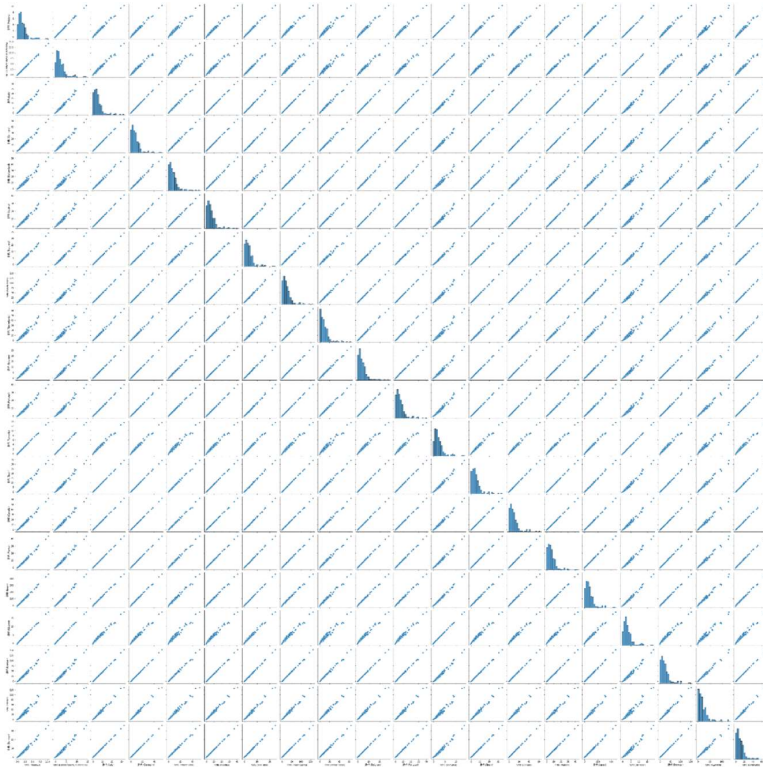


Supplementary Appendix to “Evaluation of the Global Health Security index as a predictor of COVID-19 excess mortality standardized for underreporting and age structure.”

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Figure S1. Correlation matrix comparing comparative mortality ratios derived from other standard countries with available age-specific COVID-19 mortality data.



Pearson r correlation coefficient comparing CMR using the USA as the standard country to CMR using other countries as the standard	
	CMR (United States of America)
CMR (Netherlands)	0.980
CMR (Switzerland)	0.982
CMR (Sweden)	0.984
CMR (South Korea)	0.989
CMR (Portugal)	0.990
CMR (Austria)	0.990
CMR (Denmark)	0.990
CMR (Belgium)	0.991
CMR (Norway)	0.992
CMR (Spain)	0.992
CMR (Germany)	0.992
CMR (Canada)	0.992
CMR (Italy)	0.993
CMR (France)	0.994
CMR (Scotland)	0.996
CMR (Japan)	0.997
CMR (Moldova)	0.999
CMR (Ukraine)	0.999
CMR (Romania)	1.000
CMR (United States of America)	1.000

Figure S2. Global distribution of Global Health Security index scores in 2021.

