Supplementary Information

Temperature–brucellosis associations in China, 2005–2020: limited evidence for modification by rural depopulation

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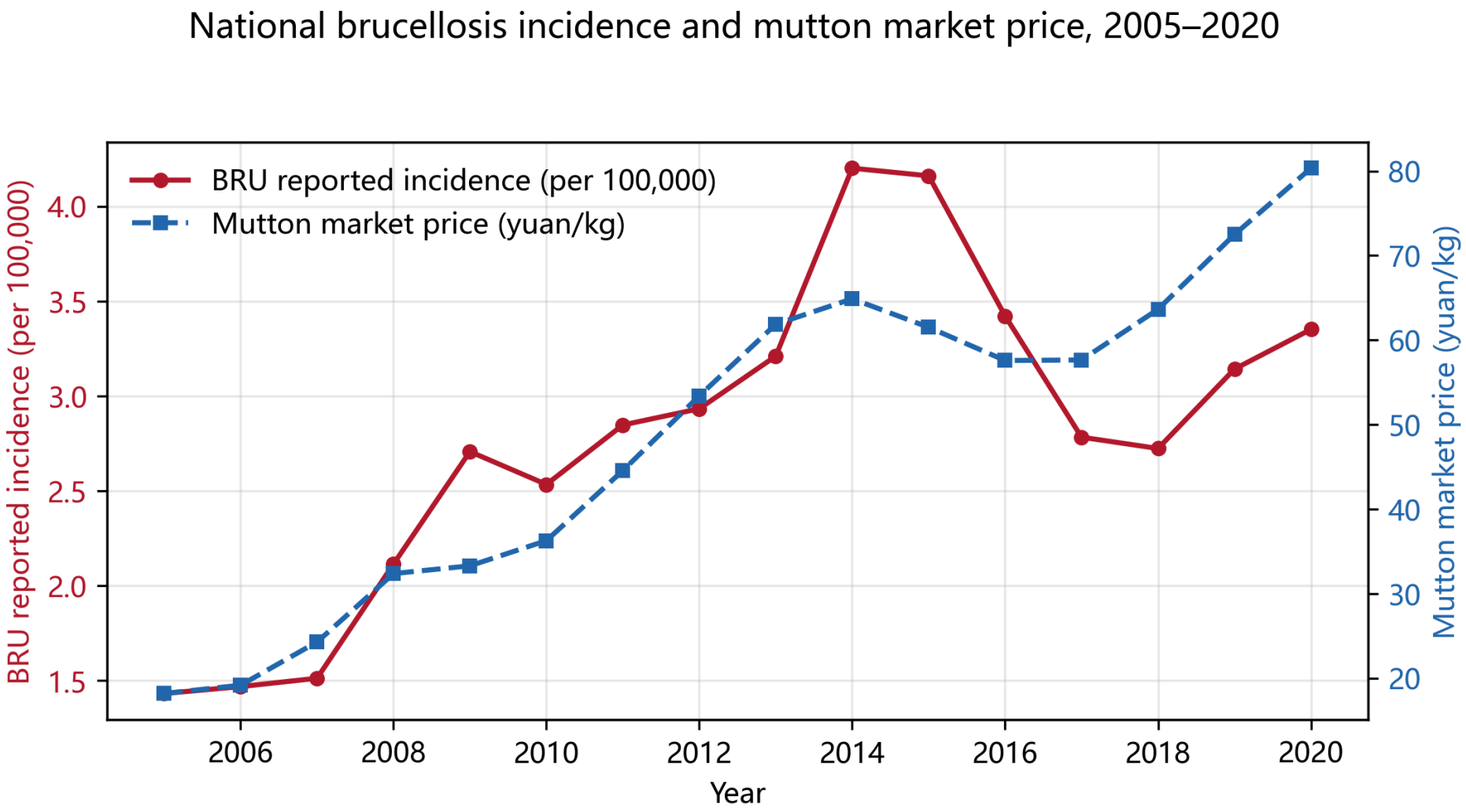
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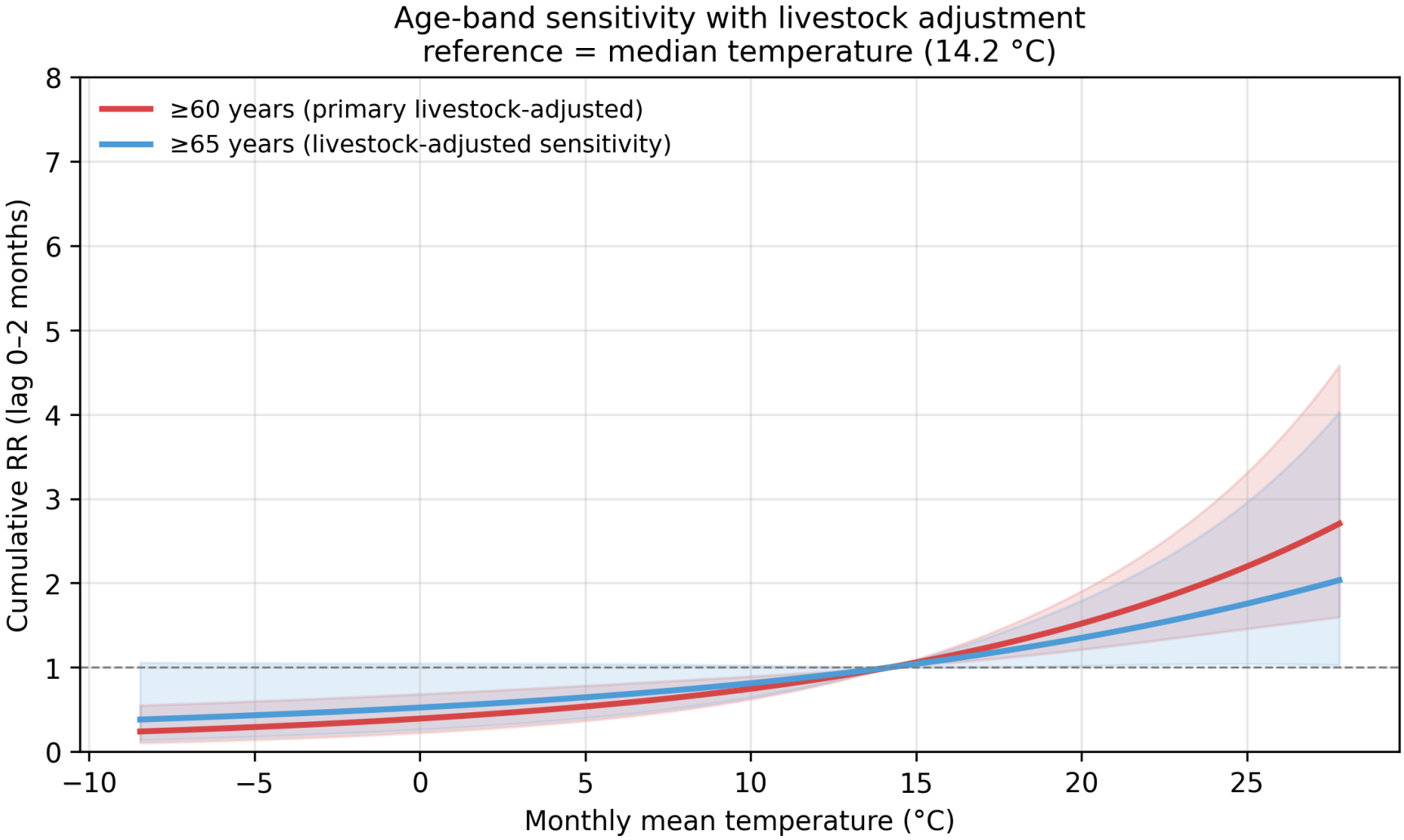
