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Effects of the COVID-19 pandemic, vaccination, and return to in-person classes on dengue incidence in major Brazilian cities: an interrupted time-series analysis

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ATA DO 361ª. TRABALHO DE FIM DE CURSO DE ESPECIALIZAÇÃO EM ESTATÍSTICA DE RENZO JOEL FLORES ORTIZ.

Aos dezessete dias do mês de dezembro de 2025, às 09:00 horas, com utilização de recursos de videoconferência a distância, reuniram-se os professores abaixo relacionados, formando a Comissão Examinadora homologada pela Comissão do Curso de Especialização em Estatística Computacional Aplicada, para julgar a apresentação do trabalho de fim de curso do aluno **Renzo Joel Flores Ortiz** intitulado: "Effects of the COVID-19 pandemic, vaccination, and return to in-person classes on dengue incidence in major Brazilian cities: an interrupted time-series analysis", como requisito para obtenção do Grau de Especialista em Estatística Computacional Aplicada. Abrindo a sessão, a Presidente da Comissão, Ela Mercedes Medrano de Toscano – Orientadora, após dar conhecimento aos presentes do teor das normas regulamentares, passou a palavra ao candidato para apresentação de seu trabalho. Seguiu-se a arguição pelos examinadores com a respectiva defesa do candidato. Após a defesa, os membros da banca examinadora reuniram-se sem a presença do candidato e do público, para julgamento e expedição do resultado final. Foi atribuída a seguinte indicação: o candidato foi considerado aprovado condicional às modificações sugeridas pela banca examinadora no prazo de 30 dias a partir da data de hoje por unanimidade. O resultado final foi comunicado publicamente ao candidato pela Presidente da Comissão. Nada mais havendo a tratar, a Presidente encerrou a reunião e lavrou a presente Ata, que será assinada por todos os membros participantes da banca examinadora. Belo Horizonte, 17 de dezembro de 2025.

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RESUMO

A transmissão da dengue está estreitamente ligada à mobilidade humana e às atividades de controle vetorial, ambas substancialmente afetadas durante a pandemia de COVID-19. Foi realizada uma análise de séries temporais interrompidas de 477 semanas epidemiológicas (2015–2023) para estimar os efeitos da pandemia, da campanha nacional de vacinação contra COVID-19 e do retorno total às aulas presenciais sobre a incidência semanal de dengue em dez grandes cidades brasileiras. Foram ajustados modelos binomiais negativos específicos para cada cidade com ajuste por variáveis meteorológicas, e as estimativas de efeito foram combinadas utilizando metanálise de efeitos aleatórios. No nível de efeitos combinados, tanto o início da pandemia como o início da campanha de vacinação não estiveram associados a mudanças imediatas significativas na incidência de dengue. No entanto, ambas as intervenções estiveram associadas a mudanças significativas nas tendências de incidência, incluindo um declínio moderado após o início da pandemia e um aumento gradual após o início da vacinação. Não foram detectados efeitos imediato ou de tendência significativos para o retorno total às aulas presenciais no nível de efeitos combinados. Análises para cada cidade revelaram heterogeneidade substancial na direção, magnitude e significância estatística dos efeitos imediato e de tendência para cada intervenção. A heterogeneidade entre as cidades foi alta (I^2 = 75–91%), destacando uma acentuada dependência contextual dos efeitos das intervenções. Análises de sensibilidade produziram resultados consistentes. Esses resultados indicam que a pandemia de COVID-19 e as intervenções relacionadas em nível populacional tiveram impactos heterogêneos na incidência de dengue em grandes centros urbanos brasileiros, ressaltando a necessidade de estratégias reforçadas e adaptadas localmente para a vigilância e o controle vetorial da dengue durante períodos de importante ruptura sistêmica.

Palavras-chave: dengue; COVID-19; séries temporais interrompidas; análise do efeito da intervenção.

ABSTRACT

Dengue transmission is closely linked to human mobility and vector-control activities, both of which were substantially disrupted during the COVID-19 pandemic. We conducted an interrupted time-series analysis of 477 epidemiological weeks (2015–2023) to estimate the effects of the pandemic, the national COVID-19 vaccination campaign, and the full resumption of in-person classes on weekly dengue incidence in ten major Brazilian cities. City-specific negative binomial models were fitted with adjustment for meteorological variables, and effect estimates were pooled using random-effects meta-analysis. At the pooled level, no significant immediate changes in weekly dengue incidence were observed after pandemic onset or vaccination initiation. However, both interventions were associated with significant changes in incidence trends, including a modest decline following pandemic onset and a gradual increase after vaccination initiation. No significant immediate or trend effects were detected for the full resumption of in-person classes at the pooled level. City-specific analyses revealed substantial heterogeneity in the direction, magnitude, and statistical significance of immediate and trend effects for each intervention. Between-city heterogeneity was high (I^2 = 75–91%), highlighting marked context dependence of intervention effects. Sensitivity analyses yielded consistent results. These findings indicate that the COVID-19 pandemic and related population-level interventions had heterogeneous impacts on dengue incidence across major Brazilian urban centers, underscoring the need for strengthened, locally adapted dengue surveillance and vector-control strategies during periods of major systemic disruption.

Keywords: dengue; COVID-19; interrupted time series; intervention effect analysis.

CONTENTS

1 INTRODUCTION

Dengue is the most common mosquito-borne viral disease globally, and its burden has increased substantially over time.[1] Reported cases rose from 505,430 in 2000 to 14.6 million in 2024, including 13.1 million in the Americas, of which Brazil accounted for the largest share (10.3 million).[2] Dengue virus is transmitted to humans by mosquitoes of the *Aedes* genus, primarily *Aedes aegypti* and, to a lesser extent, *Aedes albopictus*.[3] Transmission is shaped by multiple factors, including climatic conditions, characteristics of the natural and built environment—such as urban infrastructure and water management—and patterns of human mobility.[4] With the onset of the coronavirus disease 2019 (COVID-19) pandemic in March 2020, public health measures involving social distancing and restrictions on population mobility were implemented in many countries to curb the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). These measures also influenced the incidence of dengue.[5–7]

The effects of the COVID-19 pandemic and associated mobility restrictions on dengue incidence, however, remain unclear, with empirical studies reporting both decreases and increases in transmission.[5–7] For example, Chen et al.[5] analyzed monthly dengue data from 23 dengue-endemic countries in Southeast Asia and Latin America and found that 19 countries experienced lower dengue incidence in 2020 compared with the pre-pandemic period (2014–2019), whereas Brazil, Peru, Bolivia, and Singapore showed increases. Despite this contrast, plausible mechanisms exist that could explain both effect directions. Given the limited flight range of *Aedes aegypti*, the spatial spread of dengue virus is strongly shaped by human mobility.[8] Accordingly, one potential explanation for reduced incidence is that declines in population mobility during the pandemic—whether voluntary or imposed through public health measures such as stay-at-home orders—limited opportunities for virus transmission during house-to-house human movement, a key driver of dengue virus transmission.[9] Conversely, reduced mobility may have disrupted routine vector-control operations, including larval-site elimination, fumigation, and door-to-door inspections. Such reductions in operational capacity could have facilitated *Aedes aegypti* proliferation, thereby increasing dengue virus transmission.[5] This is a plausible mechanism, particularly given that, in the absence of widespread access to an effective dengue vaccine, dengue prevention has relied primarily on vector-control activities.[10]

The direction of the COVID-19 pandemic's impact on dengue incidence has varied not only between countries[5], but also within individual countries.[6] For example, although Brazil experienced an overall increase in dengue incidence following the onset of the pandemic,[5] this pattern was not uniform across states.[6] Roster et al.[6] conducted an interrupted time-series analysis of weekly dengue cases across 25 Brazilian states and found that, during March–April 2020, 19 states reported fewer dengue cases than predicted, whereas 6 states recorded excess cases relative to model forecasts. Beyond differences in direction, the magnitude of these effects also varied substantially, with observed cases ranging from 65% below predicted levels in Sergipe to 307% above predicted levels in Santa Catarina.[6]

Similar evidence has been reported in Southeast Asia.[7] In an interrupted time-series analysis evaluating the impact of the COVID-19 lockdown in Sri Lanka, Liyanage et al.[7] found substantial reductions in dengue cases at both the national level and across climate zones, with the largest decline observed in the dry zone (91% reduction; relative risk (RR) 0.09, 95% CI 0.05–0.15) and the smallest in the wet zone (83% reduction; RR 0.17, 95% CI 0.09–0.30). Highlighting additional within-country heterogeneity, the authors also estimated age-specific effects and found larger reductions among children (92% reduction; RR 0.08, 95% CI 0.03–0.25) than among adults (86% reduction; RR 0.14, 95% CI 0.05–0.35).[7]

These heterogeneous findings indicate that the impact of the COVID-19 pandemic—and the interventions implemented in response—on dengue incidence is highly context-dependent, varying, for example, across geographic settings and population groups.[5–7] They also underscore the importance of subnational analyses, particularly at the municipal level, where mobility-restriction policies were primarily implemented and varied in intensity across cities.[11,12] Such analyses are especially critical in tropical and subtropical urban settings, where high population density, in combination with climatic and built-environment factors, creates conditions conducive to *Aedes aegypti* breeding and dengue transmission.[13]

The objective of this study was to estimate the effect of the COVID-19 pandemic on dengue incidence in ten major Brazilian cities. Although the early phase of the pandemic involved restrictions on population mobility, these measures were progressively relaxed.[12] Two key population-level interventions associated with this relaxation and the restoration of population mobility were the initiation of the national COVID-19 vaccination campaign and the full resumption of in-person classes[14,15], whose effects on dengue incidence were also assessed.

2 METHODS

2.1 Study design

An interrupted time-series (ITS) analysis was conducted to evaluate the effects of the COVID-19 pandemic, the national COVID-19 vaccination campaign, and the full resumption of in-person classes on weekly dengue incidence in ten major Brazilian cities between 1 January 2015 and 31 December 2023. The cities included Belo Horizonte, Brasília, Campo Grande, Fortaleza, Goiânia, Natal, Rio de Janeiro, Salvador, São Paulo, and Teresina. These cities were selected because dengue constitutes a relevant component of their infectious disease burden[16], and because they provide consistent surveillance data and standardized meteorological measurements suitable for use as covariates.

ITS analyses were conducted separately for each city to account for city-specific epidemiological patterns and differences in intervention start dates across cities. To summarize effects across cities, pooled intervention estimates and between-city heterogeneity were estimated using a two-stage random-effects meta-analysis.[17]

The ITS design is well suited to this study, as it leverages routinely collected longitudinal surveillance data to assess population-level effects of interventions implemented at clearly defined time points.[18] By modeling pre-intervention trends as the counterfactual, ITS estimates the expected outcome trajectory in the absence of each intervention, enabling the evaluation of both immediate (level) and gradual (slope) changes in dengue incidence.[18]

The study design and reporting adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines and the RECORD extension for studies using routinely collected health data.[19]

2.2 Data sources

Weekly dengue case count data for each city were obtained from the Sistema de Informação de Agravos de Notificação (SINAN), Brazil’s national surveillance system for notifiable diseases. Reporting of suspected and laboratory-confirmed dengue cases is mandatory across healthcare facilities nationwide, ensuring comprehensive coverage and consistent surveillance data. All dengue case notifications recorded in SINAN between January 2015 and December 2023 were extracted.

Annual population estimates for each city were obtained from the Instituto Brasileiro de Geografia e Estatística (IBGE), Brazil's national statistical agency. These estimates, based on census data and demographic projections, were used as denominators to compute weekly dengue incidence rates.

Daily meteorological data on air temperature (°C), relative humidity (%), wind speed (m/s), and global solar radiation (kJ/m²) for each city were obtained from the Instituto Nacional de Meteorologia (INMET), Brazil's National Institute of Meteorology. For each variable, weekly median values were calculated to align with the epidemiological week structure used in dengue surveillance. These meteorological variables were extracted for potential inclusion as covariates in the ITS models, given the well-established influence of climatic conditions on *Aedes aegypti* ecology and dengue virus transmission.[3] In ITS analyses, adjustment for relevant outcome-related covariates is standard practice[18] and can help reduce confounding when estimating the effects of the COVID-19 pandemic and related interventions on dengue incidence.

All datasets were extracted and harmonized in December 2024. Each city contributed 477 epidemiological weeks of data covering the period 2015–2023.

2.3 Outcome

The primary outcome was the weekly incidence rate of dengue cases reported to SINAN between January 2015 and December 2023, including both laboratory-confirmed and clinically suspected cases. According to SINAN case definitions, a suspected dengue case is an individual residing in or having traveled within the previous 14 days to an area with ongoing dengue transmission or documented presence of *Aedes aegypti*, who presents with fever, usually lasting 2–7 days, and at least two of the following manifestations: nausea, vomiting, rash, myalgia, headache or retro-orbital pain, petechiae or a positive tourniquet test, and laboratory evidence of leukopenia.[20]

Weekly incidence rates were calculated as the number of reported dengue cases per week divided by city-specific annual population estimates from IBGE, assuming a constant population size within each calendar year. Weekly aggregation was selected to align with national surveillance reporting practices and to capture short-term variations in dengue transmission.

2.4 Timing of interventions

Three major population-level interventions with potential relevance for dengue transmission were evaluated: the COVID-19 pandemic, the national COVID-19 vaccination campaign, and the full resumption of in-person classes. Because the timing of these interventions varied across cities (Appendix A), the ITS analyses incorporated city-specific intervention start dates (Figure 1).

