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Supplemental Material

Association between Heat Exposure and Hospitalization for Diabetes in Brazil during 2000–2015: A Nationwide Case-Crossover Study

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Table of Contents

Figure S2. The linearity of the relationship between daily mean temperature during the hot seasons and diabetes hospitalization at the national level, modelled by a distributed lag non-linear model with nature cubic spline of df=3 for both temperature and lag.

Figure S3. The lag pattern across 0-3 lag days of the association between heat exposure (every 5°C increase in daily mean temperature during the hot season) and diabetes hospitalization (odds ratios with 95% CI), stratified by sex and age group.

Figure S4. The lag pattern across 0-3 lag days of the association between heat exposure (every 5°C increase in daily mean temperature during the hot season) and diabetes hospitalization (odds ratios with 95% CI), stratified by regions.

Figure S5. The lag pattern across 0-3 lag days of the association between heat exposure (every 5°C increase in daily mean temperature during the hot season) and diabetes hospitalization (odds ratios with 95% CI), stratified by complications.

Figure S6. The association between heat exposure (every 5°C increase in daily mean temperature during the hot season) and diabetes hospitalization (odds ratios with 95% CI), stratified by diabetes subtype and by region.

Figure S7. The association between heat exposure (every 5°C increase in daily mean temperature during the hot season) and diabetes hospitalization (odds ratios with 95% CI), stratified by diabetes subtype and by complication.

Table S1. ICD-10 codes of different types of diabetes mellitus with different complications

	Type 1 diabetes mellitus	Type 2 diabetes mellitus	Malnutrition-related diabetes mellitus	Other specified diabetes mellitus	Unspecified diabetes mellitus
With coma	E10.0	E11.0	E12.0	E13.0	E14.0
With ketoacidosis	E10.1	E11.1	E12.1	E13.1	E14.1
With renal complications	E10.2	E11.2	E12.2	E13.2	E14.2
With ophthalmic complications	E10.3	E11.3	E12.3	E13.3	E14.3
With neurological complications	E10.4	E11.4	E12.4	E13.4	E14.4
With peripheral circulatory complications	E10.5	E11.5	E12.5	E13.5	E14.5
With other specified complications	E10.6	E11.6	E12.6	E13.6	E14.6
With multiple complications	E10.7	E11.7	E12.7	E13.7	E14.7
With unspecified complications	E10.8	E11.8	E12.8	E13.8	E14.8
Without complications	E10.9	E11.9	E12.9	E13.9	E14.9

Note: See https://icd.who.int/browse10/2016/en for detail

Table S2. Comparison of daily mean temperature between case days and controls days that included in analyses

Region	Daily mean temperature (℃), mean±sd		Student's t-test.	
	Case days	Control days	t	*P*-value
North	28.15±1.52	28.13±1.52	1.62	0.104
Northeast	27.35±1.84	27.33±1.84	2.39	0.017
Central west	25.74±2.45	25.70±2.47	3.75	<0.001
Southeast	24.62±2.30	24.57±2.32	8.73	<0.001
South	23.85±2.64	23.78±2.66	7.21	<0.001
Overall	25.44±2.65	25.40±2.67	9.51	<0.001

Note: sd, standard deviation.

Table S3. The association between heat exposure (every 5°C increase in daily mean temperature during the hot season) and diabetes hospitalization at lag0-3 days