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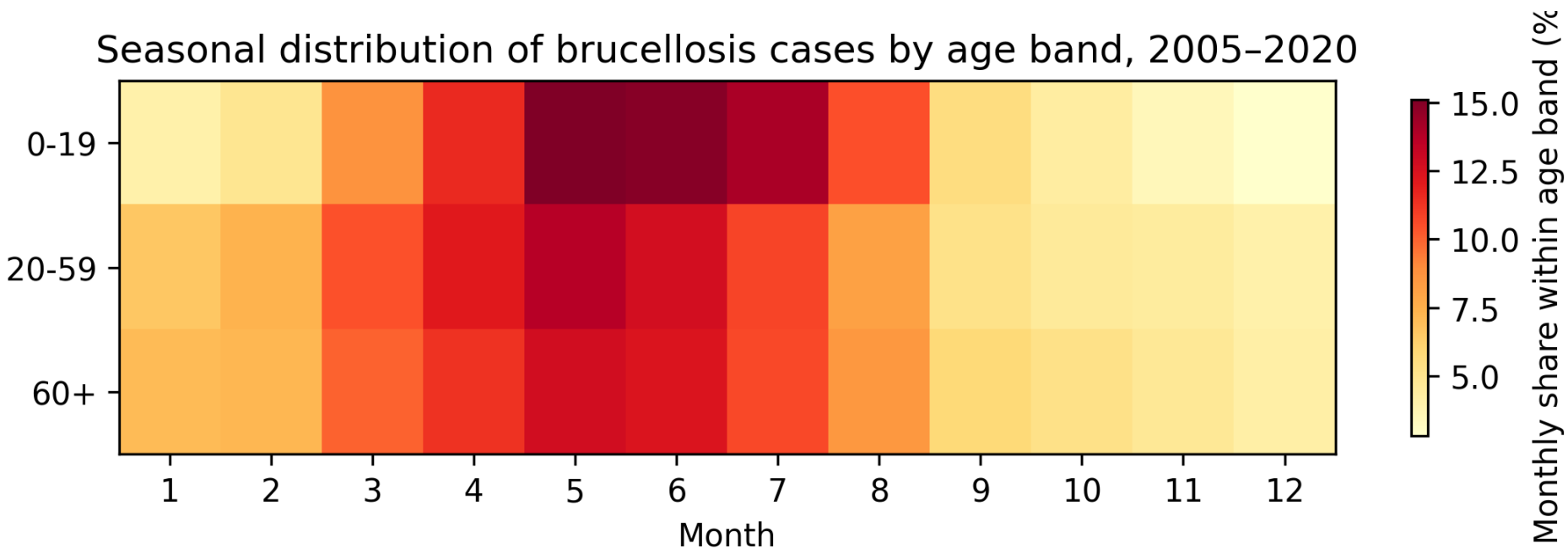
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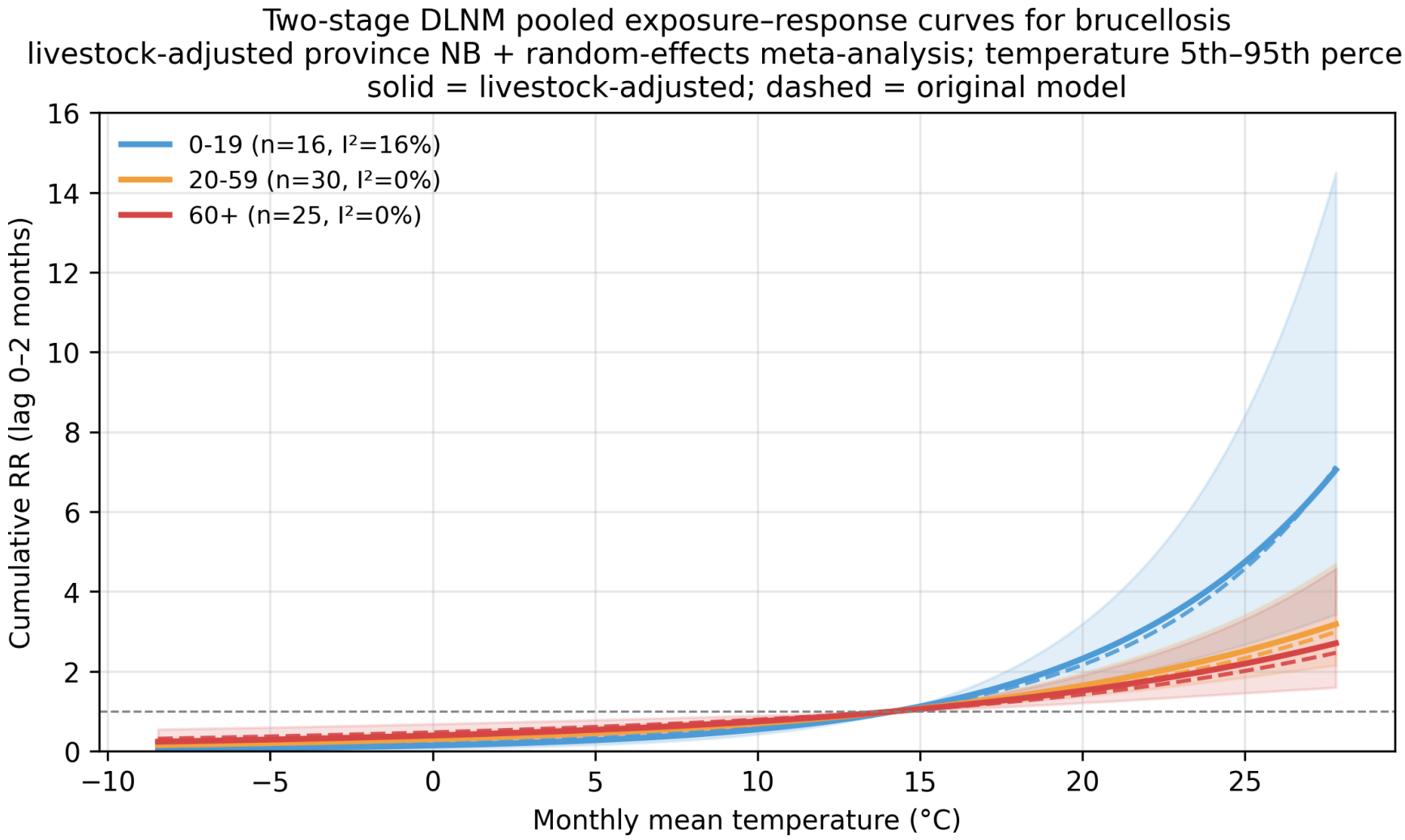
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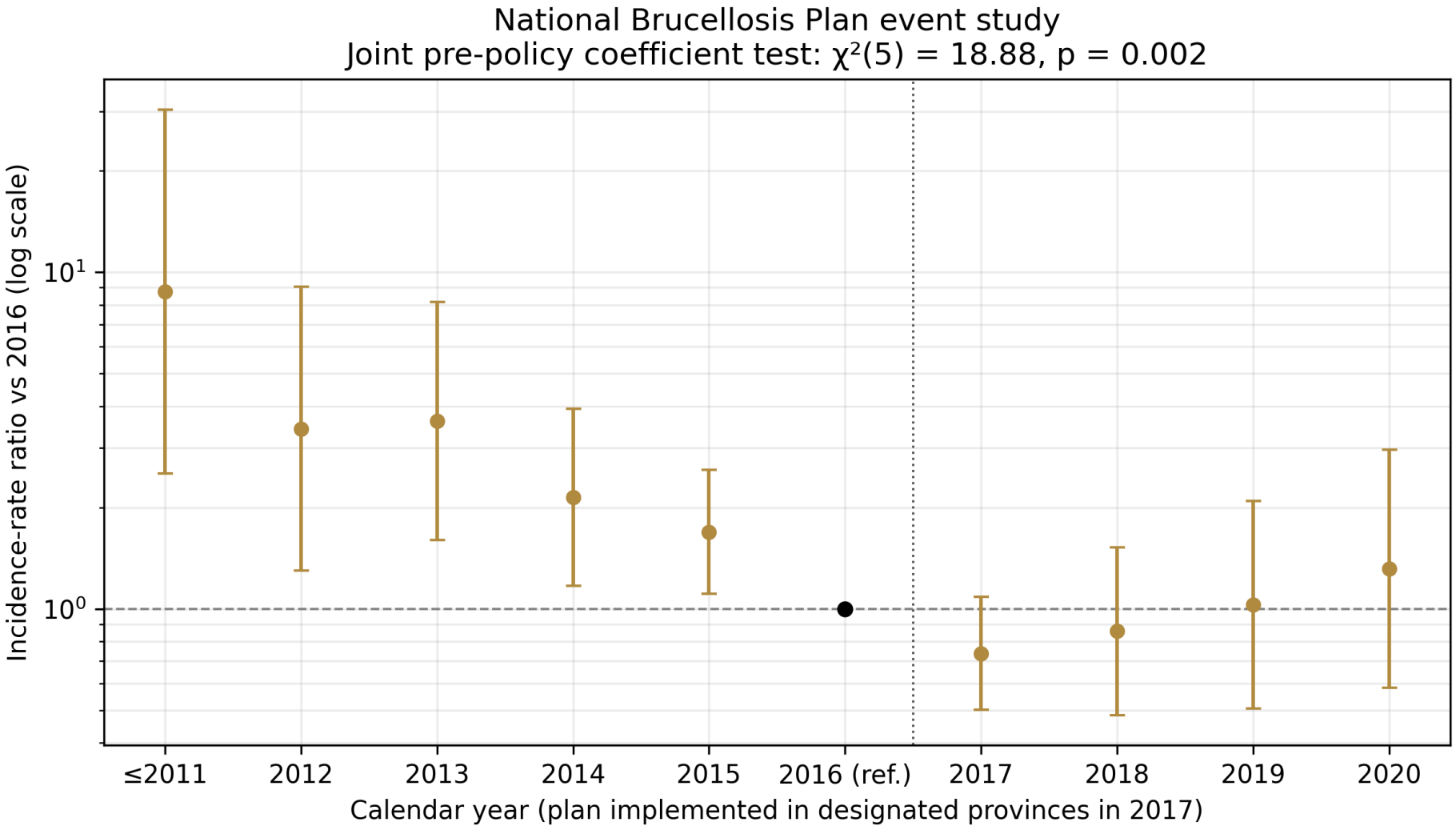