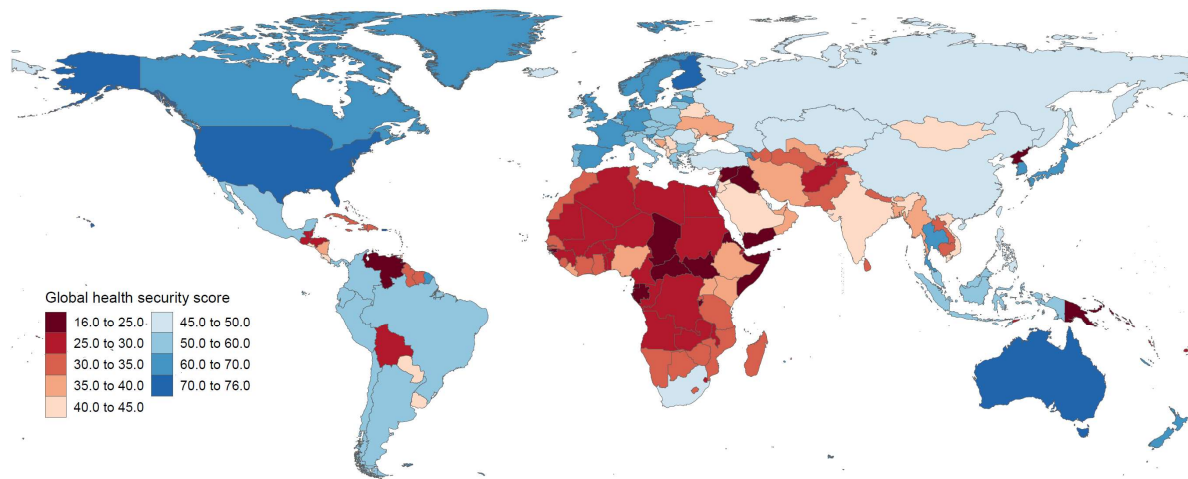


Figure S3. Global distribution of comparative mortality ratios for excess COVID-19 mortality, 2020 – 2021.

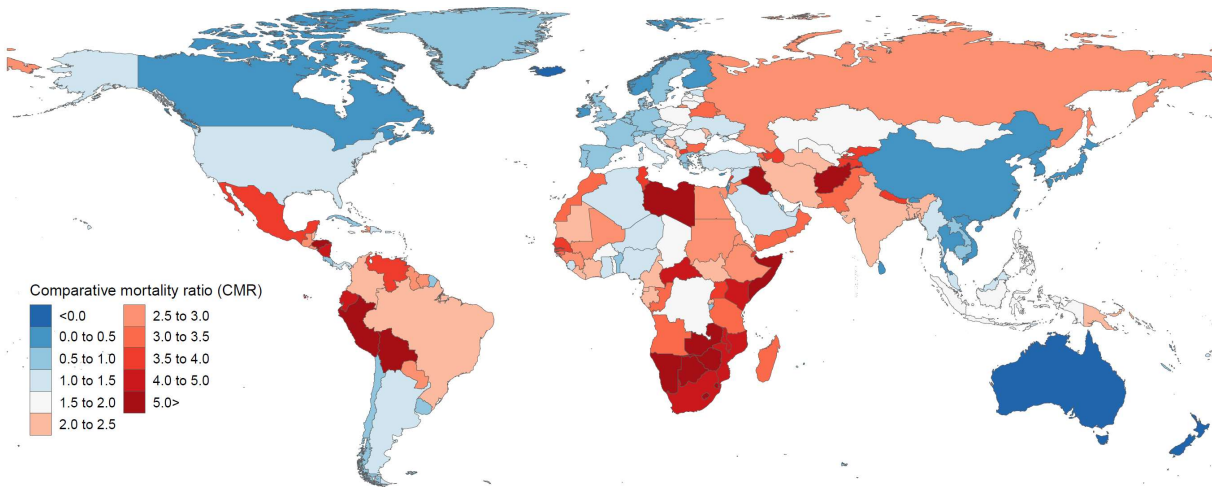


Figure S4. Scatterplot of Global Health Security index scores against (A) observed excess mortality rate and (B) expected excess mortality rate.

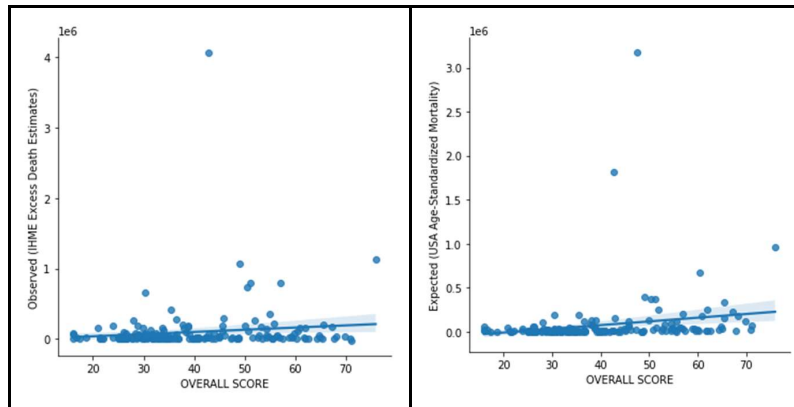


Table S1. Population-weighted averages of comparative COVID-19 excess mortality ratios, Global Health Security index scores, and category scores by IHME regions.