	Odds ratio (95% CI) at different lag days			
Subgroup	**lag0**	**lag1**	**lag2**	**lag3**
Overall	1.08 (1.07, 1.10)	1.01 (1.00, 1.02)	0.98 (0.97, 0.99)	0.99 (0.98, 1.00)
Type of diabetes				
Type 1	1.08 (1.06, 1.10)	1.01 (1.00, 1.03)	0.98 (0.97, 1.00)	0.97 (0.95, 0.99)
Type 2	1.07 (1.02, 1.11)	1.01 (0.98, 1.05)	0.99 (0.97, 1.02)	1.00 (0.96, 1.04)
Malnutrition-related	1.19 (1.08, 1.32)	0.92 (0.85, 0.99)	0.92 (0.86, 0.98)	1.10 (1.00, 1.21)
Other specified	1.08 (1.03, 1.13)	1.03 (0.99, 1.07)	1.00 (0.97, 1.03)	0.99 (0.95, 1.03)
Unspecified	1.08 (1.07, 1.10)	1.00 (0.99, 1.01)	0.98 (0.97, 0.99)	0.99 (0.98, 1.01)
Sex				
Male	1.08 (1.06, 1.10)	1.01 (1.00, 1.02)	0.98 (0.97, 0.99)	0.99 (0.97, 1.00)
Female	1.09 (1.07, 1.11)	1.00 (0.99, 1.02)	0.98 (0.97, 0.99)	0.99 (0.97, 1.01)
Age group (years)				
0~19	1.00 (0.96, 1.05)	0.98 (0.95, 1.02)	0.99 (0.96, 1.02)	1.01 (0.97, 1.06)
20~39	1.03 (0.99, 1.06)	0.96 (0.94, 0.99)	0.97 (0.95, 0.99)	1.02 (0.98, 1.05)
40~59	1.08 (1.06, 1.11)	1.00 (0.98, 1.01)	0.97 (0.96, 0.98)	0.98 (0.96, 1.00)
60~79	1.10 (1.08, 1.12)	1.02 (1.01, 1.04)	0.99 (0.98, 1.00)	0.98 (0.96, 0.99)
≥80	1.13 (1.09, 1.18)	1.03 (1.00, 1.07)	1.00 (0.98, 1.03)	1.01 (0.97, 1.04)
Region				
North	1.08 (0.99, 1.18)	1.03 (0.96, 1.09)	0.99 (0.94, 1.05)	0.97 (0.89, 1.05)
Northeast	1.12 (1.08, 1.16)	1.00 (0.97, 1.02)	0.96 (0.94, 0.98)	0.98 (0.95, 1.02)
Central west	1.10 (1.06, 1.15)	1.00 (0.98, 1.03)	0.98 (0.96, 1.00)	1.00 (0.97, 1.04)
Southeast	1.08 (1.06, 1.09)	1.01 (0.99, 1.02)	0.98 (0.97, 0.99)	0.99 (0.97, 1.00)
South	1.08 (1.05, 1.10)	1.01 (1.00, 1.03)	0.99 (0.97, 1.00)	0.98 (0.96, 1.00)
Complications				
Without complication	1.12 (1.09, 1.15)	1.00 (0.98, 1.02)	0.97 (0.95, 0.99)	1.00 (0.97, 1.02)
Coma	1.10 (1.05, 1.16)	1.02 (0.99, 1.06)	0.99 (0.96, 1.02)	0.99 (0.95, 1.03)
Ketoacidosis	1.05 (1.00, 1.09)	1.00 (0.97, 1.03)	0.98 (0.95, 1.00)	0.98 (0.94, 1.02)
Peripheral circulatory complications	1.04 (1.00, 1.07)	1.00 (0.98, 1.03)	1.00 (0.98, 1.03)	1.03 (0.99, 1.06)
Other complications	1.08 (1.06, 1.10)	1.01 (1.00, 1.02)	0.98 (0.97, 0.99)	0.98 (0.97, 0.99)
With multiple complications	1.14 (1.06, 1.23)	1.03 (0.98, 1.09)	0.99 (0.94, 1.03)	0.98 (0.92, 1.05)

Notes: The odds ratios are for lag0-3 days and came from time-stratified case-crossover analyses modelled by conditional logistic regression with a cross-basis function for daily mean temperature. The model adjusted for public holiday. Hot season was the city-specific 4 adjacent hottest months and varied by city (e.g., Dec-Mar for São Paulo, Aug-Nov for Manaus).

Table S4. The association between heat exposure (every 5°C increase in daily mean temperature during the hot season) and diabetes hospitalization, stratified by diabetes subtypes, and by sex, age, region, and complications.

	Odds ratio (95% CI), by diabetes subtypes			
Subgroups	**Type 1**	**Type 2**	**Malnutrition-related and other specified**	**Unspecified**
Sex				
Female	1.05 (1.02, 1.08)	1.05 (0.99, 1.12)	1.08 (1.01, 1.15)	1.06 (1.03, 1.08)
Male	1.04 (1.01, 1.08)	1.10 (1.03, 1.18)	1.14 (1.06, 1.22)	1.05 (1.02, 1.07)
Age group (years)				
0~19	0.96 (0.89, 1.03)	1.14 (0.89, 1.46)	0.93 (0.75, 1.15)	1.00 (0.93, 1.08)
20~39	0.95 (0.89, 1.01)	0.95 (0.82, 1.10)	1.08 (0.93, 1.25)	0.98 (0.93, 1.03)
40~59	1.02 (0.98, 1.06)	1.06 (0.98, 1.14)	1.10 (1.02, 1.20)	1.03 (1.00, 1.06)
60~79	1.12 (1.08, 1.16)	1.11 (1.03, 1.19)	1.12 (1.04, 1.20)	1.06 (1.04, 1.09)
≥80	1.10 (1.02, 1.19)	1.07 (0.93, 1.25)	1.15 (0.98, 1.35)	1.25 (1.18, 1.32)
Region				
North	0.99 (0.78, 1.24)	1.17 (0.82, 1.66)	1.23 (0.91, 1.65)	1.03 (0.88, 1.22)
Northeast	1.07 (0.99, 1.16)	1.17 (0.98, 1.39)	1.13 (0.97, 1.33)	1.02 (0.97, 1.08)
Central west	1.09 (1.01, 1.17)	1.21 (1.04, 1.41)	1.05 (0.93, 1.19)	1.08 (1.01, 1.15)
Southeast	1.02 (0.99, 1.05)	1.05 (0.99, 1.12)	1.10 (1.02, 1.19)	1.06 (1.04, 1.09)
South	1.08 (1.04, 1.13)	1.04 (0.95, 1.14)	1.11 (1.03, 1.19)	1.03 (1.00, 1.07)
Complications				
Without complication	1.07 (0.99, 1.15)	0.99 (0.87, 1.12)	1.14 (1.04, 1.25)	1.08 (1.04, 1.12)
Coma	1.14 (1.08, 1.21)	0.97 (0.79, 1.19)	1.15 (0.85, 1.55)	1.02 (0.91, 1.14)
Ketoacidosis	0.97 (0.91, 1.03)	0.95 (0.84, 1.09)	1.16 (0.93, 1.43)	1.07 (0.97, 1.17)
Peripheral circulatory complications	1.05 (0.98, 1.12)	1.16 (1.03, 1.31)	1.03 (0.90, 1.18)	1.08 (1.02, 1.14)
Other complications	1.03 (1.00, 1.06)	1.11 (1.04, 1.18)	1.10 (1.03, 1.17)	1.04 (1.02, 1.06)
With multiple complications	1.17 (1.05, 1.30)	1.10 (0.92, 1.32)	1.00 (0.68, 1.46)	1.13 (0.97, 1.32)