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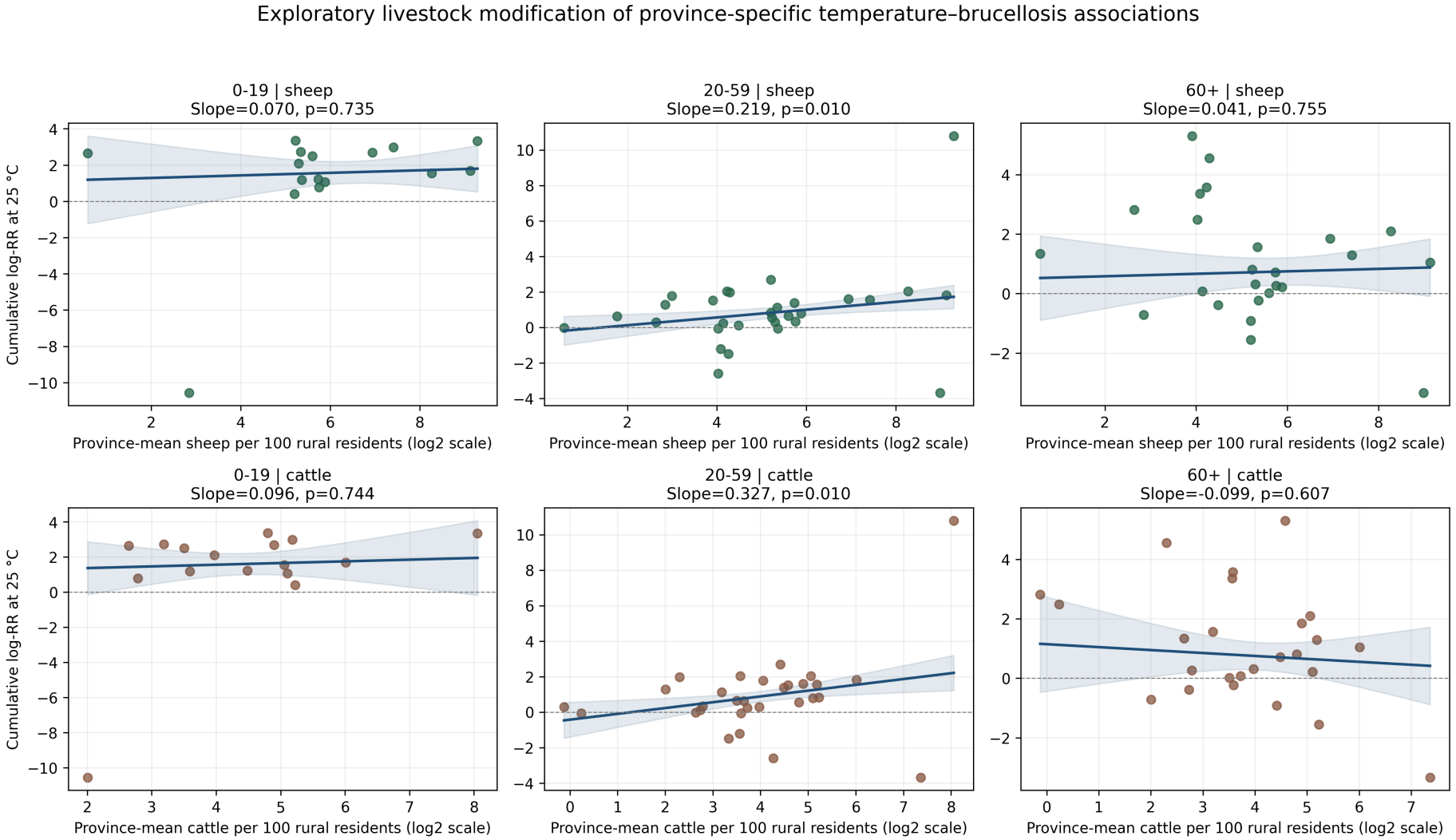
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Supplementary Fig. S6. Exploratory livestock modification of province-specific temperature–brucellosis associations. Points are province-specific cumulative log-RRs at 25 °C; lines and shading are model-based mean fits and 95% confidence intervals. Displayed p values are unadjusted primary meta-regression p values. These analyses are exploratory; adjusted, weighting and influence diagnostics are reported in Supplementary Tables S7–S13.