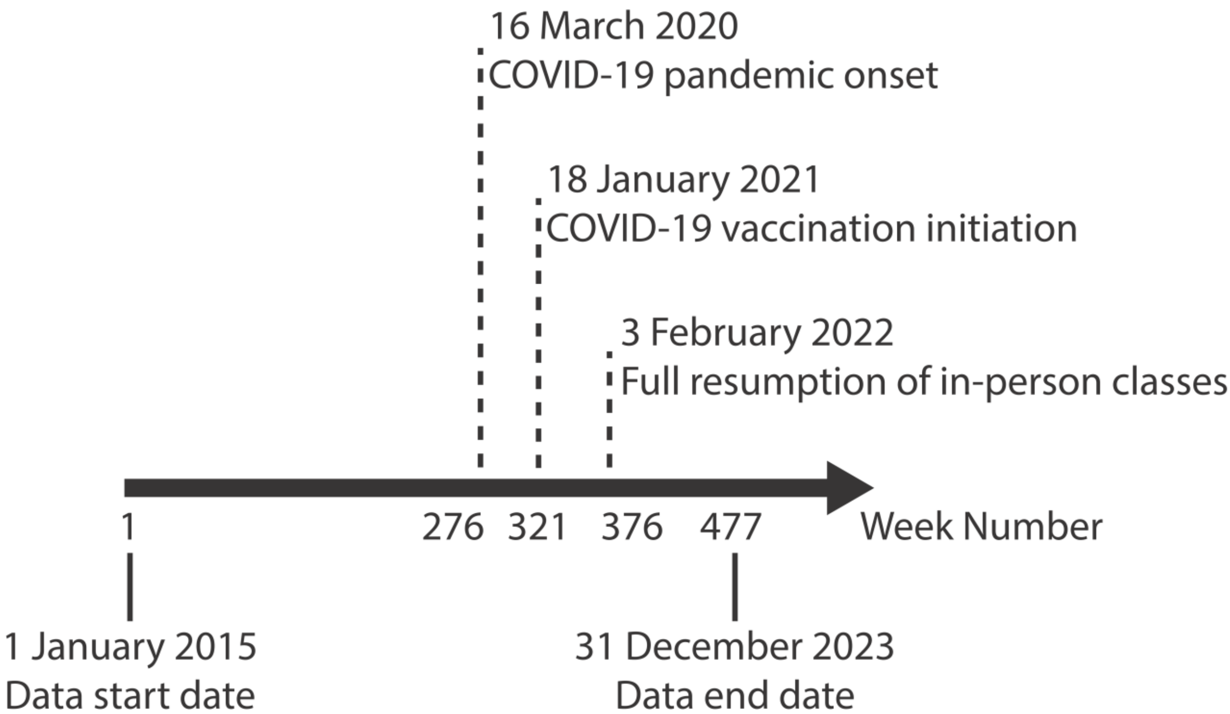

Figure 1. Timeline of study interventions in Belo Horizonte, Brazil (2015–2023). Vertical dashed lines indicate the onset of the COVID-19 pandemic (16 March 2020), the initiation of the COVID-19 vaccination campaign (18 January 2021), and the full resumption of in-person classes (3 February 2022).

Onset of the COVID-19 pandemic

The onset of the COVID-19 pandemic was defined as the date of the first laboratory-confirmed COVID-19 case reported in each city. This definition captures the earliest documented local detection of SARS-CoV-2 and provides a standardized, city-specific reference point for early pandemic-related changes in population behavior, public health responses, and healthcare-system functioning relevant to dengue transmission.[6] The city-specific onset dates were: 26 February 2020 (São Paulo); 6 March 2020 (Rio de Janeiro, Salvador); 7 March 2020 (Brasília); 12 March 2020 (Goiânia, Natal); 14 March 2020 (Campo Grande); 15 March 2020 (Fortaleza); 16 March 2020 (Belo Horizonte); and 19 March 2020 (Teresina).

Initiation of the COVID-19 vaccination campaign

The initiation of the COVID-19 vaccination campaign was defined as the date on which the first COVID-19 vaccine dose was administered in each city, marking the onset of population-level immunization against SARS-CoV-2. Vaccination may have indirectly influenced dengue incidence through changes in population mobility, healthcare-seeking behavior, and dengue surveillance and vector-control activities.[14] Although vaccination followed a national strategy, initiation dates varied slightly across cities: 17 January 2021 (São Paulo); 18 January 2021 (Belo Horizonte, Fortaleza, Goiânia, Rio de Janeiro, Teresina); and 19 January 2021 (Brasília, Campo Grande, Salvador).

Full resumption of in-person classes

The full resumption of in-person classes was defined as the date on which each municipal government officially authorized the complete return to classroom-based instruction in the public municipal school system. This intervention represents a relevant shift in mobility patterns, contact rates, and school-based social interactions, which may indirectly influence dengue transmission through changes in human mobility, time allocation between residential and community settings, and opportunities for vector–human contact.[15] The city-specific authorization dates were: 2 August 2021 (São Paulo); 3 November 2021 (Brasília, Rio de Janeiro); 19 January 2022 (Goiânia); 1 February 2022 (Fortaleza); 3 February 2022 (Belo Horizonte, Salvador); 3 March 2022 (Campo Grande); and 23 May 2022 (Teresina).

2.5 Statistical analysis

ITS analyses of weekly dengue incidence were conducted using a generalized linear modeling (GLM) approach, following a structured six-step procedure for each city.

Step 1: Data preparation. Missing observations were infrequent in both dengue case counts (<2% per city) and meteorological covariates (<3.2%; Appendix B). To maintain the continuous weekly structure required for ITS modeling[18], missing values were imputed using linear interpolation between adjacent weeks. Imputed dengue counts were rounded to the nearest integer to maintain compatibility with count-scale data.

Step 2: Distributional choice. To determine the appropriate GLM distributional family for modeling weekly dengue incidence, we first fitted a Poisson ITS model specified as:

$$\log(\mu_t) = \log(pop_t) + \beta_0 + \beta_1 t + \beta_2 COVID_t + \beta_3 TimeSinceCOVID_t + \beta_4 Vaccine_t + \beta_5 TimeSinceVaccine_t + \beta_6 ClassResumption_t + \beta_7 TimeSinceClassResumption_t$$

where $Y_t \sim Poisson(\mu_t)$ denotes the weekly dengue case count and μ_t its expected value. t represents time (in weeks) since the start of the study. The offset $\log(pop_t)$ adjusts for population size, allowing estimation of incidence rates rather than raw counts.

Each intervention was represented by (i) a binary indicator (coded 1 from the week of intervention onset and 0 otherwise), and (ii) a post-intervention time variable counting weeks since intervention onset.

The parameter β_0 represents the expected log weekly dengue incidence rate at baseline, and β_1 captures the pre-intervention linear trend. Coefficients β_2, β_4, β_6

quantify immediate (level) changes at the start of each intervention, while β_3, β_5, β_7 measure changes in the post-intervention trend relative to the pre-intervention slope.

A single ITS model incorporating the three study interventions was used to account for their sequential and potentially overlapping effects over time, minimize bias associated with attributing changes to individual interventions in isolation, and ensure consistent adjustment for seasonality, meteorological factors, and serial dependence throughout the study period.

Overdispersion was assessed using the Pearson dispersion statistic, calculated as the sum of squared Pearson residuals divided by the residual degrees of freedom.[21] Values substantially greater than one indicate extra-Poisson variation, whereby the conditional variance of the outcome exceeds its conditional mean. Because marked overdispersion was observed (Appendix C), the negative binomial GLM was selected for subsequent analyses, as it includes a dispersion parameter (θ) that accounts for extra-Poisson variation.

Step 3: Meteorological covariate screening. Pairwise correlations (Appendix D) and multicollinearity diagnostics (variance inflation factors, VIFs; Appendix E) were evaluated to guide inclusion of meteorological covariates in the ITS models. Variables exhibiting strong collinearity (absolute Pearson correlation coefficient $|r| > 0.7$ or $VIF > 5$) were flagged as potentially redundant. When redundancy was detected, the covariate with stronger biological plausibility was retained.

Step 4: ITS model building. A baseline negative binomial ITS model was specified as:

$$\log(\mu_t) = \log(pop_t) + \beta_0 + \beta_1 t + \beta_2 COVID_t + \beta_3 TimeSinceCOVID_t + \beta_4 Vaccine_t + \beta_5 TimeSinceVaccine_t + \beta_6 ClassResumption_t + \beta_7 TimeSinceClassResumption_t$$

with $Y_t \sim NegBin(\mu_t, \theta)$, where θ represents the dispersion parameter that accounts for variation beyond that expected under the Poisson model.

Model refinement proceeded by sequentially adding meteorological covariates, autoregressive terms, and Fourier pairs (sine and cosine functions of time), to account for climatic influences, serial correlation, and seasonality, respectively. Model expansion was halted when the Akaike Information Criterion (AIC) and the Bayesian

Information Criterion (BIC) no longer showed meaningful improvement, prioritizing model parsimony (Appendix F).

Model adequacy was evaluated using diagnostic checks, including visual inspection of residuals and examination of the autocorrelation function (ACF; Appendix G) to assess residual autocorrelation.

For each intervention, incidence rate ratios (IRRs), 95% confidence intervals (CIs), and p-values were reported. Confidence intervals and p-values were estimated using Newey–West standard errors to account for heteroscedasticity and serial correlation in the model residuals (Appendix G).

Step 5: Estimation of pooled intervention effects. Pooled intervention effects across cities were estimated using a two-stage random-effects meta-analysis. In the first stage, city-specific log IRRs and their Newey–West standard errors were extracted for each intervention coefficient, including immediate level and weekly trend changes. In the second stage, these estimates were pooled using restricted maximum-likelihood estimation in a random-effects meta-analysis model implemented in the metafor R package (version 4.8-0).[17] Pooled IRRs, 95% CIs, and p-values were reported. Between-city heterogeneity was quantified using the I^2 index and τ^2, representing the proportion of total variation attributable to heterogeneity and the estimated between-city variance, respectively.

Step 6: Sensitivity analysis. To assess the robustness of the findings, both the city-specific ITS models and the pooled meta-analytic estimates were re-estimated after excluding weeks with imputed dengue or meteorological data (complete-case analysis). Consistency with the primary analysis was examined to evaluate the stability of intervention effect estimates.

All analyses were conducted using R version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria; https://www.r-project.org).

2.6 Ethical considerations

This study used only aggregated, open-access data obtained from official Brazilian sources. All datasets are publicly available, contain no individual identifiers, and represent routinely collected surveillance or administrative information. In accordance with national and international ethical regulations, analyses based exclusively on publicly available, de-identified, aggregate data do not require review by a research ethics committee.

3 RESULTS

3.1 Descriptive analyses

Between January 2015 and December 2023, a total of 1,613,719 dengue cases were reported across the ten major Brazilian cities analyzed, spanning 477 epidemiological weeks (Table 1). Median weekly dengue incidence varied markedly, from 0.4 cases per 100,000 population in São Paulo to 21.9 cases per 100,000 population in Goiânia. Because the distributions of weekly dengue case counts and incidence rates were right-skewed (Appendices H and I), Table 1 reports medians and ranges (minimum–maximum). Temporal trajectories of weekly dengue incidence were highly heterogeneous across cities, with marked differences in seasonal patterns, the timing and magnitude of epidemic peaks, and the degree of interannual variation (Figure 2).

Table 1. Summary of weekly dengue case counts and incidence rates in ten major Brazilian cities, 2015–2023, by study period.

City	Study period (weeks, n)	Total cases (n)	Median weekly cases (min–max)	Median weekly incidence per 100,000 (min–max)	% change in median weekly incidence per 100,000 vs pre-COVID-19
Belo Horizonte	All (477)	339,837	38.0 (1–13,884)	1.55 (0.04–552.39)	—
	Pre-COVID-19 pandemic (275)	310,403	37.5 (1–13,884)	1.49 (0.04–552.39)	—
	COVID-19 pandemic to pre-vaccination (45)	4,173	37.0 (11–568)	1.47 (0.44–22.53)	−1%
	Vaccination to pre-full resumption of in-person classes (55)	1,677	26.0 (2–81)	1.03 (0.08–3.20)	−31%
	Post-full resumption of in-person classes (102)	23,584	80.5 (16–1,943)	3.43 (0.69–80.41)	+130%
Brasília	All (477)	260,585	222.0 (1–4,843)	7.46 (0.03–171.90)	—
	Pre-COVID-19 pandemic (274)	85,051	82.5 (1–3,438)	2.80 (0.03–114.02)	—
	COVID-19 pandemic to pre-vaccination (46)	42,460	254.0 (50–3,184)	8.26 (1.64–104.22)	+195%
	Vaccination to pre-full resumption of in-person classes (41)	14,997	285.0 (90–855)	9.21 (2.91–27.63)	+229%
	Post-full resumption of in-person classes (116)	118,077	669.5 (32–4,843)	22.43 (1.03–171.90)	+701%
Campo Grande	All (477)	108,262	46.0 (1–3,114)	5.14 (0.11–347.55)	—
	Pre-COVID-19 pandemic (275)	80,712	42.0 (1–3,114)	4.74 (0.11–347.55)	—
	COVID-19 pandemic to pre-vaccination (45)	6,093	89.0 (16–657)	9.82 (1.77–72.51)	+107%
	Vaccination to pre-full resumption of in-person classes (59)	736	9.0 (1–57)	0.98 (0.11–6.35)	−79%
	Post-full resumption of in-person classes (98)	20,721	109.5 (5–953)	12.19 (0.52–99.84)	+157%
Fortaleza	All (477)	132,110	115.0 (1–2,774)	4.35 (0.04–107.06)	—
	Pre-COVID-19 pandemic (275)	84,530	102.0 (1–2,774)	3.82 (0.04–107.06)	—
	COVID-19 pandemic to pre-vaccination (45)	7,840	159.0 (10–534)	5.92 (0.37–19.88)	+55%
	Vaccination to pre-full resumption of in-person classes (55)	15,249	134.0 (4–1,048)	4.96 (0.15–38.77)	+30%
	Post-full resumption of in-person classes (102)	24,491	119.0 (9–1,324)	4.74 (0.35–54.51)	+24%
Goiânia	All (477)	348,076	327.0 (2–4,373)	21.91 (0.13–305.66)	—
	Pre-COVID-19 pandemic (275)	246,615	479.5 (5–4,373)	31.70 (0.35–305.66)	—
	COVID-19 pandemic to pre-vaccination (45)	9,756	148.0 (25–628)	9.63 (1.63–40.88)	−70%
	Vaccination to pre-full resumption of in-person classes (53)	15,684	170.0 (2–1,678)	10.93 (0.13–116.74)	−66%
	Post-full resumption of in-person classes (104)	76,021	354.5 (120–3,108)	24.63 (8.03–216.23)	−22%
Natal	All (477)	87,162	73.0 (1–1,749)	8.53 (0.11–199.28)	—
	Pre-COVID-19 pandemic (275)	62,298	100.5 (1–1,749)	11.45 (0.11–199.28)	—
	COVID-19 pandemic to pre-vaccination (45)	772	16.0 (1–56)	1.80 (0.11–6.29)	−84%