Notes: The odds ratios represent the cumulative association over lag0-3 days and came from time-stratified case-crossover analyses modelled by conditional logistic regression with a cross-basis function for daily mean temperature. The model adjusted for public holiday. Hot season was the city-specific 4 adjacent hottest months and varied by city (e.g., Dec-Mar for São Paulo, Aug-Nov for Manaus).

Table S5. Results of sensitivity analysis by changing maximum lag of daily mean temperature from three to seven days and df of lag days from three to four.

Model	Odds ratio (95% CI)	*p*-values for difference*
All diabetes mellitus combined		
Primary	1.06(1.04, 1.07)	Ref
Lag 0-4 days	1.05(1.04, 1.06)	0.517
Lag 0-5 days	1.04(1.03, 1.06)	0.258
Lag 0-6 days	1.04(1.02, 1.06)	0.118
Lag 0-7 days	1.03(1.01, 1.05)	0.024
Df of lag days = 4	1.06(1.04, 1.07)	0.983
Type 1 diabetes mellitus		
Primary	1.05(1.02, 1.07)	Ref
Lag 0-4 days	1.04(1.01, 1.06)	0.402
Lag 0-5 days	1.03(1.01, 1.06)	0.161
Lag 0-6 days	1.03(1.01, 1.06)	0.503
Lag 0-7 days	1.03(1.00, 1.06)	0.477
Df of lag days = 4	1.05(1.02, 1.07)	0.980
Type 2 diabetes mellitus		
Primary	1.07(1.02, 1.12)	Ref
Lag 0-4 days	1.07(1.02, 1.12)	0.395
Lag 0-5 days	1.05(1.00, 1.11)	0.139
Lag 0-6 days	1.05(0.99, 1.11)	0.575
Lag 0-7 days	1.05(0.99, 1.11)	0.525
Df of lag days = 4	1.07(1.02, 1.12)	0.982
Malnutrition-related diabetes mellitus		
Primary	1.11(1.00, 1.24)	Ref
Lag 0-4 days	1.11(0.98, 1.24)	0.394
Lag 0-5 days	1.10(0.97, 1.25)	0.138
Lag 0-6 days	1.08(0.94, 1.23)	0.711
Lag 0-7 days	1.05(0.91, 1.21)	0.493
Df of lag days = 4	1.11(1.00, 1.24)	0.982
Other specified diabetes mellitus		
Primary	1.10(1.04, 1.16)	Ref
Lag 0-4 days	1.12(1.06, 1.18)	0.452
Lag 0-5 days	1.13(1.07, 1.20)	0.192
Lag 0-6 days	1.12(1.05, 1.19)	0.713
Lag 0-7 days	1.10(1.03, 1.17)	0.963
Df of lag days = 4	1.10(1.04, 1.16)	0.983
Unspecified diabetes mellitus		
Primary	1.05(1.04, 1.07)	Ref
Lag 0-4 days	1.05(1.03, 1.07)	0.360
Lag 0-5 days	1.04(1.02, 1.06)	0.110
Lag 0-6 days	1.03(1.01, 1.05)	0.141
Lag 0-7 days	1.02(1.00, 1.04)	0.030
Df of lag days = 4	1.05(1.03, 1.07)	0.976

Note: Odds ratios represent the cumulative association between every 5°C increase in daily mean temperature over lag 0-3 days and diabetes hospitalization during hot season. The odds ratios came from time-stratified case-crossover analyses modelled by conditional logistic regression with a cross-basis function for daily mean temperature. The model adjusted for public holiday. Hot season was the city-specific 4 adjacent hottest months and varied by city (e.g., Dec-Mar for São Paulo, Aug-Nov for Manaus). *p*-values for difference testing the difference between different models were estimated by meta-regression.

Table S6. Results of sensitivity analysis by adjusting for relative humidity using data of 193 cities.