Supplementary Table S1. Data sources and variables

Domain	Variable	Source	Resolution	Period
Outcome	Monthly reported brucellosis cases/deaths, by age	Public Health Science Data Center, China CDC	Province × month × single-year age	2005–2020
Population	Age-band population (0–19, 20–59, ≥60)	2010/2020 censuses, intercensal interpolation, annual yearbook totals	Province × year	2005–2020
Climate	Daily Tmax/Tmin, precipitation (CN05.1, 0.25°)	Arid Land Ecology and Resources Science Data Center; refs. [9,10]	Grid → province × month (area-weighted)	2005–2020
Climate	Monthly relative humidity	NASA POWER	Grid → province × month	2005–2020
Socioeconomic	Urbanisation rate, GDP per capita, cattle/sheep stocks	China Statistical Yearbooks [11]	Province × year	2005–2020
Health system	Hospital beds, practising (assistant) physicians per 1,000	China (Health) Statistical Yearbooks 2006–2008; China Health Statistical Yearbooks 2009–2021	Province × year	2005–2020
Economic driver	National mutton market-fair price (yuan/kg)	China Agricultural Product Price Survey Yearbook (2006–2021 volumes)	National × year	2005–2020
Policy	National Brucellosis Plan 2016–2020 (11 provinces, from 2017)	National Brucellosis Prevention and Control Plan [12]	Province × year (indicator)	—

Reference numbers correspond to the main article.

Supplementary Table S2. Robustness analyses for livestock adjustment, temporal effect modification and policy evaluation

Analysis	Estimate	Result	Note
Livestock adjustment	0–19: RR at 27.8 °C	7.14 → 7.05	Adjusted 95% CI 3.43–14.50
Livestock adjustment	20–59: RR at 27.8 °C	2.99 → 3.18	Adjusted 95% CI 2.15–4.70
Livestock adjustment	≥60: RR at 27.8 °C	2.47 → 2.70	Adjusted 95% CI 1.60–4.58
Common-province period	0–19: change-on-change	Slope −0.036; p = 0.917	11 provinces; 25 °C
Common-province period	20–59: change-on-change	Slope −0.262; p = 0.075	20 provinces; 25 °C
Common-province period	≥60: change-on-change	Slope −0.091; p = 0.679	14 provinces; 25 °C
Legacy continuous interaction	0–19: interaction block	Wald p < 0.001	Condition number 2.68×10^3
Legacy continuous interaction	20–59: interaction block	Wald p < 0.001	Condition number 2.42×10^3
Legacy continuous interaction	≥60: interaction block	Wald p < 0.001	Condition number 2.37×10^3
Policy event study	Joint pre-policy test	$\chi^2(5) = 18.88$; p = 0.002	Parallel pre-policy trends rejected
Average post-2017 association	Policy IRR	0.264 (95% CI 0.100–0.698)	Descriptive only; not a causal effect

Common-province period estimates use the same provinces in both periods. Legacy continuous interaction results are exploratory and do not corroborate the two-stage findings. The policy event study uses province-clustered standard errors and 2016 as the reference year.