IHME Region	CMR	GHS index score	Prevention score	Detection score	Response score	Health system score	International norms score	Risk environment score
Global	1.79	45.2	36.1	45.3	39.2	42.8	50.7	57.1
Sub-Saharan Africa	2.85	32.9	18.0	31.3	34.9	20.3	51.8	41.2
North Africa and Middle East	2.90	33.1	26.5	25.4	30.0	28.5	40.2	47.9
South Asia	2.41	40.5	27.6	41.5	28.7	41.8	46.3	57.1
Central Europe, Eastern Europe, and Central Asia	2.26	46.7	42.4	37.7	39.7	49.6	54.8	56.1
Southeast Asia, East Asia, and Oceania	0.43	47.3	40.2	50.5	40.1	46.7	46.0	60.1
Latin America and Caribbean	3.28	47.9	40.9	47.0	50.8	45.9	49.9	53.2
High-income	0.75	65.8	60.2	68.5	57.8	63.1	70.9	74.3

NOTE: Population weighed averages computed utilizing UN country-specific population sizes in 2020. The IHME regions grouped countries on the basis of epidemiological homogeneity and geographic proximity.
CMR=Comparative mortality ratio

Table S2. Unadjusted and income adjusted effect sizes and corresponding 95% confidence intervals using robust standard errors [no Bonferroni correction] of 2021 Global Health Security measures on comparative COVID-19 excess mortality ratio.

Pandemic preparedness capacity	Unadjusted analysis		Income adjusted analysis	
	Coefficient (95% CI)	P value	Coefficient (95% CI)	P value
Global Health Security Index Score	-0.29 (-0.39, -0.19)	<0.0001	-0.21 (-0.33, -0.10)	0.0004
Prevention score	-0.19 (-0.26, -0.11)	<0.0001	-0.11 (-0.20, -0.03)	0.0086
1.1) Antimicrobial resistance (AMR)	-0.09 (-0.14, -0.05)	<0.0001	-0.05 (-0.10, 0.00)	0.0670
1.2) Zoonotic disease	-0.15 (-0.23, -0.08)	<0.0001	-0.09 (-0.17, -0.02)	0.0200
1.3) Biosecurity	-0.11 (-0.17, -0.06)	<0.0001	-0.05 (-0.11, 0.01)	0.1325
1.4) Biosafety	-0.07 (-0.11, -0.03)	0.0007	-0.03 (-0.08, 0.01)	0.1577
1.5) Dual-use research and culture of responsible science	-0.12 (-0.22, -0.02)	0.0206	-0.04 (-0.11, 0.04)	0.3027
1.6) Immunization	-0.09 (-0.15, -0.04)	0.0011	-0.08 (-0.13, -0.02)	0.0047
Detection score	-0.14 (-0.21, -0.07)	<0.0001	-0.09 (-0.17, -0.02)	0.0140
2.1) Laboratory systems strength and quality	-0.06 (-0.11, -0.02)	0.0097	-0.05 (-0.09, 0.00)	0.0540
2.1.1) Lab capacity for detecting priority diseases	-0.07 (-0.12, -0.02)	0.0042	-0.06 (-0.10, -0.01)	0.0166
2.1.2) Laboratory quality systems	-0.03 (-0.07, 0.01)	0.0963	-0.02 (-0.06, 0.02)	0.2774
2.2) Laboratory supply chains	-0.04 (-0.10, 0.02)	0.2397	0.02 (-0.05, 0.09)	0.5140
2.3) Real-time surveillance and reporting	-0.04 (-0.08, 0.01)	0.1163	-0.02 (-0.07, 0.02)	0.3634
2.4) Surveillance data accessibility and transparency	-0.09 (-0.13, -0.05)	<0.0001	-0.04 (-0.09, 0.01)	0.1103
2.5) Case-based investigation	-0.12 (-0.18, -0.05)	0.0005	-0.09 (-0.15, -0.03)	0.0042
2.6) Epidemiology workforce	-0.06 (-0.12, 0.00)	0.0673	-0.07 (-0.13, -0.01)	0.0332
Response score	-0.27 (-0.39, -0.15)	<0.0001	-0.19 (-0.32, -0.05)	0.0072
3.1) Emergency preparedness and response planning	-0.11 (-0.18, -0.05)	0.0005	-0.07 (-0.14, -0.01)	0.0270
3.1.1) National public health emergency preparedness plan	-0.09 (-0.13, -0.04)	<0.0001	-0.05 (-0.09, -0.00)	0.0398
3.1.3) Non-pharmaceutical interventions planning`	-0.06 (-0.10, -0.02)	0.0028	-0.04 (-0.08, -0.01)	0.0274
3.2) Exercising response plans	-0.09 (-0.22, 0.05)	0.2130	-0.11 (-0.24, 0.02)	0.1003
3.3) Emergency response operation	-0.04 (-0.12, 0.03)	0.2590	-0.06 (-0.14, 0.01)	0.1020
3.4) Linking public health and security authorities	-0.05 (-0.08, -0.02)	0.0014	-0.02 (-0.05, 0.02)	0.3364
3.5) Risk communication	-0.11 (-0.19, -0.04)	0.0027	-0.07 (-0.15, 0.00)	0.0523
3.6) Access to communications infrastructure	-0.20 (-0.29, -0.12)	<0.0001	-0.17 (-0.27, -0.07)	0.0007
3.7) Trade and travel restrictions	0.03 (-0.02, 0.08)	0.307	0.03 (-0.02, 0.08)	0.1835
Health system score	-0.18 (-0.26, -0.09)	<0.0001	-0.10 (-0.20, -0.01)	0.0366
4.1) Health capacity in clinics, hospitals and community care centers	-0.18 (-0.24, -0.11)	<0.0001	-0.10 (-0.18, -0.01)	0.0247
4.1.2) Facilities capacity	-0.10 (-0.15, -0.05)	0.0001	-0.06 (-0.11, -0.00)	0.0436