Model	Odds ratio(95% CI)	*p*-value for difference*
All diabetes mellitus combined		
Primary	1.03(1.01, 1.06)	Ref
Adjusted for humidity	1.03(1.00, 1.05)	0.751
Type 1 diabetes mellitus		
Primary	1.03(0.99, 1.08)	Ref
Adjusted for humidity	1.03(0.98, 1.07)	0.696
Type 2 diabetes mellitus		
Primary	1.04(0.95, 1.13)	Ref
Adjusted for humidity	1.03(0.95, 1.13)	0.694
Malnutrition-related diabetes mellitus		
Primary	0.99(0.78, 1.24)	Ref
Adjusted for humidity	0.97(0.77, 1.23)	0.690
Other specified diabetes mellitus		
Primary	1.03(0.92, 1.15)	Ref
Adjusted for humidity	1.04(0.93, 1.16)	0.713
Unspecified diabetes mellitus		
Primary	1.03(1.00, 1.06)	Ref
Adjusted for humidity	1.02(0.99, 1.06)	0.663

Note: Odds ratios represent the cumulative association between every 5°C increase in daily mean temperature and diabetes hospitalization during the hot season. The odds ratios came from time-stratified case-crossover analyses modelled by conditional logistic regression with a cross-basis function for daily mean temperature. The model adjusted for public holiday and relative humidity. We adjusted for relative humidity by adding the average relative humidity in lag 0-3 days using natural cubic spline with three degrees of freedom (df=3). *P*-values testing the difference between different models were estimated by meta-regression. Hot season was the city-specific 4 adjacent hottest months and varied by city (e.g., Dec-Mar for São Paulo, Aug-Nov for Manaus).

Table S7. Sensitivity analyses by changing the definition of hot season

Hot season definition	No. of cases	Odds ratio (95%CI)	*p*-value for difference
4 adjacent hottest months	553,351	1.06 (1.04, 1.07)	Ref
5 adjacent hottest months	689,272	1.05 (1.04, 1.06)	0.656
6 adjacent hottest months	827,232	1.05 (1.04, 1.06)	0.850

Note: Odds ratios represent the cumulative association between every 5°C increase in daily mean temperature during the hot season and hospitalization for diabetes over lag 0-3 days. The odds ratios came from time-stratified case-crossover analyses modelled by conditional logistic regression with a cross-basis function for daily mean temperature. The model adjusted for public holiday. *p*-value for difference were estimated by meta-regression. The exact calendar months of hot season varied by city (e.g., Dec-Mar for São Paulo, Aug-Nov for Manaus, when using the first definition).

Table S8. The association between temperature and hospitalization for diabetes in different seasons.

Season	No. of cases	Odds ratio (95%CI)	*p*-value for difference
Hot	553,351	1.06 (1.04, 1.07)	Ref
Moderate	551,446	1.04 (1.03, 1.05)	0.169
Cold	558,594	1.02 (1.01, 1.03)	<0.001

Note: Odds ratios represent the cumulative association between every 5°C increase in daily mean temperature and hospitalization for diabetes over lag0-3 days. The odds ratios came from time-stratified case-crossover analyses modelled by conditional logistic regression with a cross-basis function for daily mean temperature. The model adjusted for public holiday. *p*-value for difference were estimated by meta-regression. Hot season was the city-specific 4 adjacent hottest months and varied by city (e.g., Dec-Mar for São Paulo, Aug-Nov for Manaus); cold season was the city-specific 4 coldest months; the city-specific remained months were categorized as moderate season.