	Vaccination to pre-full resumption of in-person classes (43)	1,165	25.0 (5–58)	2.79 (0.56–6.47)	−76%
	Post-full resumption of in-person classes (114)	22,927	60.0 (1–1,278)	7.64 (0.11–170.11)	−33%
Rio de Janeiro	All (477)	101,385	81.0 (1–2,565)	1.23 (0.01–39.47)	—
	Pre-COVID-19 pandemic (274)	72,705	103.0 (21–2,565)	1.57 (0.32–39.47)	—
	COVID-19 pandemic to pre-vaccination (46)	640	10.0 (4–54)	0.15 (0.06–0.80)	−90%
	Vaccination to pre-full resumption of in-person classes (41)	767	16.0 (3–45)	0.24 (0.04–0.66)	−85%
	Post-full resumption of in-person classes (116)	27,273	142.0 (1–1,033)	2.24 (0.01–15.35)	+43%
Salvador	All (477)	49,750	51.0 (2–687)	1.78 (0.07–25.38)	—
	Pre-COVID-19 pandemic (274)	25,129	50.0 (10–493)	1.72 (0.34–17.08)	—
	COVID-19 pandemic to pre-vaccination (46)	7,998	55.0 (7–687)	1.91 (0.24–23.80)	+11%
	Vaccination to pre-full resumption of in-person classes (55)	796	14.0 (2–32)	0.48 (0.07–1.10)	−72%
	Post-full resumption of in-person classes (102)	15,827	91.5 (9–652)	3.56 (0.37–25.38)	+107%
São Paulo	All (477)	143,345	49.0 (2–9,649)	0.41 (0.02–80.62)	—
	Pre-COVID-19 pandemic (273)	104,381	38.0 (6–9,649)	0.31 (0.05–80.62)	—
	COVID-19 pandemic to pre-vaccination (47)	1,590	14.5 (2–183)	0.12 (0.02–1.48)	−61%
	Vaccination to pre-full resumption of in-person classes (28)	8,239	169.0 (30–920)	1.36 (0.24–7.42)	+339%
	Post-full resumption of in-person classes (129)	29,135	86.5 (11–1,705)	0.73 (0.09–14.89)	+135%
Teresina	All (477)	43,207	29.0 (1–1,778)	3.35 (0.12–205.24)	—
	Pre-COVID-19 pandemic (276)	18,051	31.0 (1–502)	3.67 (0.12–59.46)	—
	COVID-19 pandemic to pre-vaccination (44)	700	13.0 (4–47)	1.50 (0.46–5.41)	−59%
	Vaccination to pre-full resumption of in-person classes (71)	14,730	23.0 (3–1,778)	2.64 (0.34–205.24)	−28%
	Post-full resumption of in-person classes (86)	9,726	42.0 (8–657)	4.65 (0.89–75.84)	+27%

Weekly incidence was calculated as the number of newly reported dengue cases divided by the annual city-specific population estimate and multiplied by 100,000. Median weekly incidence refers to the median of these week-level values within each period. Population denominators were obtained from official census projections and assumed constant within each calendar year.

Percentage change was calculated as the relative difference in median weekly incidence compared with the pre-COVID-19 baseline: (median weekly incidence during each period − median weekly incidence in the pre-COVID-19 period) ÷ median weekly incidence in the pre-COVID-19 period × 100.

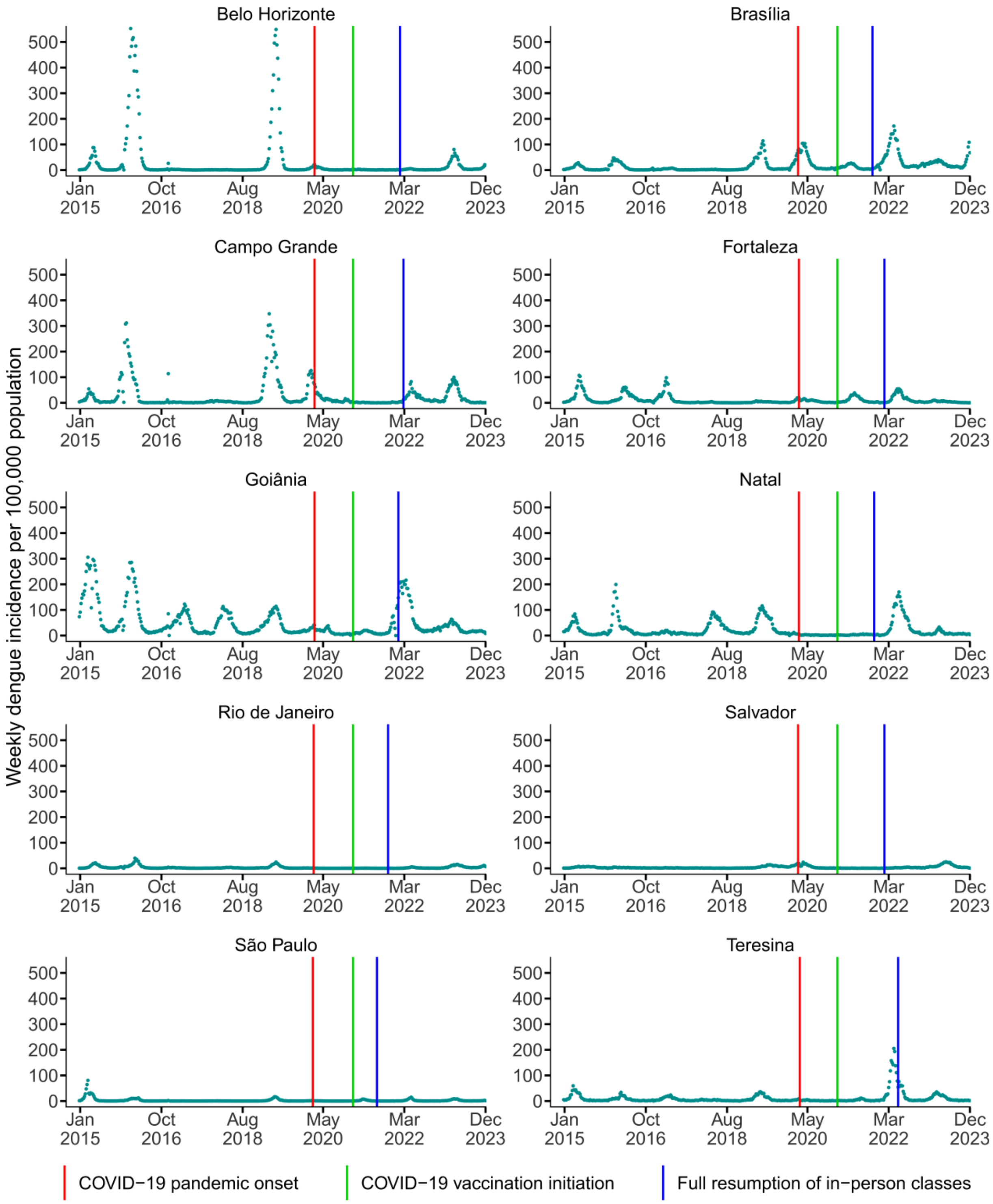

Figure 2. Weekly dengue incidence per 100,000 population in ten major Brazilian cities, 2015–2023. Vertical colored lines indicate key intervention points: onset of the COVID-19 pandemic (red), initiation of the COVID-19 vaccination campaign (green), and full resumption of in-person classes (blue).

During the pre–COVID-19 period (January 2015–February 2020), weekly dengue incidence showed marked seasonal fluctuations and episodic outbreaks, but remained overall stable within most cities, with no clear evidence of sustained upward or downward trends. However, median weekly dengue incidence varied substantially across locations: southeastern cities such as São Paulo and Belo Horizonte had the lowest baseline incidence, whereas northeastern and midwestern cities, including Fortaleza, Natal, Salvador, and Goiânia, consistently showed higher incidence.

Relative to the pre-COVID-19 period, median weekly dengue incidence during the pandemic–pre-vaccination period declined in Belo Horizonte, Goiânia, Natal, Rio de Janeiro, São Paulo, and Teresina, while other cities experienced temporary increases. Percentage changes ranged from a 90% reduction in Rio de Janeiro to a 195% increase in Brasília.

With the exception of Brasília, Fortaleza, and São Paulo, the remaining cities experienced declines in median weekly dengue incidence during the vaccination–pre–full resumption of in-person classes period relative to the pre-COVID-19 period. Following the full resumption of in-person classes, median weekly dengue incidence increased relative to pre-COVID-19 levels in all cities except Goiânia and Natal. The largest post-resumption increases were observed in Brasília (+701%), Campo Grande (+157%), and Belo Horizonte (+130%) relative to pre-COVID-19 incidence.

3.2 Main interrupted time-series analysis

Results from the negative binomial interrupted time-series models (Table 2) demonstrated substantial heterogeneity in the effects of the interventions on weekly dengue incidence across cities.

Table 2. Estimated immediate and trend effects of the COVID-19 pandemic, COVID-19 vaccination campaign, and full resumption of in-person classes on weekly dengue incidence in ten major Brazilian cities, 2015–2023.

	COVID-19 pandemic						**COVID-19 vaccination campaign**						**Full resumption of in-person classes**				
	Immediate effect (level change)			**Weekly trend change (slope change)**			**Immediate effect (level change)**			**Weekly trend change (slope change)**			**Immediate effect (level change)**			**Weekly trend change (slope change)**	
City	**IRR (95% CI)**	**P value**		**IRR (95% CI)**	**P value**		**IRR (95% CI)**	**P value**		**IRR (95% CI)**	**P value**		**IRR (95% CI)**	**P value**		**IRR (95% CI)**	**P value**
Belo Horizonte	1.81 (0.52–6.25)	0.347		0.97 (0.95–0.99)	0.007		0.82 (0.29–2.28)	0.7		1.04 (1.02–1.06)	<0.001		0.84 (0.33–2.11)	0.71		1.02 (0.996–1.04)	0.117
Brasília	1.46 (0.52–4.07)	0.472		1.00 (0.97–1.03)	0.847		0.79 (0.35–1.82)	0.587		1.01 (0.97–1.05)	0.696		0.70 (0.30–1.64)	0.41		1.00 (0.97–1.02)	0.698
Campo Grande	3.81 (1.85–7.83)	<0.001		0.97 (0.95–0.98)	<0.001		0.08 (0.02–0.30)	<0.001		1.04 (1.01–1.07)	0.009		30.19 (7.39–123.31)	<0.001		0.98 (0.95–1.01)	0.299
Fortaleza	4.87 (2.33–10.17)	<0.001		0.96 (0.95–0.97)	<0.001		5.99 (2.96–12.11)	<0.001		1.02 (0.99–1.04)	0.143		4.27 (2.26–8.07)	<0.001		1.01 (0.99–1.04)	0.212
Goiânia	1.30 (0.66–2.58)	0.452		0.97 (0.95–0.99)	0.003		0.90 (0.55–1.47)	0.681		1.07 (1.04–1.09)	<0.001		1.10 (0.70–1.70)	0.686		0.96 (0.95–0.97)	<0.001
Natal	0.27 (0.17–0.41)	<0.001		0.99 (0.98–1.005)	0.22		0.85 (0.46–1.58)	0.605		1.05 (1.03–1.07)	<0.001		1.11 (0.58–2.12)	0.744		0.96 (0.94–0.98)	<0.001
Rio de Janeiro	0.25 (0.10–0.61)	0.002		0.99 (0.96–1.02)	0.634		1.53 (0.65–3.59)	0.329		1.01 (0.97–1.04)	0.686		2.23 (1.05–4.71)	0.036		1.02 (0.999–1.04)	0.065
Salvador	0.80 (0.39–1.63)	0.541		1.00 (0.98–1.02)	0.904		0.69 (0.47–1.02)	0.066		0.99 (0.97–1.01)	0.482		4.48 (2.92–6.88)	<0.001		1.01 (0.998–1.02)	0.094
São Paulo	1.97 (0.97–4.02)	0.061		0.94 (0.92–0.96)	<0.001		11.04 (3.57–34.11)	<0.001		1.07 (1.03–1.12)	0.001		0.59 (0.27–1.28)	0.183		1.00 (0.95–1.04)	0.869
Teresina	0.38 (0.17–0.85)	0.018		1.02 (1.004–1.04)	0.013		0.46 (0.19–1.13)	0.09		1.00 (0.98–1.03)	0.754		0.83 (0.40–1.74)	0.629		0.97 (0.95–0.996)	0.019
Pooled estimate	1.08 (0.56–2.11)	0.814		0.98 (0.97–0.996)	0.012		1.05 (0.49–2.26)	0.906		1.03 (1.01–1.05)	<0.001		1.74 (0.90–3.37)	0.099		0.99 (0.98–1.01)	0.338

Incidence rate ratios (IRRs) and 95% confidence intervals (CIs) were obtained from city-specific negative binomial interrupted time-series models estimated by maximum likelihood. Newey–West standard errors were applied to adjust for heteroskedasticity and serial correlation in the model residuals (Appendix G). Model specifications are provided in Appendix F. Pooled effect estimates across cities were obtained using random-effects meta-analysis with restricted maximum-likelihood estimation. Between-city heterogeneity was quantified using the I^2 index and the between-city variance (τ^2) (Appendix J).