Supplementary Table S3. Same-20-province decomposition of livestock adjustment and τ² for ages 20–59

Specification	Temperature basis	Slope per pp Δrural	SE	p	τ²
No livestock; fixed effect	Current common	−0.408	0.139	0.009	0
No livestock; random τ²	Current common	−0.426	0.159	0.016	0.679
Livestock; fixed effect	Current common	−0.256	0.135	0.073	0
Livestock; random τ²	Current common	−0.262	0.139	0.075	0.131
No livestock; fixed effect	Legacy age-band	−0.415	0.142	0.009	0

All models used the same 20 provinces and evaluated Δlog-RR at 25 °C per percentage-point change in rural population share.

Supplementary Table S4. Sensitivity of climatic attribution to the MRT search range

Age band	MRT lower percentile	MRT, °C	AF, %	Warming cases	Warming share, %
0–19	5th	−8.308	66.96	+302	1.82
0–19	1st	−15.649	85.90	+128	0.60
20–59	5th	−8.308	48.93	+7,100	3.04
20–59	1st	−15.649	71.52	+3,959	1.16
≥60	5th	−8.308	51.51	+1,369	2.67
≥60	1st	−15.649	67.70	+912	1.35

The upper search bound remained the 95th percentile. AF is the model-estimated fraction attributable to non-MRT temperatures; warming share is the percentage of attributable cases estimated as excess under observed versus detrended temperatures.

Supplementary Table S5. Alternative single-stage period-interaction models with province-clustered inference

Age band	Provinces	Single-stage slope per 10 pp (95% CI)	Slope p	Joint-block p	Two-stage slope per 10 pp (p)
0–19	11	+3.880 (−1.322 to 9.081)	0.128	1.74×10^{-9}	−0.355 (0.917)
20–59	20	+0.946 (−1.668 to 3.560)	0.458	0.074	−2.619 (0.075)
≥60	14	+1.966 (−3.342 to 7.275)	0.438	0.178	−0.908 (0.679)

This model used a linear year trend rather than the two-stage year spline and was not fully aligned. Joint tests cover the entire three-way cross-basis interaction block, not the 25 °C slope. Condition numbers were 5.70×10^5, 5.17×10^5 and 5.42×10^5, supporting exploratory interpretation only.

Supplementary Table S6. Revised livestock-adjusted age-definition and physician-density sensitivities

Analysis	Age band	Provinces	Covered cases	RR at 27.8 °C (95% CI)	RR at 29.2 °C (95% CI)
Age definition	≥65	22	48,018	2.03 (1.03–4.03)	2.19 (1.01–4.76)
Physician density	0–19	16	24,779	7.46 (3.62–15.41)	9.16 (4.10–20.45)
Physician density	20–59	30	477,176	3.32 (2.32–4.74)	3.75 (2.52–5.58)
Physician density	≥60	25	99,448	2.87 (1.71–4.81)	3.19 (1.79–5.68)

All models included log sheep and cattle stocks. The ≥65-year numerator was rebuilt from single-year-age records, but the available ≥60-year population denominator was retained.

Supplementary Table S7. Primary exploratory livestock-density meta-regression at 25 °C

Age band	Species	Provinces	Slope per doubling	95% CI	RR ratio per doubling	p	BH-adjusted p
0-19	sheep	16	0.070	-0.366 to 0.506	1.073	0.7349	0.7550
0-19	cattle	16	0.096	-0.522 to 0.714	1.101	0.7439	0.7550
20-59	sheep	30	0.219	0.058 to 0.380	1.245	0.0095	0.0309
20-59	cattle	30	0.327	0.084 to 0.571	1.387	0.0103	0.0309
≥60	sheep	25	0.041	-0.230 to 0.312	1.042	0.7550	0.7550
≥60	cattle	25	-0.099	-0.491 to 0.293	0.906	0.6069	0.7550

The outcome is province-specific cumulative log-RR at 25 °C versus the age-band-specific median temperature. Livestock density is province-mean stock per 100 rural residents. Six primary tests were adjusted using the Benjamini–Hochberg procedure.

Supplementary Table S8. Adjusted and alternative-denominator sensitivity analyses for livestock-density modification