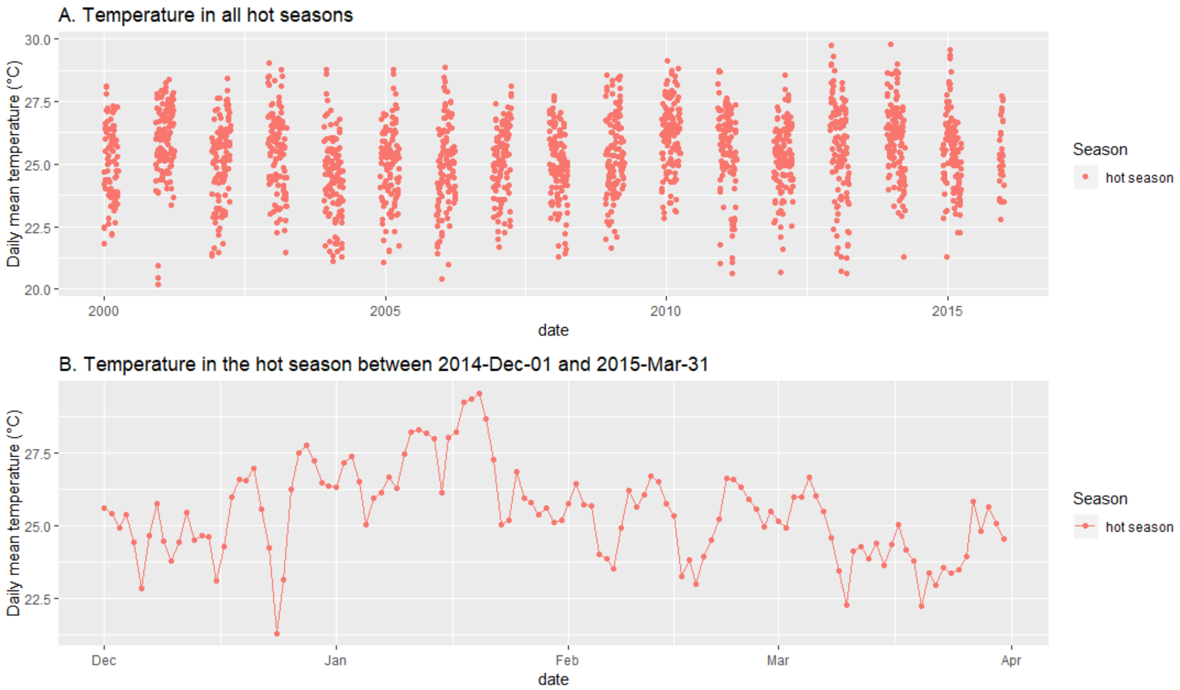

Figure S1. Time-series plot of daily mean temperature in a selected city (São Joaquim) during the hot season between 2000 and 2015.

Notes: the city (São Joaquim) selected for this figure is the city with median standard deviation of daily mean temperature during the study period. Hot season was defined as the city-specific adjacent four hottest months.

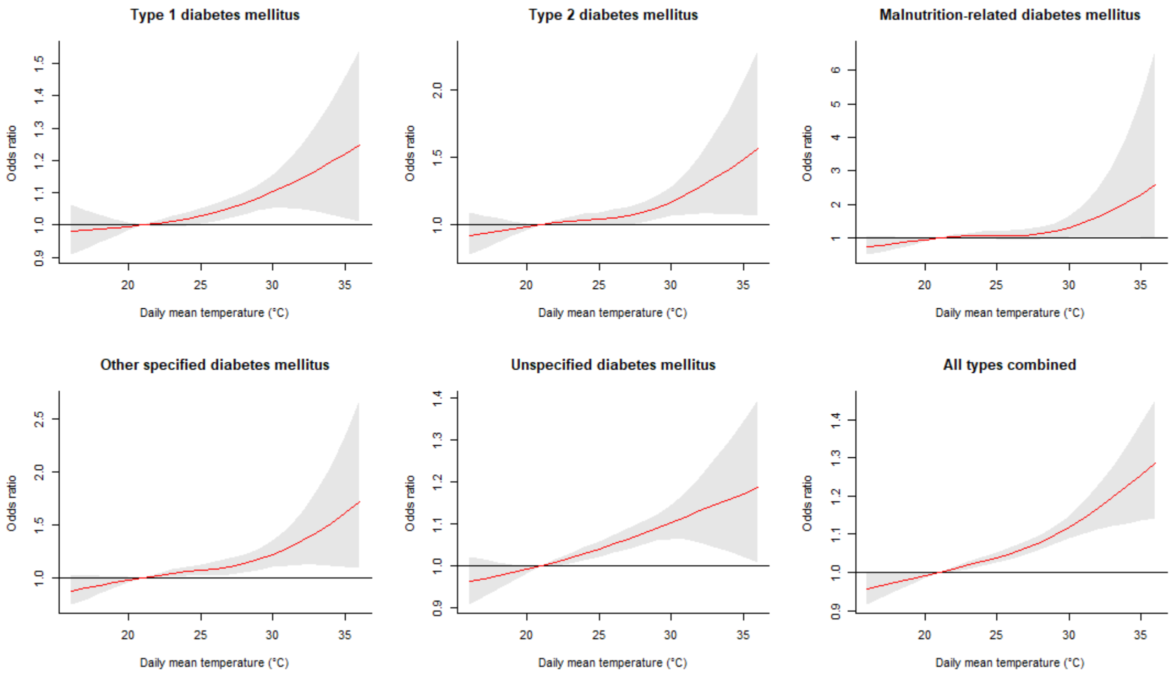

Figure S2. The linearity of the relationship between daily mean temperature during the hot seasons and diabetes hospitalization at the national level, modelled by a distributed lag non-linear model with nature cubic spline of df=3 for both temperature and lag.

Notes: Hot season was defined as the city-specific adjacent four hottest months and varied by city (e.g., Dec-Mar for São Paulo, Aug-Nov for Manaus). The solid lines represent the point estimates of odds ratio, and the shaded areas represent the 95% confidence interval (CI).