COVID-19 pandemic

The onset of the COVID-19 pandemic was associated with significant immediate decreases in weekly dengue incidence in Natal (IRR 0.27, 95% CI 0.17–0.41), Rio de Janeiro (IRR 0.25, 95% CI 0.10–0.61), and Teresina (IRR 0.38, 95% CI 0.17–0.85), whereas significant immediate increases were observed in Campo Grande (IRR 3.81, 95% CI 1.85–7.83) and Fortaleza (IRR 4.87, 95% CI 2.33–10.17).

Following the onset of the COVID-19 pandemic, weekly dengue incidence trends declined significantly in Belo Horizonte, Campo Grande, Fortaleza, Goiânia, and São Paulo (IRRs 0.94–0.97, $p < 0.05$), whereas Teresina showed a significant increase (IRR 1.02, $p < 0.05$).

COVID-19 vaccination campaign

The initiation of the COVID-19 vaccination campaign was associated with a significant immediate decrease in weekly dengue incidence in Campo Grande (IRR 0.08, 95% CI 0.02–0.30), whereas significant immediate increases were observed in Fortaleza (IRR 5.99, 95% CI 2.96–12.11) and São Paulo (IRR 11.04, 95% CI 3.57–34.11).

Following the initiation of the COVID-19 vaccination campaign, weekly dengue incidence trends increased significantly in Belo Horizonte, Campo Grande, Goiânia, Natal, and São Paulo (IRRs 1.04–1.07, $p < 0.05$).

Full resumption of in-person classes

The full resumption of in-person classes was associated with significant immediate increases in weekly dengue incidence in Campo Grande (IRR 30.19, 95% CI 7.39–123.31), Fortaleza (IRR 4.27, 95% CI 2.26–8.07), Rio de Janeiro (IRR 2.23, 95% CI 1.05–4.71), and Salvador (IRR 4.48, 95% CI 2.92–6.88).

Following the full resumption of in-person classes, weekly dengue incidence trends decreased significantly in Goiânia, Natal, and Teresina (IRRs 0.96–0.97, $p < 0.05$).

Pooled intervention effects

Across the ten cities, the onset of the COVID-19 pandemic was not associated with a significant immediate change in weekly dengue incidence (pooled IRR 1.08, 95% CI 0.56–2.11; $p = 0.81$), but was associated with a modest, statistically significant decline in the weekly dengue incidence trend (pooled IRR 0.98, 95% CI 0.97–0.996; $p = 0.012$). Similarly, the initiation of the COVID-19 vaccination campaign was not associated with a significant immediate effect (pooled IRR 1.05, 95% CI 0.49–2.26; $p = 0.91$), but was associated with a small, statistically significant increase in the weekly dengue incidence trend (pooled IRR 1.03, 95% CI 1.01–1.05; $p < 0.001$). No significant immediate or trend changes were observed following the full resumption of in-person classes. Between-city heterogeneity was substantial, with I^2 values ranging from 74.6% to 91.3% across pooled effect estimates (Appendix J).

3.3 Sensitivity analyses (complete-case models)

Excluding all weeks with imputed dengue or meteorological data yielded results consistent with the main ITS analysis (Table 3). For most interventions, both the direction and statistical significance of city-specific estimates were unchanged. For example, the COVID-19 pandemic remained associated with significant immediate reductions in weekly dengue incidence in Natal, Rio de Janeiro, and Teresina, while the full resumption of in-person classes was again associated with immediate increases in weekly dengue incidence in Campo Grande, Fortaleza, Rio de Janeiro, and Salvador. Similarly, post-pandemic-onset changes in weekly dengue incidence trends remained statistically significant in Belo Horizonte, Campo Grande, Fortaleza, Goiânia, São Paulo, and Teresina.

At the pooled level, intervention effects derived from the complete-case models closely mirrored those of the primary random-effects meta-analysis, with only minor differences in precision. For example, weekly dengue incidence trend changes associated with the pandemic onset (pooled IRR 0.98, 95% CI 0.96–0.997; $p = 0.023$) and the initiation of the COVID-19 vaccination campaign (pooled IRR 1.03, 95% CI

1.01–1.05; $p = 0.001$) were nearly identical to the main estimates, as were the pooled immediate effect estimates for all three interventions.

Taken together, these findings indicate that the limited imputation applied in the primary analysis did not materially affect the estimated intervention effects, supporting the robustness and internal validity of the main ITS results.

Table 3. Estimated immediate and trend effects from complete-case analyses of the COVID-19 pandemic, COVID-19 vaccination campaign, and full resumption of in-person classes on weekly dengue incidence in ten major Brazilian cities, 2015–2023.

	COVID-19 pandemic				**COVID-19 vaccination campaign**				**Full resumption of in-person classes**			
	Immediate effect (level change)		**Weekly trend change (slope change)**		**Immediate effect (level change)**		**Weekly trend change (slope change)**		**Immediate effect (level change)**		**Weekly trend change (slope change)**	
City	**IRR (95% CI)**	**P value**	**IRR (95% CI)**	**P value**	**IRR (95% CI)**	**P value**	**IRR (95% CI)**	**P value**	**IRR (95% CI)**	**P value**	**IRR (95% CI)**	**P value**
Belo Horizonte	1.78 (0.52–6.09)	0.359	0.97 (0.95–0.99)	0.006	0.84 (0.30–2.35)	0.741	1.04 (1.02–1.06)	<0.001	0.86 (0.33–2.22)	0.757	1.02 (0.996–1.04)	0.109
Brasília	1.48 (0.52–4.19)	0.458	1.00 (0.97–1.03)	0.932	0.79 (0.34–1.84)	0.582	1.01 (0.97–1.05)	0.605	0.67 (0.29–1.59)	0.366	0.99 (0.97–1.02)	0.653
Campo Grande	3.98 (1.86–8.50)	<0.001	0.97 (0.95–0.98)	<0.001	0.09 (0.03–0.29)	<0.001	1.04 (1.01–1.07)	0.004	24.57 (6.59–91.62)	<0.001	0.99 (0.96–1.02)	0.436
Fortaleza	5.24 (2.31–11.89)	<0.001	0.96 (0.95–0.97)	<0.001	6.06 (2.97–12.36)	<0.001	1.02 (0.99–1.04)	0.146	4.23 (2.22–8.07)	<0.001	1.02 (0.99–1.04)	0.205
Goiânia	1.30 (0.64–2.62)	0.47	0.97 (0.95–0.99)	0.003	0.90 (0.55–1.47)	0.673	1.07 (1.04–1.09)	<0.001	1.10 (0.71–1.71)	0.662	0.96 (0.95–0.97)	<0.001
Natal	0.27 (0.17–0.42)	<0.001	0.99 (0.98–1.004)	0.176	0.85 (0.46–1.55)	0.591	1.05 (1.03–1.08)	<0.001	1.06 (0.54–2.09)	0.863	0.96 (0.94–0.98)	<0.001
Rio de Janeiro	0.25 (0.10–0.62)	0.002	0.99 (0.96–1.02)	0.594	1.55 (0.67–3.60)	0.311	1.01 (0.97–1.05)	0.621	2.45 (1.18–5.10)	0.017	1.02 (0.996–1.04)	0.102
Salvador	0.84 (0.41–1.72)	0.641	1.00 (0.98–1.02)	0.844	0.71 (0.48–1.03)	0.069	0.99 (0.97–1.01)	0.536	4.30 (2.78–6.63)	<0.001	1.01 (0.999–1.02)	0.068
São Paulo	2.07 (1.03–4.16)	0.041	0.94 (0.92–0.96)	<0.001	17.02 (5.90–49.11)	<0.001	1.07 (1.03–1.11)	0.001	0.73 (0.33–1.61)	0.435	1.01 (0.97–1.05)	0.72
Teresina	0.32 (0.15–0.67)	0.002	1.03 (1.01–1.04)	<0.001	0.38 (0.12–1.16)	0.089	0.99 (0.97–1.02)	0.612	0.90 (0.38–2.14)	0.814	0.98 (0.95–1.001)	0.059
Pooled estimate	1.08 (0.55–2.15)	0.821	0.98 (0.96–0.997)	0.023	1.08 (0.46–2.52)	0.856	1.03 (1.01–1.05)	0.001	1.78 (0.95–3.35)	0.071	0.99 (0.98–1.01)	0.425

Incidence rate ratios (IRRs) and 95% confidence intervals (CIs) were obtained from city-specific negative binomial interrupted time-series models estimated by maximum likelihood. Newey–West standard errors were applied to adjust for heteroskedasticity and serial correlation in the model residuals (Appendix G). Model specifications matched those of the primary analysis (Appendix F). Pooled effect estimates across cities were obtained using random-effects meta-analysis with restricted maximum-likelihood estimation. Between-city heterogeneity was quantified using the I^2 index and the between-city variance (τ^2) (Appendix J).

4 DISCUSSION

In this multi-city interrupted time-series analysis, we evaluated the effects of the COVID-19 pandemic and two subsequent population-level interventions—the COVID-19 vaccination campaign and the full resumption of in-person classes—on weekly dengue incidence in ten major Brazilian cities. At the pooled level, no significant immediate changes in weekly dengue incidence were observed following the onset of the pandemic or the initiation of vaccination; however, both were associated with modest but statistically significant changes in trend: pandemic onset with a gradual decline and vaccination initiation with a small increase. No significant immediate or trend effects were detected for the full resumption of in-person classes at the pooled level. City-specific analyses revealed substantial heterogeneity across cities in the direction, magnitude, and statistical significance of both immediate and trend effects for each intervention. Collectively, these findings indicate that pandemic-related societal disruptions affected dengue transmission unevenly across settings, underscoring the central role of local context in shaping dengue transmission dynamics and the need for locally tailored dengue prevention and control strategies.

Our findings are consistent with prior research indicating that the impact of the COVID-19 pandemic on dengue incidence varied markedly across geographic contexts.[5–7] Notably, this study extends the literature by demonstrating substantial heterogeneity in the effects of the pandemic and related population-level interventions across major Brazilian urban centers with a long-standing dengue burden. This heterogeneity likely reflects setting-specific differences in key mechanisms operating during the pandemic, including variation in mobility reductions, disruption of routine vector-control activities, and changes in healthcare-seeking behavior and health-system capacity.[12,14,15] Evidence from Brazil suggests that these mechanisms did not operate uniformly across cities during the pandemic.[12,14,15]

The absence of significant immediate pooled effects does not imply that the pandemic and related interventions had no influence on dengue incidence. Rather, the significant pooled trend effects indicate that their impacts were predominantly gradual, unfolding over longer time horizons rather than through abrupt changes. Although these trend effects were modest in magnitude, their direction is consistent with mechanisms proposed in prior research. The pooled trend decline following pandemic onset is consistent with reduced within-neighborhood mobility, which may have lowered opportunities for human–mosquito interactions and, consequently, dengue transmission.[12,14,15] The subsequent pooled trend increase after vaccination initiation may reflect the gradual restoration of mobility and municipal services.[12,14,15]

The study limitations warrant consideration. First, outcome misclassification is a potential concern, as dengue and COVID-19 share overlapping clinical manifestations that may have affected diagnostic accuracy.[6] Second, dengue case reporting may have been influenced by changes in healthcare-seeking behavior, disruptions to routine surveillance systems, and increased strain on health services during the pandemic.[6,10] Third, although the interrupted time-series design accounts for pre-intervention trends and models were adjusted for key meteorological covariates, residual confounding cannot be excluded given the complex and multifactorial nature of dengue transmission.[3] Finally, the pronounced between-city heterogeneity observed in this study cautions against extrapolating the results to settings with markedly different ecological, social, or infrastructural contexts.

5 CONCLUSIONS

This multi-city interrupted time-series analysis demonstrates marked variation in the effects of the COVID-19 pandemic and related population-level interventions on dengue incidence across major Brazilian urban centers. Although pooled estimates suggested only modest changes in dengue trends following pandemic onset and vaccination initiation, city-specific analyses revealed substantial heterogeneity in the direction, magnitude, and statistical significance of both immediate and trend effects associated with each intervention. Collectively, these findings indicate that large-scale societal disruptions can reshape dengue transmission in complex, context-dependent ways, underscoring the limitations of relying on national-level averages to inform policy planning. Strengthened, resilient surveillance and vector-control strategies tailored to city-specific conditions are essential for sustaining dengue prevention and control capacity during periods of major systemic disruption.

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APPENDIX A – Start dates of study interventions in ten major Brazilian cities, 2015–2023.

	Onset of the COVID-19 pandemic		Initiation of the COVID-19 vaccination campaign		Full resumption of in-person classes
Belo Horizonte	16/03/2020[1]		18/01/2021[2]		03/02/2022[3]
Brasília	07/03/2020[4]		19/01/2021[5]		03/11/2021[6]
Campo Grande	14/03/2020[7]		19/01/2021[8]		03/03/2022[9]
Fortaleza	15/03/2020[10]		18/01/2021[11]		01/02/2022[12]
Goiânia	12/03/2020[13]		18/01/2021[14]		19/01/2022[15]
Natal	12/03/2020[16]		19/01/2021[17]		16/11/2021[18]
Rio de Janeiro	06/03/2020[19]		18/01/2021[20]		03/11/2021[21]
Salvador	06/03/2020[22]		19/01/2021[23]		03/02/2022[24]
São Paulo	26/02/2020[25]		17/01/2021[26]		02/08/2021[27]
Teresina	19/03/2020[28]		18/01/2021[29]		23/05/2022[30]

Dates are reported as day/month/year.

The onset of the COVID-19 pandemic was defined as the date of the first laboratory-confirmed COVID-19 case reported in each city. The initiation of the COVID-19 vaccination campaign was defined as the date on which the first COVID-19 vaccine dose was administered in each city. The full resumption of in-person classes was defined as the date on which each municipal government officially authorized the complete return to classroom-based instruction in the public municipal school system.