Age band	Species	Adjustment/denominator	Provinces	Slope per doubling	95% CI	p
0-19	sheep	rural_share_plus_log_GDP	16	0.029	-0.443 to 0.502	0.8956
0-19	sheep	rural_GDP_plus_mean_temperature	16	0.383	-0.383 to 1.150	0.2946
0-19	sheep	mutual_livestock_rural_GDP_adjustment	16	-0.082	-0.774 to 0.609	0.7978
0-19	sheep	per100_total_population	16	0.087	-0.348 to 0.522	0.6742
0-19	sheep	absolute_stock	16	0.044	-0.491 to 0.579	0.8616
0-19	cattle	rural_share_plus_log_GDP	16	0.131	-0.524 to 0.787	0.6706
0-19	cattle	rural_GDP_plus_mean_temperature	16	0.602	-0.360 to 1.564	0.1960
0-19	cattle	mutual_livestock_rural_GDP_adjustment	16	0.214	-0.745 to 1.173	0.6332
0-19	cattle	per100_total_population	16	0.143	-0.505 to 0.791	0.6436
0-19	cattle	absolute_stock	16	0.015	-0.663 to 0.693	0.9632
20-59	sheep	rural_share_plus_log_GDP	30	0.223	0.052 to 0.394	0.0127
20-59	sheep	rural_GDP_plus_mean_temperature	30	0.298	-0.064 to 0.660	0.1021
20-59	sheep	mutual_livestock_rural_GDP_adjustment	30	0.124	-0.114 to 0.361	0.2939
20-59	sheep	per100_total_population	30	0.197	0.046 to 0.347	0.0121
20-59	sheep	absolute_stock	30	0.116	-0.076 to 0.307	0.2261
20-59	cattle	rural_share_plus_log_GDP	30	0.352	0.089 to 0.616	0.0107
20-59	cattle	rural_GDP_plus_mean_temperature	30	0.305	-0.040 to 0.649	0.0803
20-59	cattle	mutual_livestock_rural_GDP_adjustment	30	0.221	-0.145 to 0.586	0.2259
20-59	cattle	per100_total_population	30	0.286	0.063 to 0.510	0.0139
20-59	cattle	absolute_stock	30	0.054	-0.203 to 0.312	0.6677
≥60	sheep	rural_share_plus_log_GDP	25	0.025	-0.279 to 0.329	0.8645
≥60	sheep	rural_GDP_plus_mean_temperature	25	0.590	0.072 to 1.109	0.0278
≥60	sheep	mutual_livestock_rural_GDP_adjustment	25	0.193	-0.266 to 0.652	0.3898
≥60	sheep	per100_total_population	25	0.031	-0.224 to 0.286	0.8038
≥60	sheep	absolute_stock	25	-0.047	-0.350 to 0.255	0.7494
≥60	cattle	rural_share_plus_log_GDP	25	-0.126	-0.563 to 0.311	0.5549
≥60	cattle	rural_GDP_plus_mean_temperature	25	0.007	-0.598 to 0.611	0.9816
≥60	cattle	mutual_livestock_rural_GDP_adjustment	25	-0.333	-0.988 to 0.321	0.3006
≥60	cattle	per100_total_population	25	-0.099	-0.470 to 0.273	0.5889
≥60	cattle	absolute_stock	25	-0.249	-0.623 to 0.125	0.1811

Models are random-effects meta-regressions. Baseline-climate adjustment adds province-mean temperature to rural-share and GDP adjustment. Mutual adjustment includes the other livestock species. The isolated ≥60-year sheep-density result after baseline-climate adjustment (p = 0.028) should be interpreted within this full family of sensitivity analyses, not as a selected positive finding.

Supplementary Table S9. Robust-variance and weighting diagnostics for primary livestock-density models

Age band	Species	Method	Slope per doubling	SE	p
0-19	sheep	precision_weighted_HC3	0.070	0.108	0.5151
0-19	sheep	unweighted_OLS_HC3	0.559	0.814	0.4920
0-19	cattle	precision_weighted_HC3	0.096	0.290	0.7407
0-19	cattle	unweighted_OLS_HC3	1.025	0.984	0.2976
20-59	sheep	precision_weighted_HC3	0.219	0.055	0.0001
20-59	sheep	unweighted_OLS_HC3	0.357	0.412	0.3864
20-59	cattle	precision_weighted_HC3	0.327	0.107	0.0023
20-59	cattle	unweighted_OLS_HC3	0.454	0.603	0.4516
≥60	sheep	precision_weighted_HC3	0.066	0.149	0.6576
≥60	sheep	unweighted_OLS_HC3	-0.316	0.247	0.2012
≥60	cattle	precision_weighted_HC3	-0.050	0.201	0.8032
≥60	cattle	unweighted_OLS_HC3	-0.443	0.246	0.0717

HC3 denotes heteroscedasticity-consistent standard errors. Unweighted OLS estimates do not incorporate province-specific outcome precision.

Supplementary Table S10. Leave-one-province-out summary for primary livestock-density models

Age band	Species	Slope range	p-value range	Maximum absolute slope change
0-19	cattle	-0.159 to 0.162	0.5945 to 0.9255	0.255
0-19	sheep	0.026 to 0.115	0.6104 to 0.9011	0.045
20-59	cattle	0.287 to 0.384	0.0062 to 0.0262	0.057
20-59	sheep	0.186 to 0.242	0.0058 to 0.0373	0.033
≥60	cattle	-0.177 to 0.040	0.4057 to 0.9612	0.138
≥60	sheep	-0.028 to 0.136	0.4159 to 0.9510	0.095

Each model omits one province in turn.