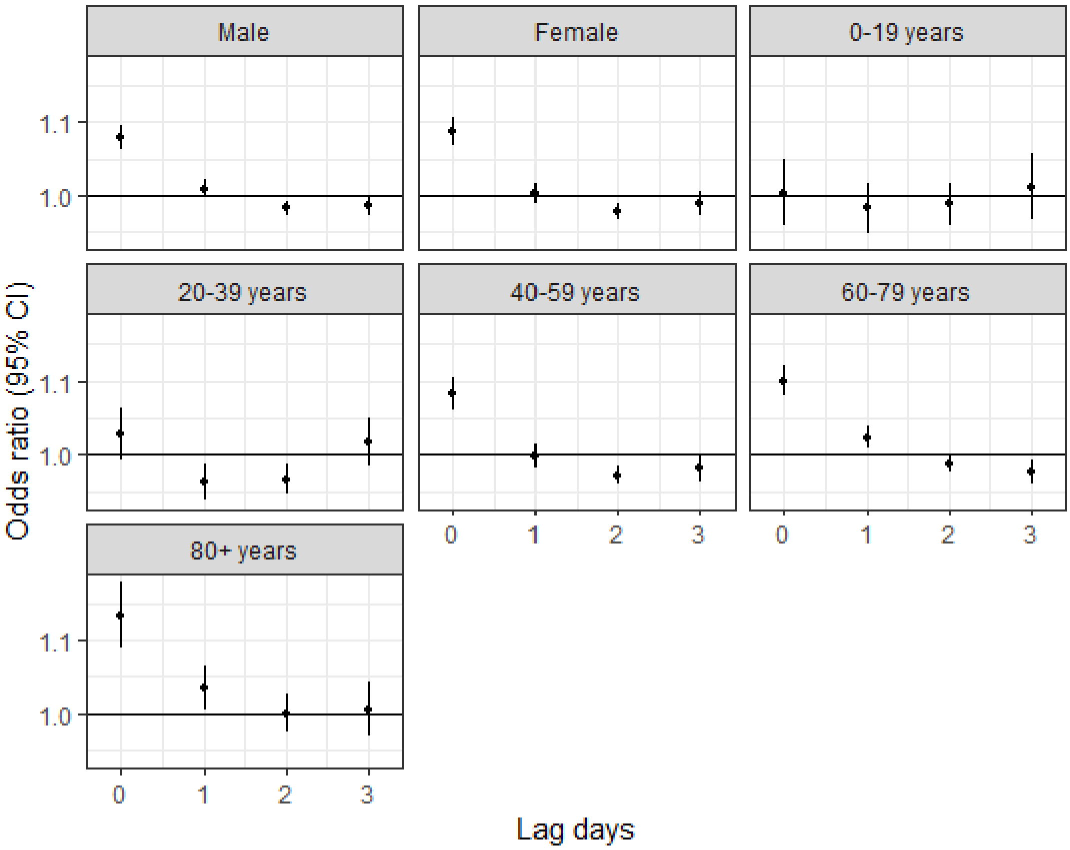

Figure S3. The lag pattern across 0-3 lag days of the association between heat exposure (every 5°C increase in daily mean temperature during the hot season) and diabetes hospitalization (odds ratios with 95% CI), stratified by sex and age group.

Notes: Hot season was defined as the city-specific adjacent four hottest months and varied by city (e.g., Dec-Mar for São Paulo, Aug-Nov for Manaus). The odds ratios were for lag0-3 days and came from time-stratified case-crossover analyses modelled by conditional logistic regression with a cross-basis function for daily mean temperature. The model adjusted for public holiday. Corresponding numeric data are provided in Table S3.