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APPENDIX B – Number and percentage of missing weekly observations for dengue case counts and meteorological covariates in ten major Brazilian cities, 2015–2023.

City	Missing dengue case counts, n (%)	Missing temperature, n (%)	Missing relative humidity, n (%)	Missing wind speed, n (%)	Missing solar radiation, n (%)
Belo Horizonte	5 (1.05)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Brasília	4 (0.84)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Campo Grande	9 (1.89)	3 (0.63)	3 (0.63)	3 (0.63)	6 (1.26)
Fortaleza	5 (1.05)	9 (1.89)	9 (1.89)	9 (1.89)	9 (1.89)
Goiânia	5 (1.05)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Natal	5 (1.05)	15 (3.14)	15 (3.14)	15 (3.14)	15 (3.14)
Rio de Janeiro	7 (1.47)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Salvador	6 (1.26)	2 (0.42)	2 (0.42)	2 (0.42)	2 (0.42)
São Paulo	8 (1.68)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Teresina	7 (1.47)	3 (0.63)	3 (0.63)	3 (0.63)	3 (0.63)

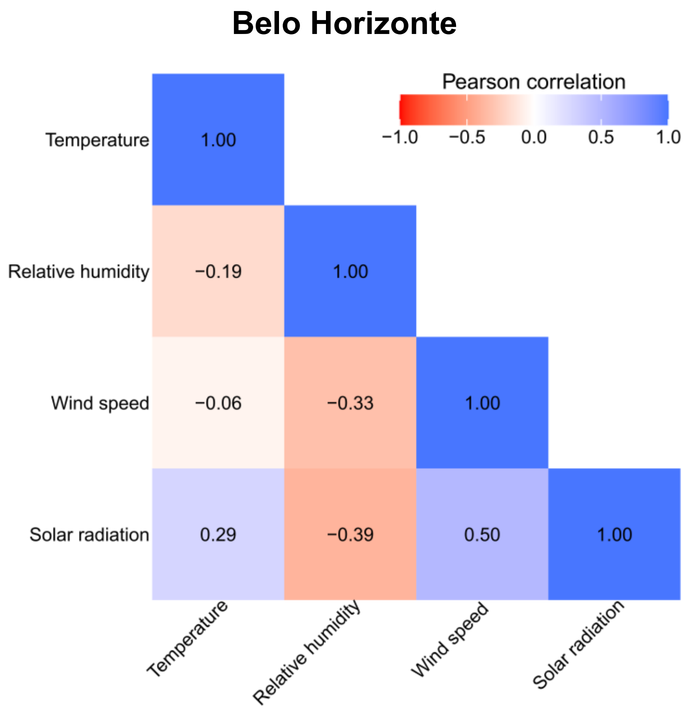
The number and proportion of missing weekly observations were calculated relative to the total study period of 477 epidemiological weeks (January 2015–December 2023). Missing observations were infrequent in both dengue case counts and meteorological covariates. To preserve temporal continuity for interrupted time-series analysis, missing values were imputed using linear interpolation between adjacent weeks. Imputed dengue counts were subsequently rounded to the nearest integer to maintain consistency with count-scale data.

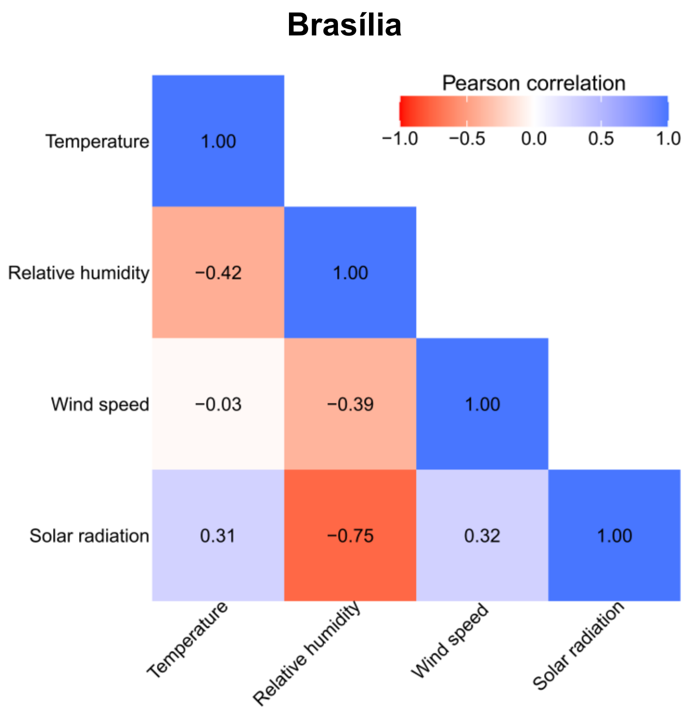
APPENDIX C – Pearson dispersion statistics used to assess overdispersion in Poisson generalized linear models used in interrupted time-series analyses of weekly dengue incidence in ten major Brazilian cities, 2015–2023.

City	Pearson dispersion statistic
Belo Horizonte	4,618.87
Brasília	696.68
Campo Grande	731.22
Fortaleza	394.03
Goiânia	469.92
Natal	277.66
Rio de Janeiro	389.19
Salvador	70.32
São Paulo	1,202.74
Teresina	92.82

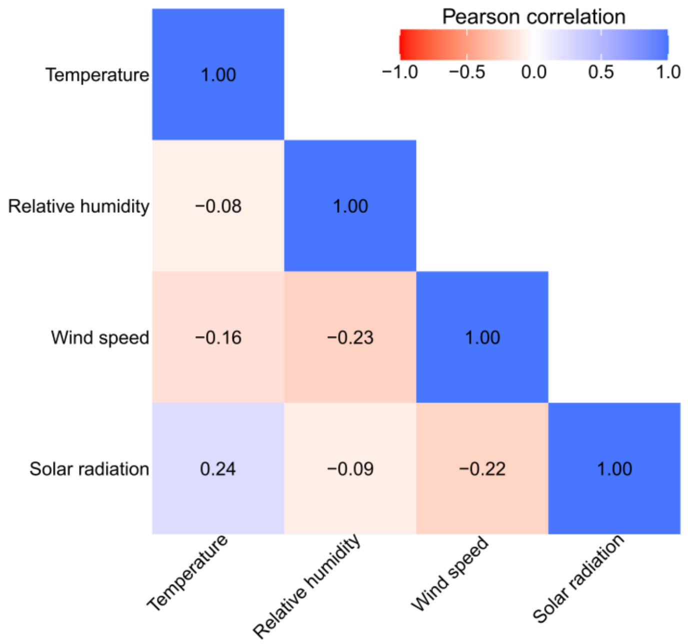
The Pearson dispersion statistic was computed as the sum of squared Pearson residuals divided by the residual degrees of freedom (i.e., the sample size minus the number of estimated parameters). Values substantially greater than one indicate overdispersion, whereby the conditional variance of the outcome exceeds its conditional mean. Evidence of overdispersion therefore provided empirical justification for using negative binomial generalized linear models in the interrupted time-series analyses.

APPENDIX D – Pearson correlation coefficients among meteorological variables in ten major Brazilian cities, 2015–2023.