Supplementary Table S11. Descriptive median-split pooled relative risks at 25 °C

Age band	Species	Density group	Provinces	RR (95% CI)	I^2, %
0-19	sheep	low	8	5.08 (1.94–13.29)	10.8
0-19	sheep	high	8	3.96 (1.86–8.42)	22.4
0-19	cattle	low	8	4.41 (1.86–10.45)	3.7
0-19	cattle	high	8	4.54 (1.91–10.80)	22.5
20-59	sheep	low	15	2.12 (1.15–3.94)	0.0
20-59	sheep	high	15	2.79 (1.82–4.28)	7.4
20-59	cattle	low	15	1.57 (1.02–2.40)	0.0
20-59	cattle	high	15	3.54 (2.20–5.71)	8.4
≥60	sheep	low	12	3.38 (1.06–10.77)	8.2
≥60	sheep	high	13	2.17 (1.39–3.37)	0.0
≥60	cattle	low	12	2.05 (1.11–3.79)	1.0
≥60	cattle	high	13	2.20 (1.19–4.04)	0.0

Reference is the age-band-specific median temperature (approximately 14.2 °C). These descriptive strata do not replace the continuous meta-regression or its sensitivity analyses.

Supplementary Table S12. Secondary temperature points and combined-stock proxy

Age band	Species/proxy	Temperature, °C	Modifier	Provinces	Slope per doubling	95% CI	p
0-19	sheep	20.0	sheep_per100_rural	16	0.056	-0.188 to 0.299	0.6303
0-19	cattle	20.0	cattle_per100_rural	16	0.113	-0.231 to 0.458	0.4915
0-19	sheep	27.8	sheep_per100_rural	16	0.069	-0.477 to 0.616	0.7892
0-19	cattle	27.8	cattle_per100_rural	16	0.051	-0.725 to 0.826	0.8903
0-19	sheep_plus_cattle	25.0	total_per100_rural	16	0.078	-0.417 to 0.574	0.7403
20-59	sheep	20.0	sheep_per100_rural	30	0.124	0.034 to 0.214	0.0089
20-59	cattle	20.0	cattle_per100_rural	30	0.195	0.060 to 0.330	0.0063
20-59	sheep	27.8	sheep_per100_rural	30	0.269	0.067 to 0.471	0.0110
20-59	cattle	27.8	cattle_per100_rural	30	0.388	0.078 to 0.698	0.0160
20-59	sheep_plus_cattle	25.0	total_per100_rural	30	0.298	0.097 to 0.499	0.0052
≥60	sheep	20.0	sheep_per100_rural	25	0.042	-0.100 to 0.185	0.5448
≥60	cattle	20.0	cattle_per100_rural	25	-0.011	-0.217 to 0.195	0.9157
≥60	sheep	27.8	sheep_per100_rural	25	0.032	-0.312 to 0.377	0.8473
≥60	cattle	27.8	cattle_per100_rural	25	-0.168	-0.666 to 0.330	0.4921
≥60	sheep_plus_cattle	25.0	total_per100_rural	25	0.043	-0.283 to 0.368	0.7891

These secondary analyses were not included in the six-test primary Benjamini–Hochberg family and are exploratory.

Supplementary Table S13. Structural correlations of livestock-density modifiers

Age band	Species	Correlate	Spearman r	p
0-19	sheep	rural_pct	0.324	0.2216
0-19	sheep	log_gdppc	-0.394	0.1309
0-19	cattle	rural_pct	0.288	0.2790
0-19	cattle	log_gdppc	-0.332	0.2085
20-59	sheep	rural_pct	0.238	0.2057
20-59	sheep	log_gdppc	-0.190	0.3140
20-59	cattle	rural_pct	0.438	0.0154
20-59	cattle	log_gdppc	-0.482	0.0070
≥60	sheep	rural_pct	0.250	0.2281
≥60	sheep	log_gdppc	-0.318	0.1208
≥60	cattle	rural_pct	0.375	0.0644
≥60	cattle	log_gdppc	-0.445	0.0257

Correlations use log2 livestock density and describe potential structural confounding across provinces.

Supplementary Methods

Exploratory livestock-density modification

Province-mean sheep and cattle stocks per 100 rural residents were calculated from annual stock and population data for 2005–2020. The analysis reused the livestock-adjusted province-specific DLNM coefficient vectors and covariance matrices from the primary models; no first-stage model was refitted. For each age band and species, a moment-based random-effects meta-regression related province-specific cumulative log-RR at 25 °C versus the age-band-specific median temperature to log2 livestock density. Slopes therefore represent the change in log-RR per doubling of livestock per 100 rural residents; exponentiated slopes are ratios of relative risks. Inference used t distributions with residual degrees of freedom, and Benjamini–Hochberg adjustment covered the six primary age-band × species tests. Sensitivity analyses controlled for rural population share and mean log GDP per capita, then added baseline province-mean temperature; mutually adjusted sheep and cattle densities; substituted stock per 100 total population or absolute stock; compared precision-weighted and unweighted HC3 estimators; and repeated fits leaving out each province. Descriptive median-split pooled RRs, secondary temperature contrasts, a combined-stock proxy and structural correlations are also reported. All livestock-density analyses are ecological and exploratory. Their sensitivity to adjustment and weighting precludes causal interpretation or selection of isolated statistically significant sensitivity results.