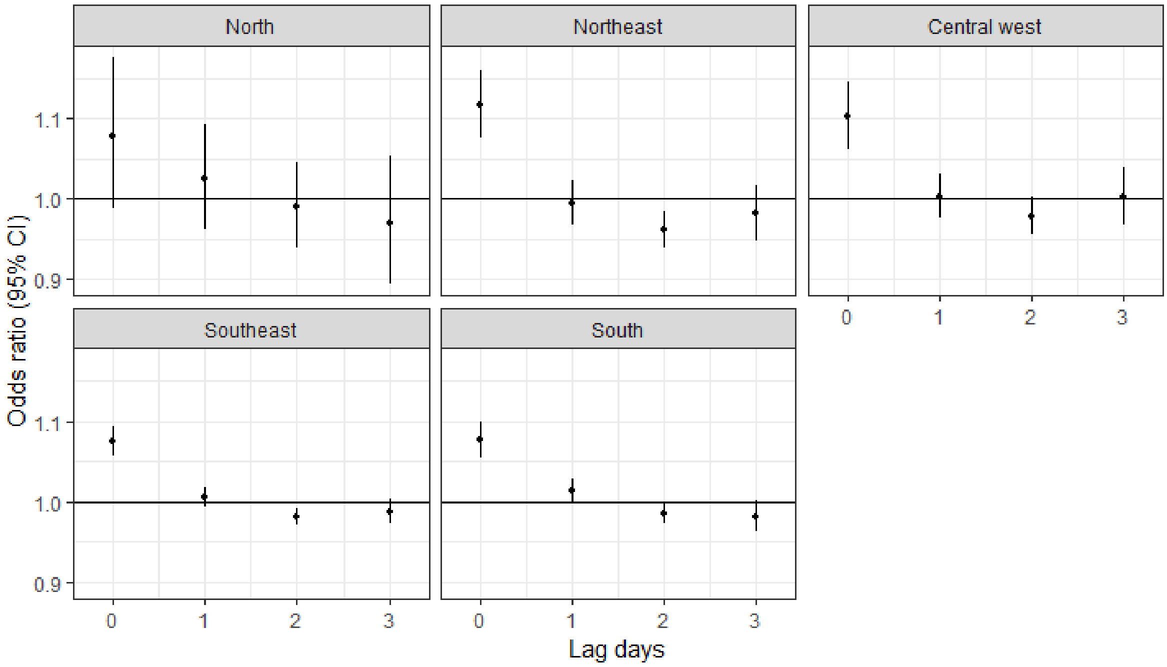

Figure S4. The lag pattern across 0-3 lag days of the association between heat exposure (every 5°C increase in daily mean temperature during the hot season) and diabetes hospitalization (odds ratios with 95% CI), stratified by regions.

Notes: Hot season was defined as the city-specific adjacent four hottest months and varied by city (e.g., Dec-Mar for São Paulo, Aug-Nov for Manaus). The odds ratios were for lag0-3 days and came from time-stratified case-crossover analyses modelled by conditional logistic regression with a cross-basis function for daily mean temperature. The model adjusted for public holiday. Corresponding numeric data are provided in Table S3.

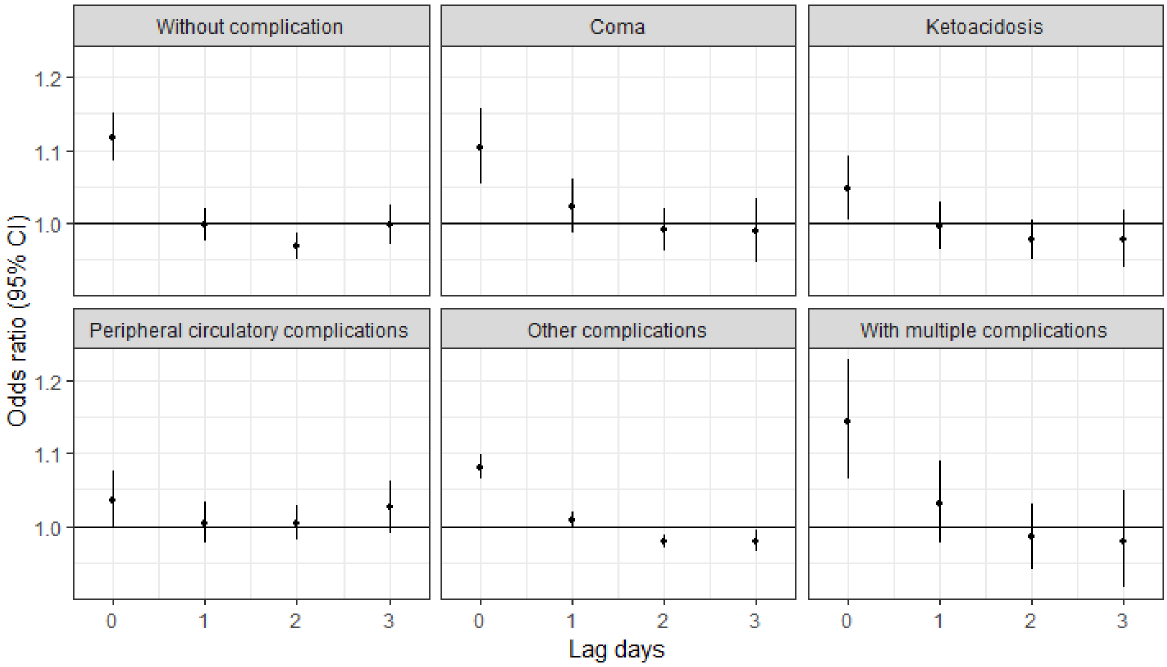

Figure S5. The lag pattern across 0-3 lag days of the association between heat exposure (every 5°C increase in daily mean temperature during the hot season) and diabetes hospitalization (odds ratios with 95% CI), stratified by complications.

Notes: Hot season was defined as the city-specific adjacent four hottest months and varied by city (e.g., Dec-Mar for São Paulo, Aug-Nov for Manaus). The odds ratios were for lag0-3 days and came from time-stratified case-crossover analyses modelled by conditional logistic regression with a cross-basis function for daily mean temperature. The model adjusted for public holiday. Corresponding numeric data are provided in Table S3.