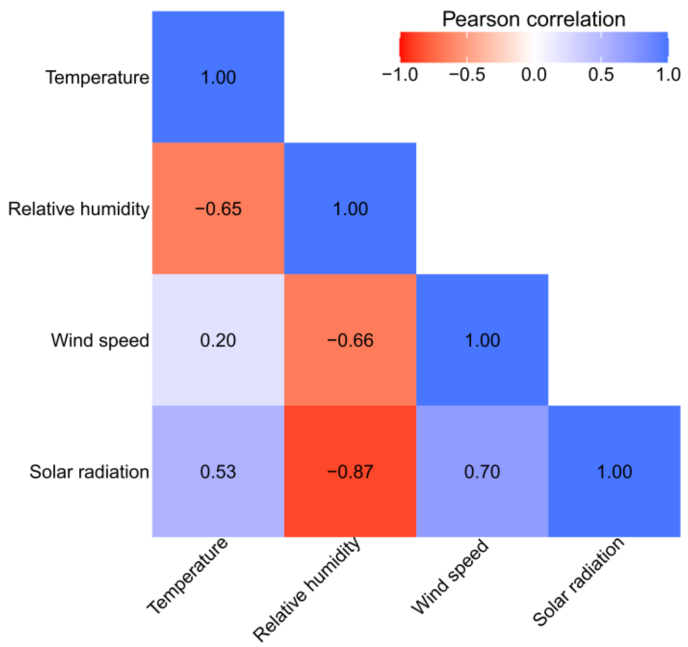


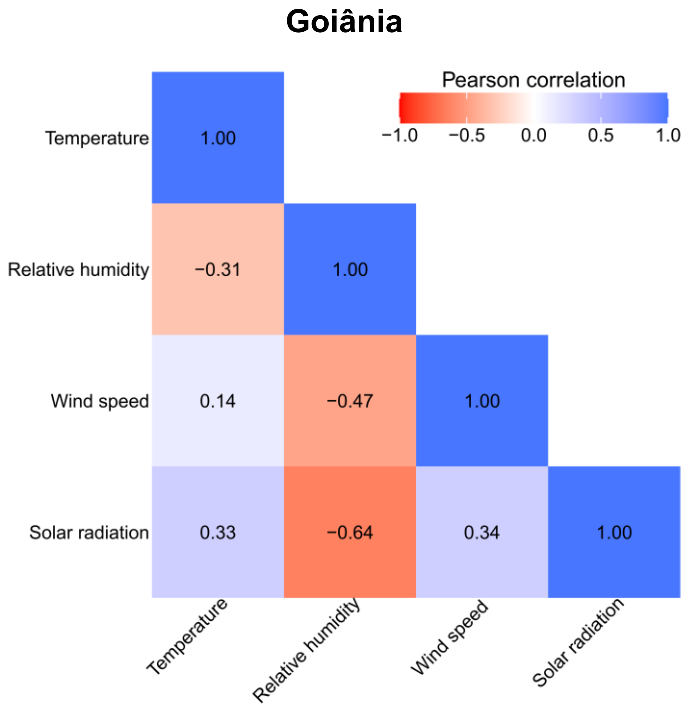


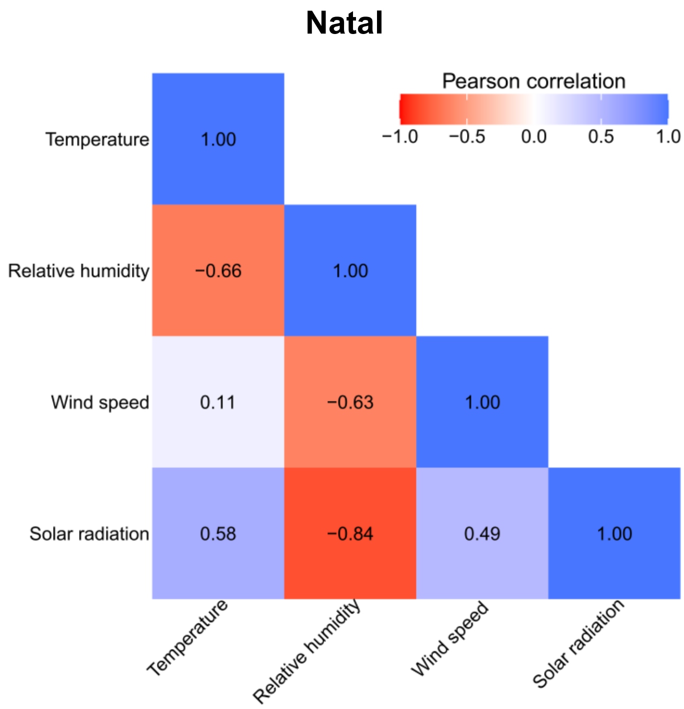
Campo Grande

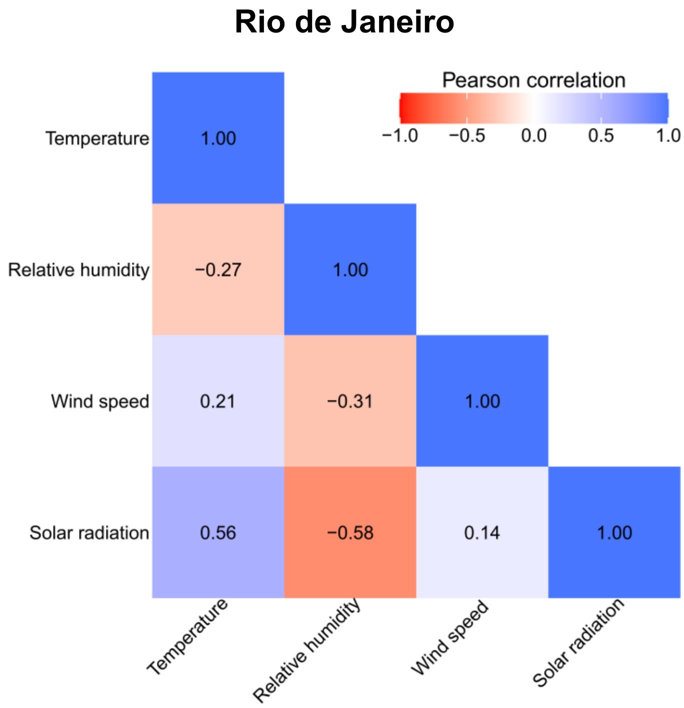


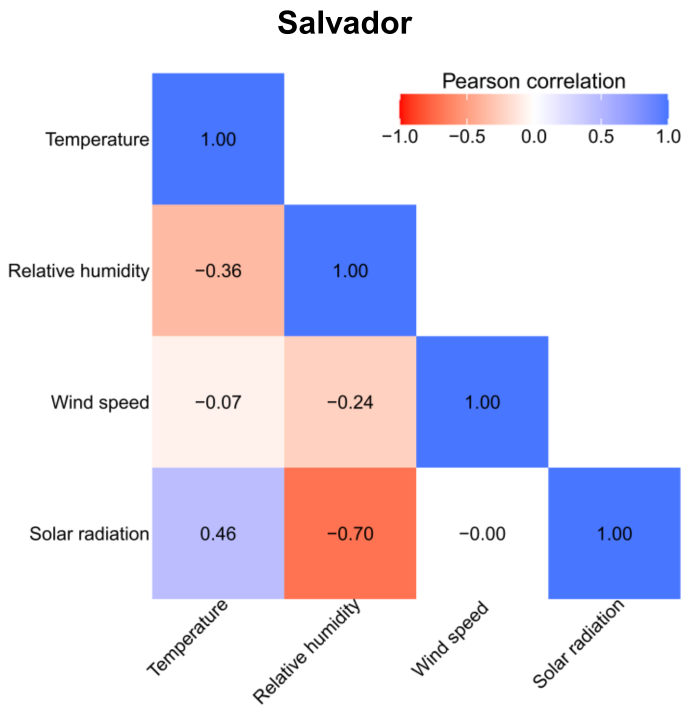
Fortaleza

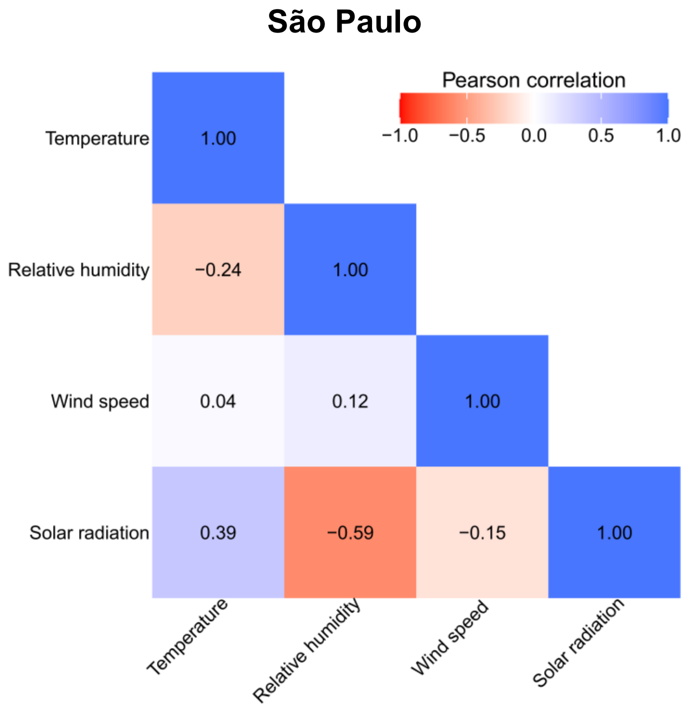


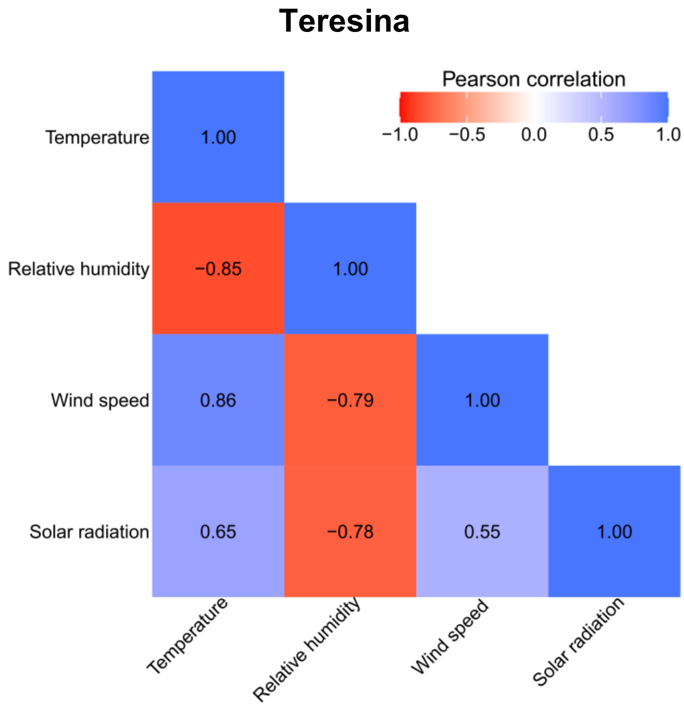

Goiânia
Pearson correlation
−1.0
−0.5
0.0
0.5
1.0
Temperature
Relative humidity
Wind speed
Solar radiation
1.00
−0.31
1.00
0.14
−0.47
1.00
0.33
−0.64
0.34
1.00
Temperature
Relative humidity
Wind speed
Solar radiation


Natal
Pearson correlation
−1.0
−0.5
0.0
0.5
1.0
Temperature
Relative humidity
Wind speed
Solar radiation
1.00
−0.66
1.00
0.11
−0.63
1.00
0.58
−0.84
0.49
1.00
Temperature
Relative humidity
Wind speed
Solar radiation


Rio de Janeiro
Pearson correlation
−1.0
−0.5
0.0
0.5
1.0
Temperature
Relative humidity
Wind speed
Solar radiation
1.00
−0.27
1.00
0.21
−0.31
1.00
0.56
−0.58
0.14
1.00
Temperature
Relative humidity
Wind speed
Solar radiation


Salvador
Pearson correlation
−1.0
−0.5
0.0
0.5
1.0
Temperature
Relative humidity
Wind speed
Solar radiation
1.00
−0.36
1.00
−0.07
−0.24
1.00
0.46
−0.70
−0.00
1.00
Temperature
Relative humidity
Wind speed
Solar radiation


São Paulo
Pearson correlation
−1.0
−0.5
0.0
0.5
1.0
Temperature
Relative humidity
Wind speed
Solar radiation
1.00
−0.24
1.00
0.04
0.12
1.00
0.39
−0.59
−0.15
1.00
Temperature
Relative humidity
Wind speed
Solar radiation


Teresina
Pearson correlation
−1.0
−0.5
0.0
0.5
1.0
Temperature
Relative humidity
Wind speed
Solar radiation
1.00
−0.85
1.00
0.86
−0.79
1.00
0.65
−0.78
0.55
1.00
Temperature
Relative humidity
Wind speed
Solar radiation

APPENDIX E – Variance inflation factors for meteorological covariates in ten major Brazilian cities, 2015–2023.

City	Temperature	Relative humidity	Wind speed	Solar radiation
Belo Horizonte	1.18	1.24	1.48	1.62
Brasília	1.29	2.73	1.25	2.27
Campo Grande	1.09	1.09	1.14	1.12
Fortaleza	2.05	5.59	2.41	4.58
Goiânia	1.14	1.97	1.29	1.75
Natal	2.42	6.30	2.27	3.35
Rio de Janeiro	1.54	1.66	1.15	2.10
Salvador	1.28	2.27	1.15	2.30
São Paulo	1.19	1.54	1.04	1.74
Teresina	5.49	5.82	4.23	2.63

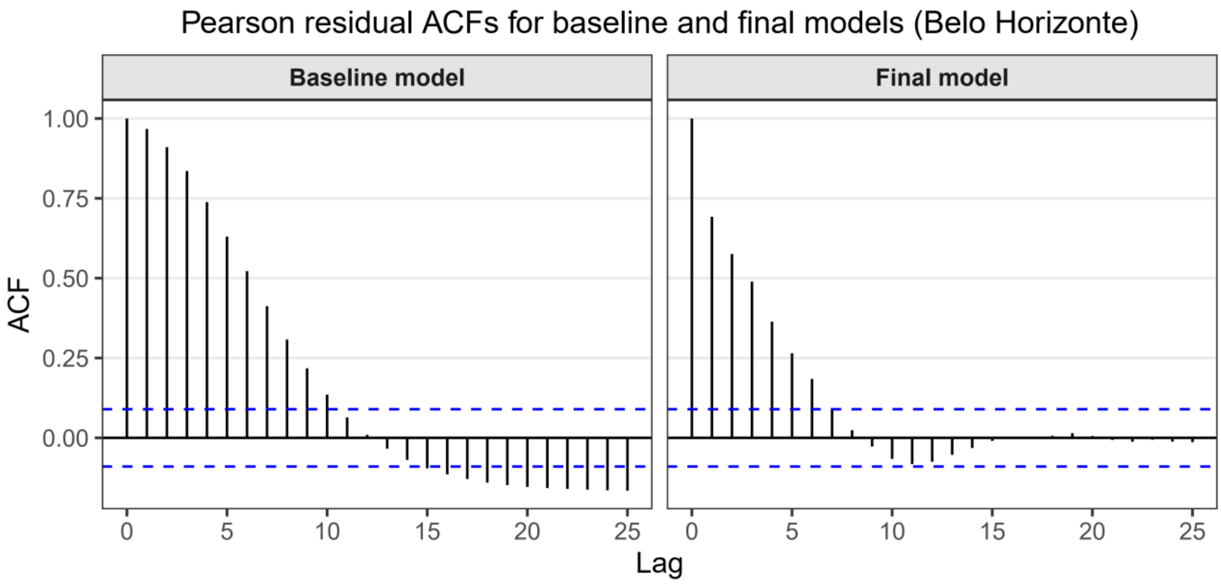
APPENDIX F – Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) values for baseline and final negative binomial interrupted time-series models in ten major Brazilian cities, 2015–2023.

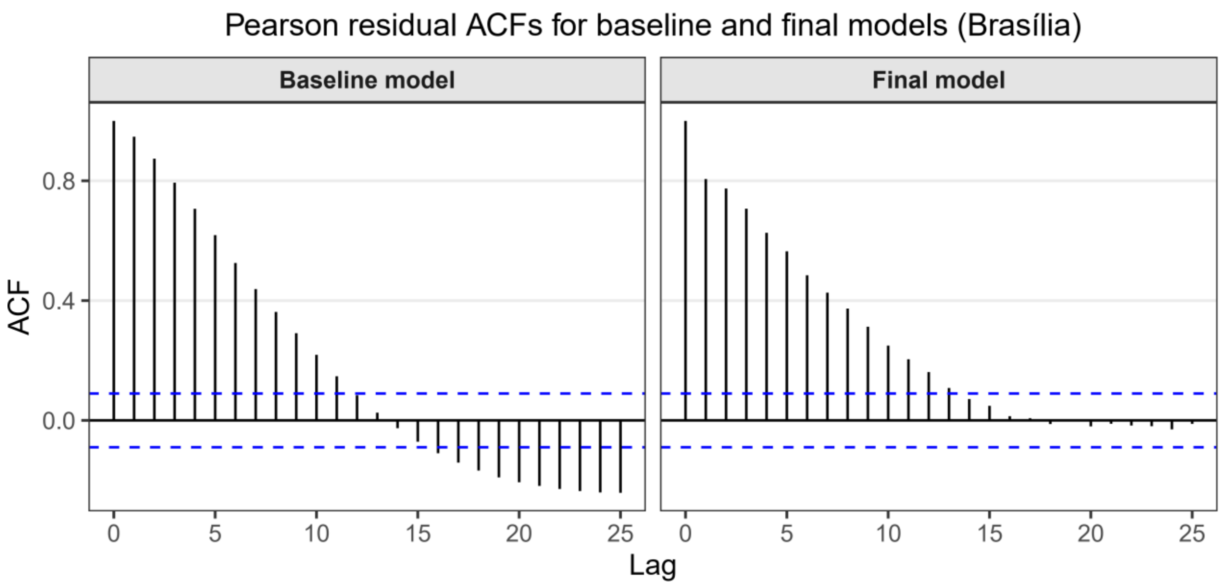
City	ITS model specification	AIC	BIC
Belo Horizonte	**Baseline model:** time + COVID + TimeSinceCOVID + Vaccine + TimeSinceVaccine + ClassResumption + TimeSinceClassResumption + Population offset	6,237	6,275
	Final model: baseline model + Lag1Outcome + Temperature lags (0–1) + WindSpeed lags (0–1) + 1 Fourier pair	5,512	5,578
Brasília	**Baseline model:** time + COVID + TimeSinceCOVID + Vaccine + TimeSinceVaccine + ClassResumption + TimeSinceClassResumption + Population offset	6,748	6,785
	Final model: baseline model + Outcome lags (1–4) + Temperature lags (0–1) + WindSpeed lags (0–1) + 1 Fourier pair	6,086	6,173
Campo Grande	**Baseline model:** time + COVID + TimeSinceCOVID + Vaccine + TimeSinceVaccine + ClassResumption + TimeSinceClassResumption + Population offset	5,684	5,721
	Final model: baseline model + Temperature + WindSpeed + Lag1Outcome	5,185	5,235
Fortaleza	**Baseline model:** time + COVID + TimeSinceCOVID + Vaccine + TimeSinceVaccine + ClassResumption + TimeSinceClassResumption + Population offset	6,058	6,096
	Final model: baseline model + Outcome lags (1–5) + Temperature lags (0–5)	5,539	5,618
Goiânia	**Baseline model:** time + COVID + TimeSinceCOVID + Vaccine + TimeSinceVaccine + ClassResumption + TimeSinceClassResumption + Population offset	6,950	6,987
	Final model: baseline model + Temperature + Outcome lags (1–5) + WindSpeed lags (0–1) + 1 Fourier pair	6,181	6,260
Natal	**Baseline model:** time + COVID + TimeSinceCOVID + Vaccine + TimeSinceVaccine + ClassResumption + TimeSinceClassResumption + Population offset	5,644	5,682
	Final model: baseline model + Outcome lags (1–2) + Temperature lags (0–2) + 2 Fourier pairs	4,910	4,985
Rio de Janeiro	**Baseline model:** time + COVID + TimeSinceCOVID + Vaccine + TimeSinceVaccine + ClassResumption + TimeSinceClassResumption + Population offset	5,683	5,721

