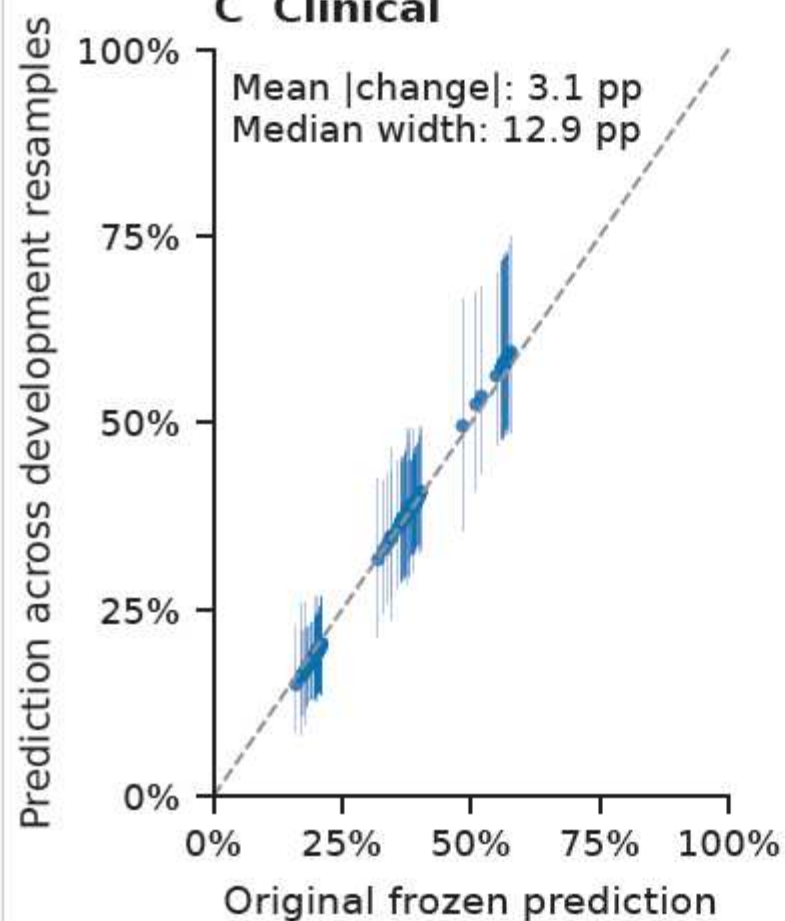
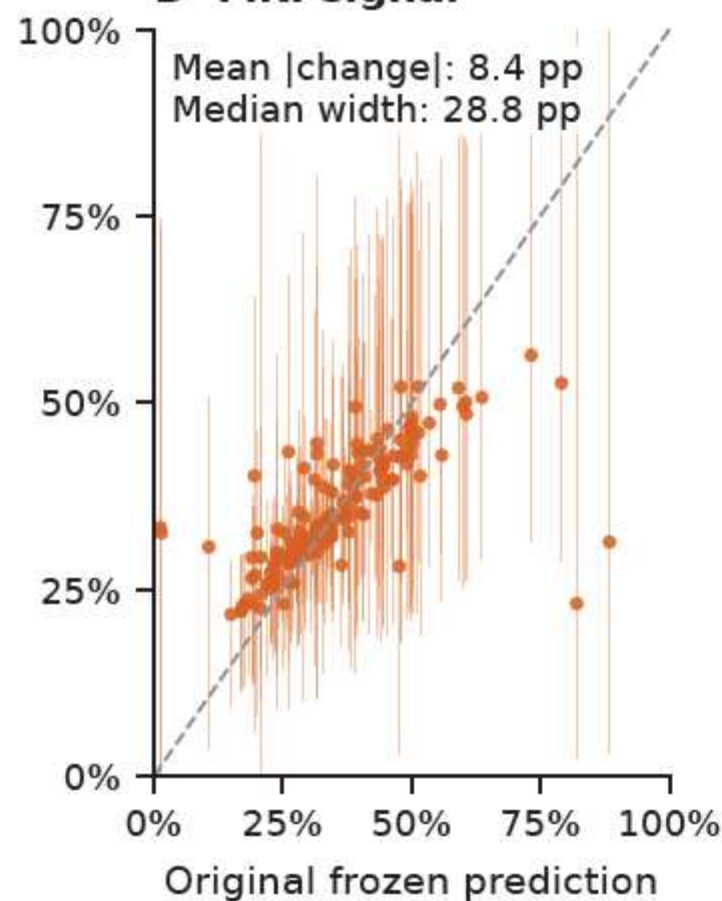
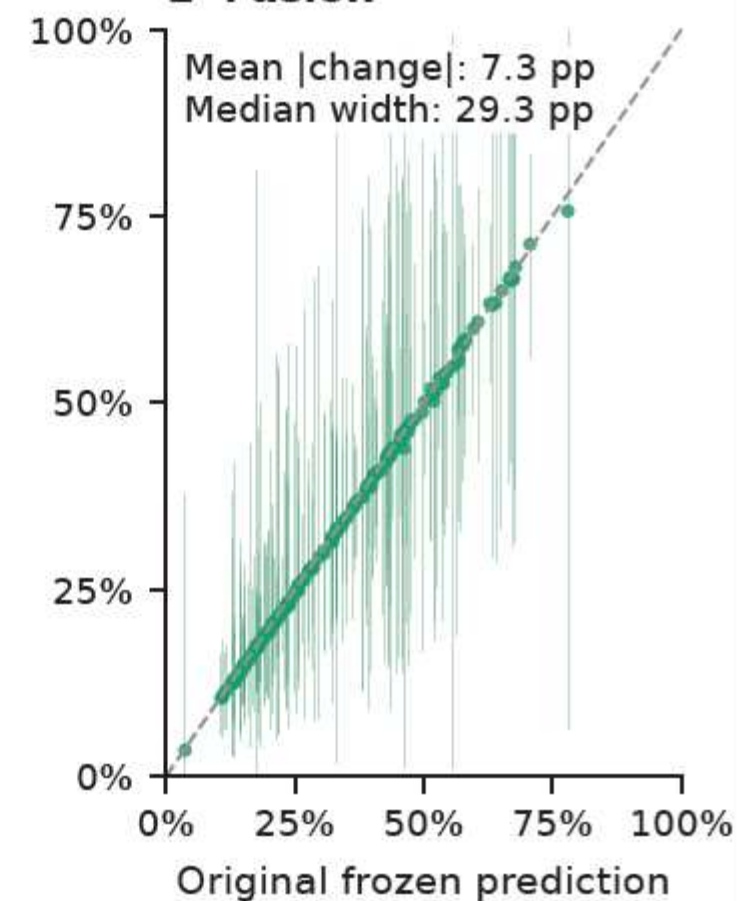
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Predicted pCR probability



A External Brier contrast**B Penalty selection****C Clinical****D MRI signal****E Fusion**

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