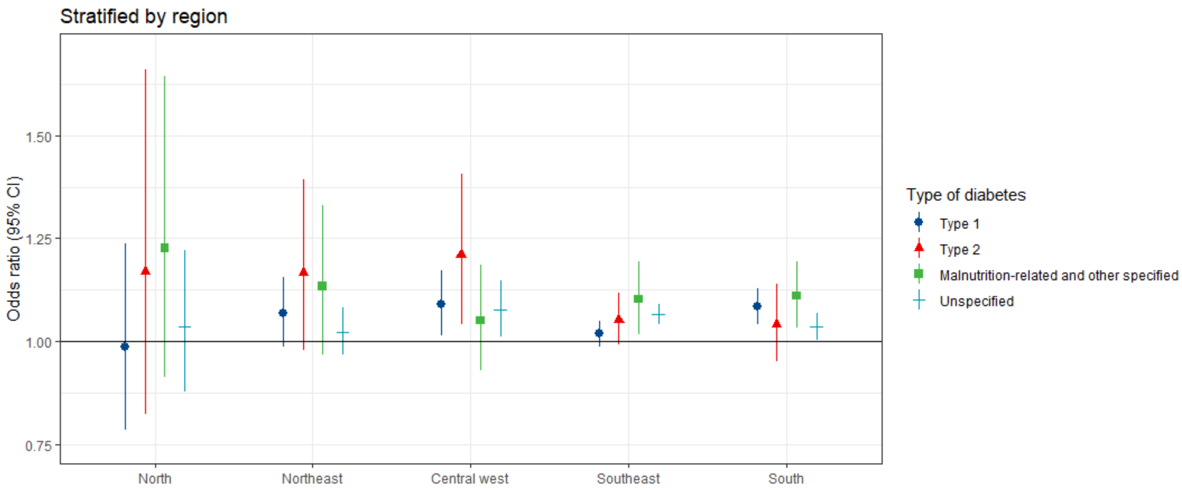

Figure S6. The association between heat exposure (every 5°C increase in daily mean temperature during the hot season) and diabetes hospitalization (odds ratios with 95% CI), stratified by diabetes subtype and by region.

Notes: Hot season was defined as the city-specific adjacent four hottest months and varied by city (e.g., Dec-Mar for São Paulo, Aug-Nov for Manaus). The odds ratios represent the cumulative associations over lag0-3 days and came from time-stratified case-crossover analyses modelled by conditional logistic regression with a cross-basis function for daily mean temperature. The model adjusted for public holiday. Corresponding numeric data are provided in Table S4.

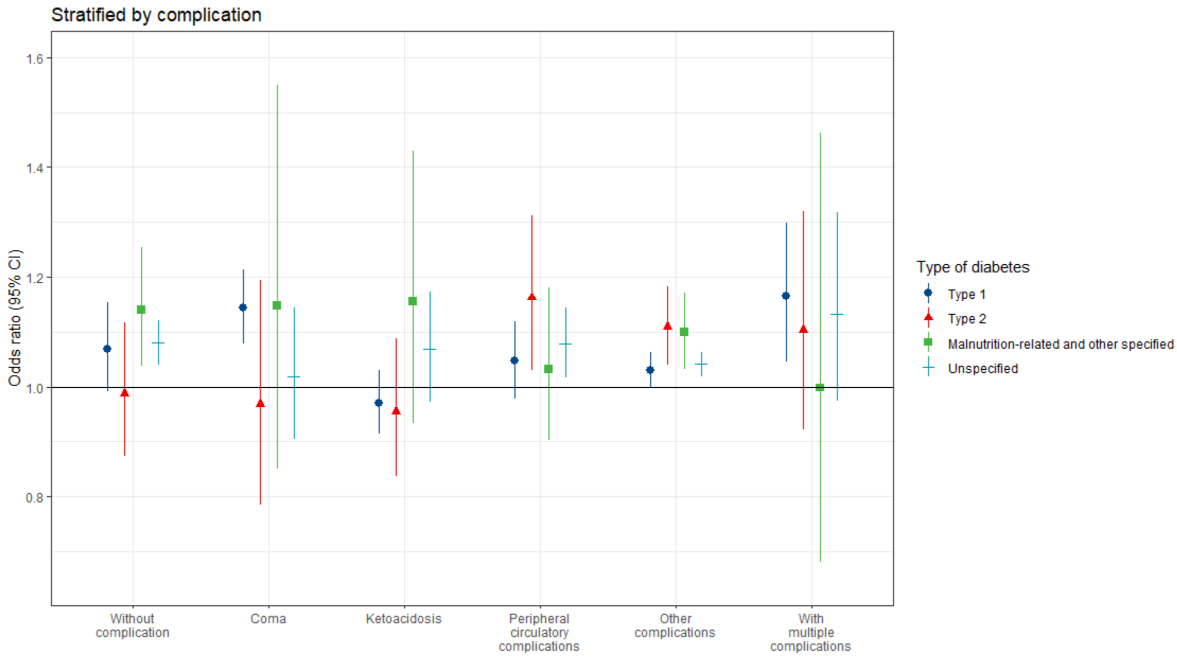

Figure S7. The association between heat exposure (every 5°C increase in daily mean temperature during the hot season) and diabetes hospitalization (odds ratios with 95% CI), stratified by diabetes subtype and by complication.

Notes: Hot season was defined as the city-specific adjacent four hottest months and varied by city (e.g., Dec-Mar for São Paulo, Aug-Nov for Manaus). The odds ratios represent the cumulative associations over lag0-3 days and came from time-stratified case-crossover analyses modelled by conditional logistic regression with a cross-basis function for daily mean temperature. The model adjusted for public holiday. Corresponding numeric data are provided in Table S4.