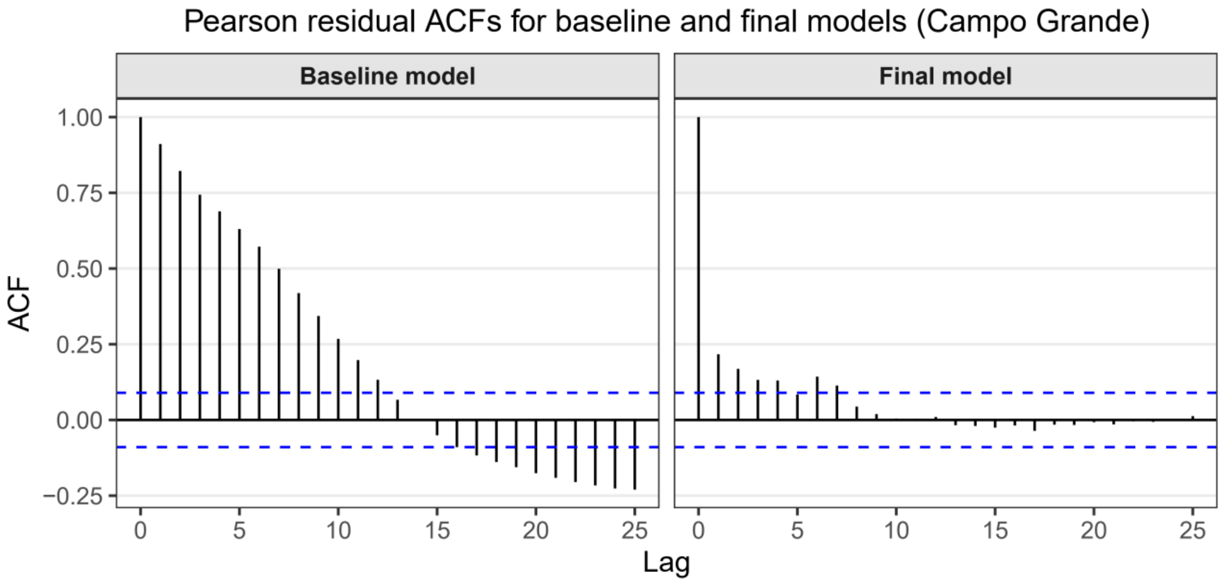
	Final model: baseline model + WindSpeed + Outcome lags (1–3) + Temperature lags (0–3) + 1 Fourier pair	4,952	5,031
Salvador	**Baseline model:** time + COVID + TimeSinceCOVID + Vaccine + TimeSinceVaccine + ClassResumption + TimeSinceClassResumption + Population offset	5,053	5,090
	Final model: baseline model + WindSpeed + Outcome lags (1–4) + Lag1Temperature	4,466	4,528
São Paulo	**Baseline model:** time + COVID + TimeSinceCOVID + Vaccine + TimeSinceVaccine + ClassResumption + TimeSinceClassResumption + Population offset	5,989	6,026
	Final model: baseline model + Outcome lags (1–4) + Temperature lags (0–1) + WindSpeed lags (0–2)	5,263	5,338
Teresina	**Baseline model:** time + COVID + TimeSinceCOVID + Vaccine + TimeSinceVaccine + ClassResumption + TimeSinceClassResumption + Population offset	4,900	4,937
	Final model: baseline model + Temperature + WindSpeed + Lag1Outcome + Lag1Temperature + Lag1WindSpeed + 1 Fourier pair	4,271	4,362

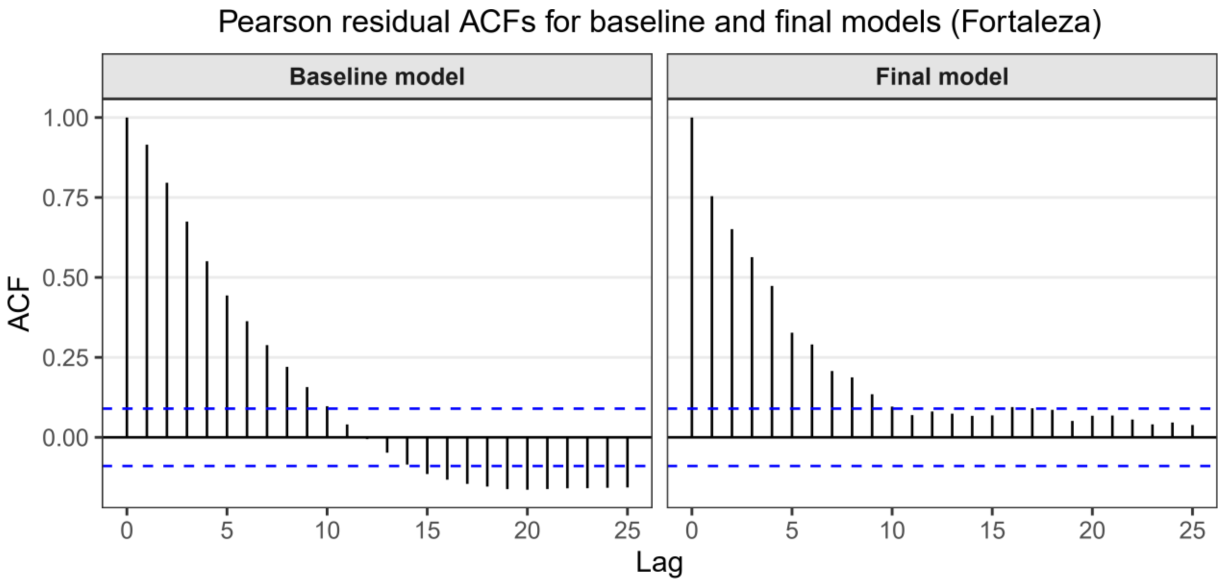
Across all cities, the final models demonstrated substantially improved fit relative to the baseline specifications, as indicated by consistently lower AIC and BIC values. These reductions in information criteria indicate that accounting for autoregressive terms, meteorological covariates, and seasonal Fourier components improved relative model fit while retaining the core intervention structure of the interrupted time-series analysis.

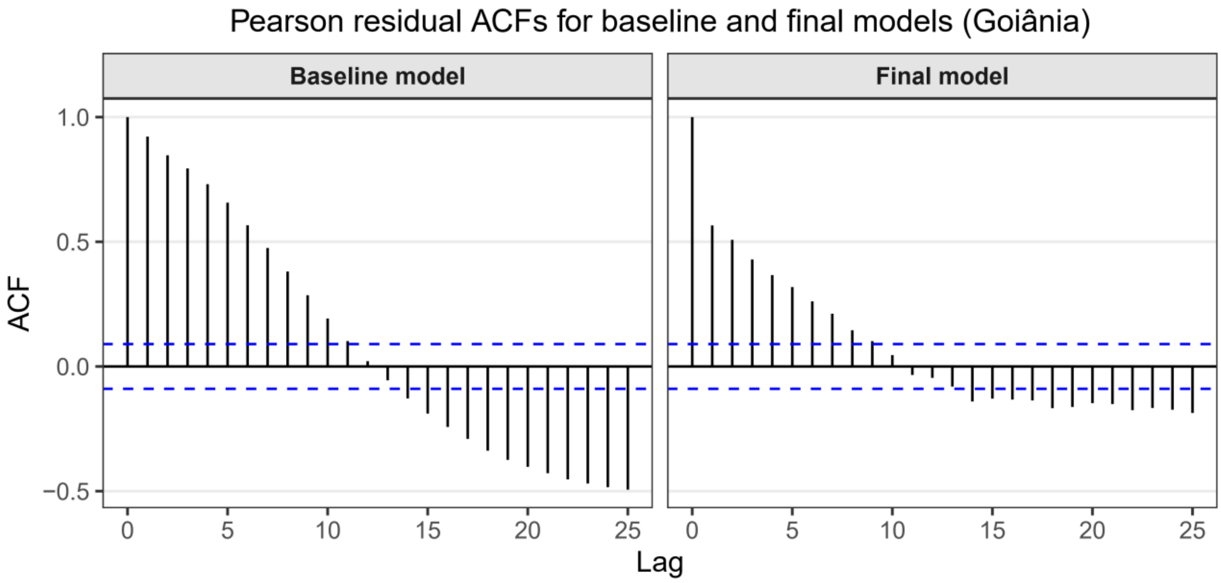
APPENDIX G – Autocorrelation functions (ACFs) of Pearson residuals from baseline and final negative binomial interrupted time-series models in ten major Brazilian cities, 2015–2023.



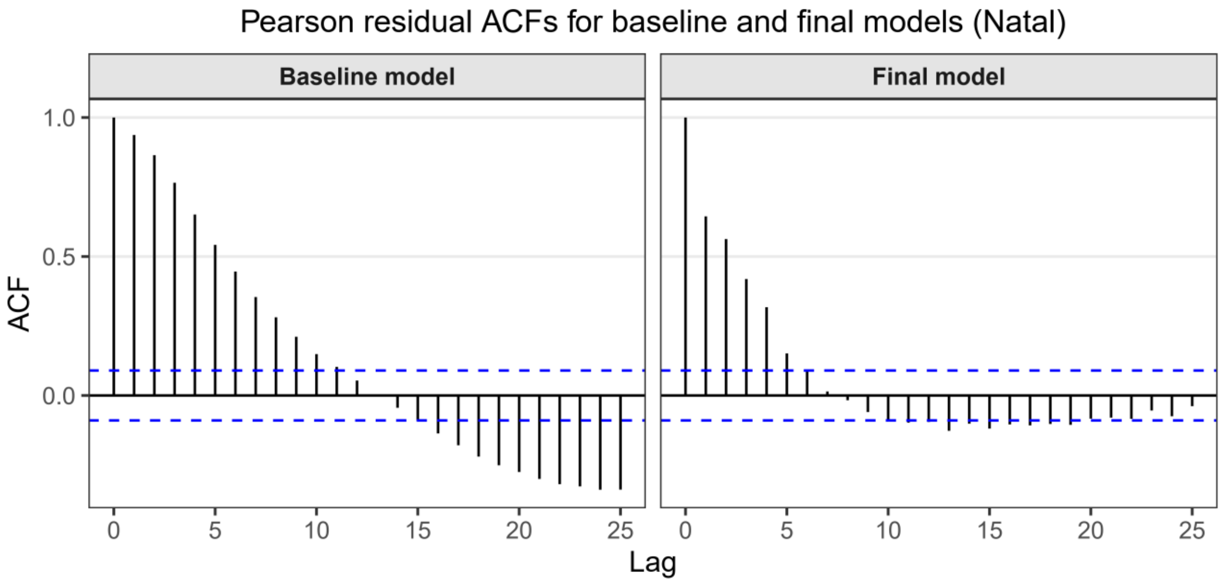



Pearson residual ACFs for baseline and final models (Campo Grande)
Baseline model
Final model
ACF
Lag
1.00
0.75
0.50
0.25
0.00
−0.25
0
5
10
15
20
25

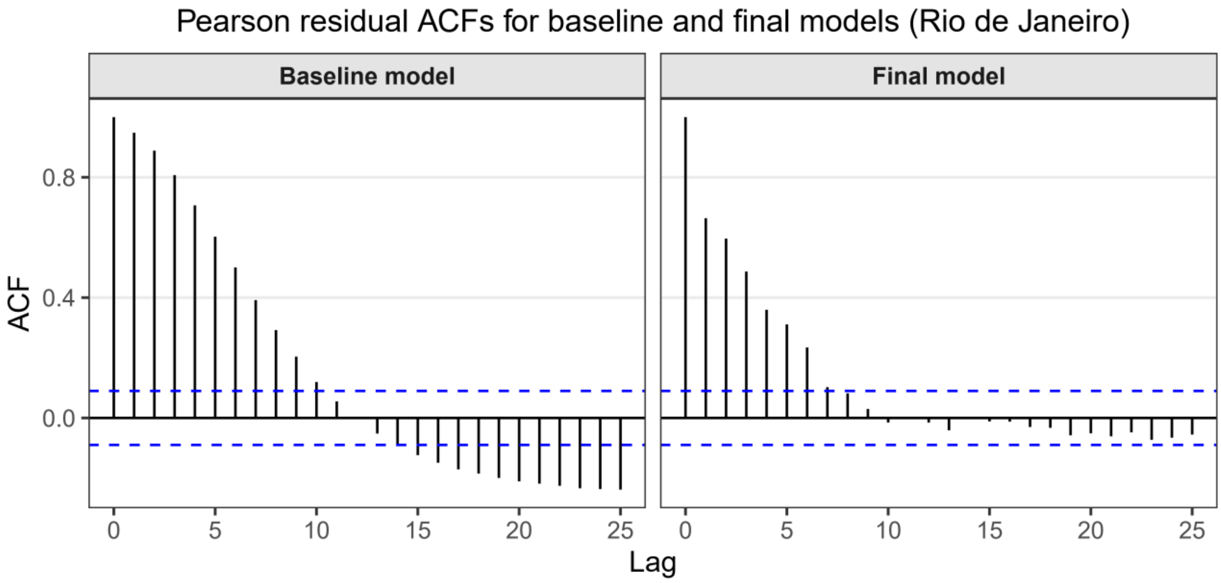

Pearson residual ACFs for baseline and final models (Fortaleza)
Baseline model
Final model
ACF
Lag
1.00
0.75
0.50
0.25
0.00
0
5
10
15
20
25

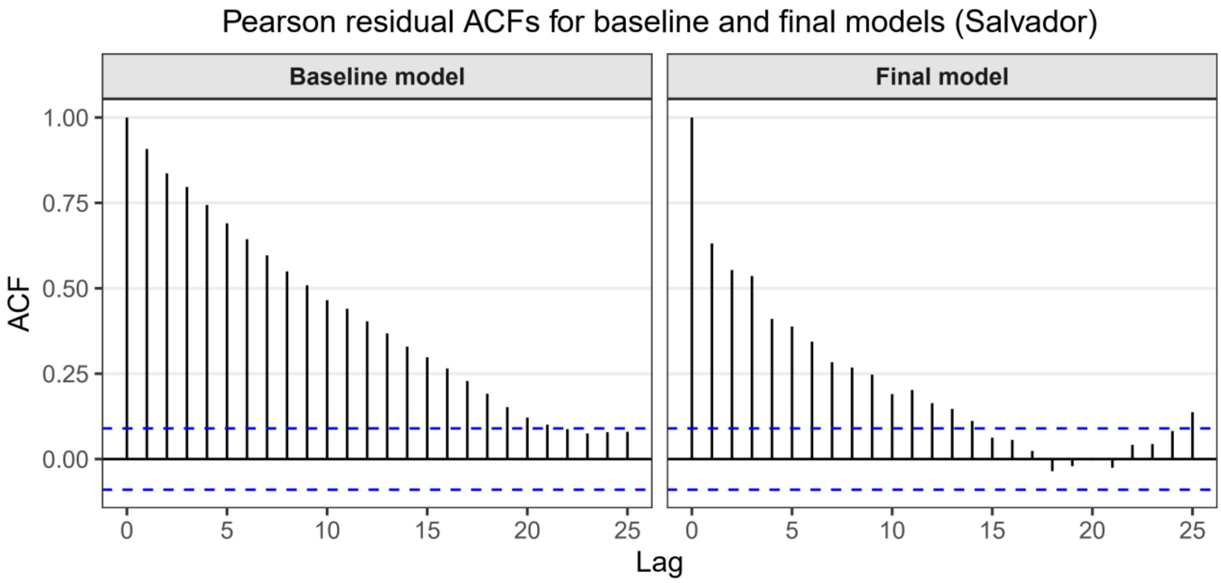


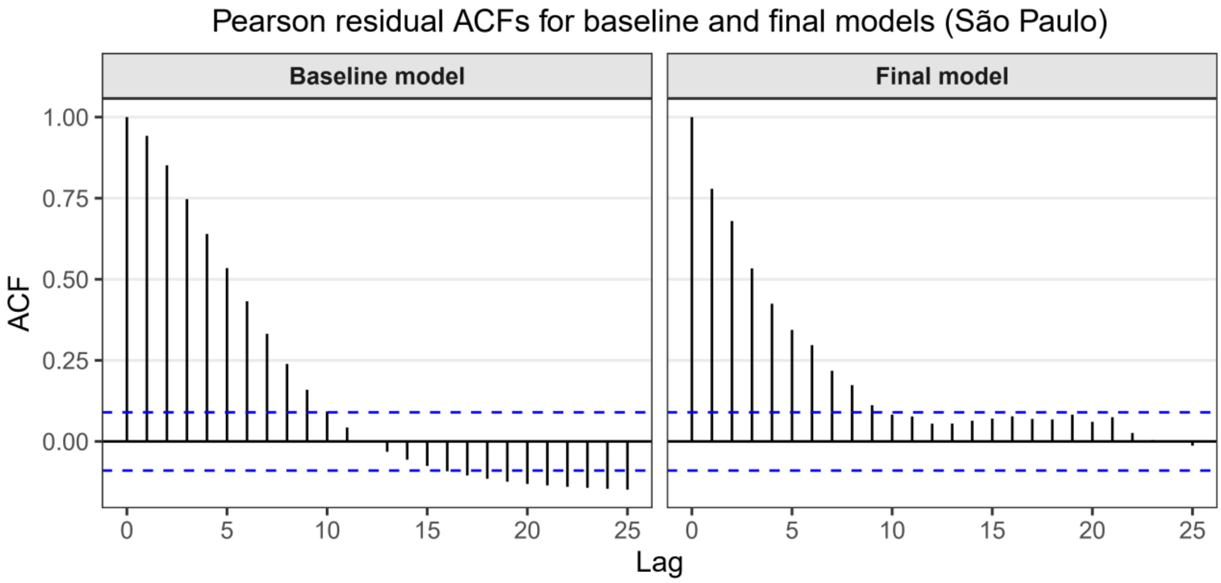
Pearson residual ACFs for baseline and final models (Goiânia)
Baseline model
Final model
ACF
1.0
0.5
0.0
−0.5
0
5
10
15
20
25
Lag

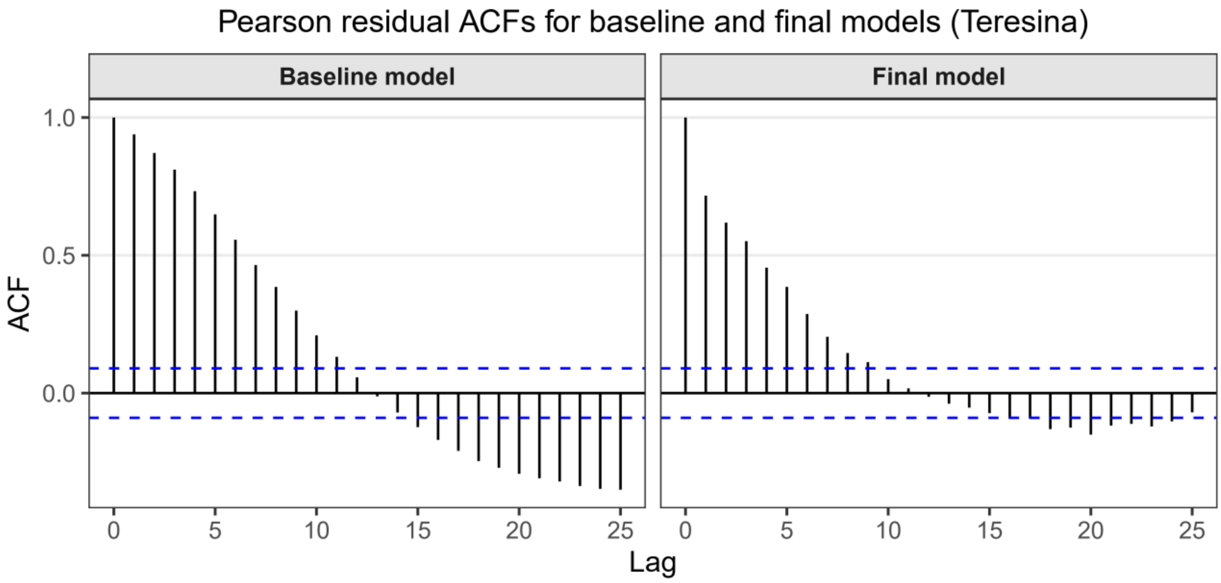


Pearson residual ACFs for baseline and final models (Natal)
Baseline model
Final model
ACF
1.0
0.5
0.0
0
5
10
15
20
25
Lag


Pearson residual ACFs for baseline and final models (Rio de Janeiro)
Baseline model
Final model
ACF
0.8
0.4
0.0
0
5
10
15
20
25
Lag

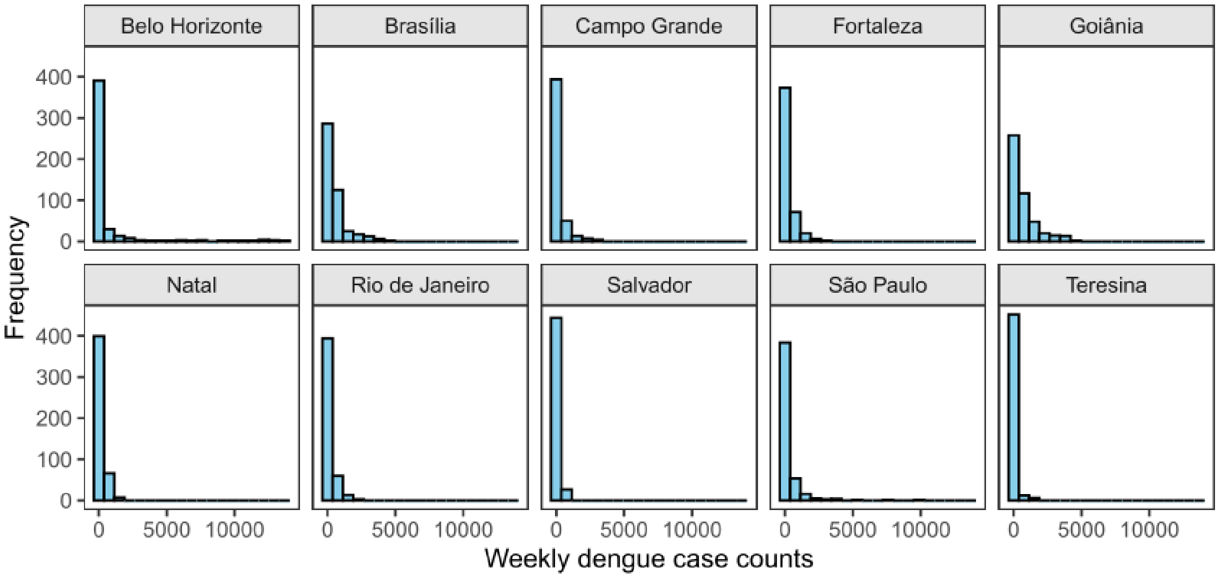

Pearson residual ACFs for baseline and final models (Salvador)
Baseline model
Final model
ACF
1.00
0.75
0.50
0.25
0.00
0
5
10
15
20
25
Lag



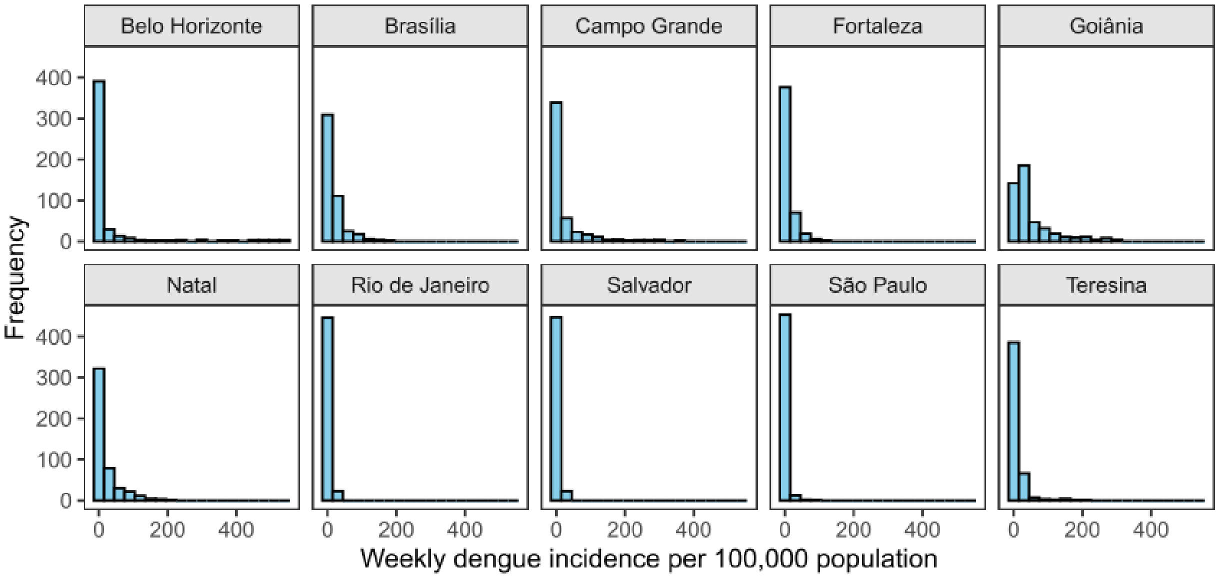


Residual ACFs indicated that the final interrupted time-series models improved in accounting for serial dependence in weekly dengue incidence through the inclusion of autoregressive terms, meteorological covariates, and seasonal Fourier components, although some residual autocorrelation persisted. Statistical inference therefore relied on Newey–West standard errors to account for remaining heteroskedasticity and serial correlation in the model residuals. Together, these diagnostics and robust variance estimators support valid statistical inference from the interrupted time-series analyses.

APPENDIX H – Distribution of weekly dengue case counts in ten major Brazilian cities, 2015–2023.



APPENDIX I – Distribution of weekly dengue incidence per 100,000 population in ten major Brazilian cities, 2015–2023.



The distributions of weekly dengue incidence in all ten cities are markedly right-skewed. This pronounced skewness and overdispersion (Appendix C) support the use of models such as the negative binomial for analyzing dengue incidence over time.

APPENDIX J – Pooled intervention effect estimates from main and complete-case interrupted time-series (ITS) analyses in ten major Brazilian cities, 2015–2023.

		Main ITS analysis				Complete-case ITS analysis			
Intervention	**Parameter**	**IRR (95% CI)**	**P value**	**I^2 (%)**	**τ^2**	**IRR (95% CI)**	**P value**	**I^2 (%)**	**τ^2**
COVID-19 pandemic	Immediate effect	1.08 (0.56–2.11)	0.814	87.6	0.985	1.08 (0.55–2.15)	0.821	88.1	1.052
	Weekly trend change	0.98 (0.97–0.996)	0.012	85.7	0.000	0.98 (0.96–0.997)	0.023	89.0	0.001
COVID-19 vaccination campaign	Immediate effect	1.05 (0.49–2.26)	0.906	91.3	1.355	1.08 (0.46–2.52)	0.856	92.9	1.678
	Weekly trend change	1.03 (1.01–1.05)	<0.001	74.6	0.001	1.03 (1.01–1.05)	0.001	76.7	0.001
Full resumption of in-person classes	Immediate effect	1.74 (0.90–3.37)	0.099	89.5	0.978	1.78 (0.95–3.35)	0.071	87.9	0.869
	Weekly trend change	0.99 (0.98–1.01)	0.338	83.7	0.000	0.99 (0.98–1.01)	0.425	83.4	0.000

Incidence rate ratios (IRRs) and 95% confidence intervals (CIs) were obtained from two-stage restricted maximum-likelihood random-effects meta-analyses pooling city-specific interrupted time-series estimates. Between-city heterogeneity was quantified using the I^2 index and τ^2, representing the proportion of total variation attributable to heterogeneity and the estimated between-city variance, respectively.