4.2) Supply chain for health system and healthcare workers	-0.10 (-0.16, -0.04)	0.0023	-0.06 (-0.12, 0.01)	0.0878
4.3) Medical countermeasures and personnel deployment	-0.06 (-0.11, -0.01)	0.0245	-0.02 (-0.07, 0.02)	0.3205
4.4) Healthcare access	0.02 (-0.21, 0.26)	0.8532	-0.05 (-0.27, 0.17)	0.6395
4.5) Communications with healthcare workers during health emergency	-0.06 (-0.11, -0.01)	0.0313	-0.02 (-0.07, 0.02)	0.3019
4.6) Infection control practices	-0.06 (-0.09, -0.03)	<0.0001	-0.03 (-0.06, 0.00)	0.0738
4.7) Capacity to test and approve new medical countermeasures	-0.08 (-0.15, -0.02)	0.0171	-0.06 (-0.13, 0.01)	0.0991
International norms score	-0.21 (-0.34, -0.08)	0.0021	-0.17 (-0.30, -0.04)	0.0127
5.1) IHR reporting compliance and disaster risk reduction	0.01 (-0.05, 0.08)	0.7009	0.01 (-0.05, 0.06)	0.8552
5.2) Cross-border agreements on public health emergency response	-0.09 (-0.13, -0.05)	<0.0001	-0.07 (-0.11, -0.03)	0.0012
5.3) International commitments	-0.10 (-0.15, -0.05)	0.0002	-0.06 (-0.12, -0.01)	0.0261
5.4) JEE and PVS	0.08 (0.01, 0.16)	0.0334	0.03 (-0.04, 0.11)	0.4266
5.5) Financing	-0.04 (-0.12, 0.03)	0.2696	-0.07 (-0.14, -0.00)	0.0432
5.6) Commitment to sharing of genetic & biological data & specimens	-0.14 (-0.27, -0.01)	0.0358	-0.05 (-0.17, 0.07)	0.4391
Risk environment score	-0.33 (-0.41, -0.25)	<0.0001	-0.30 (-0.42, -0.18)	<0.0001
6.1) Political and security risk	-0.19 (-0.25, -0.13)	<0.0001	-0.15 (-0.23, -0.06)	0.0014
6.1.1) Government effectiveness	-0.21 (-0.27, -0.16)	<0.0001	-0.21 (-0.29, -0.12)	<0.0001
6.2) Socio-economic resilience	-0.26 (-0.33, -0.18)	<0.0001	-0.23 (-0.32, -0.14)	<0.0001
6.2.3) Social inclusion	-0.17 (-0.22, -0.11)	<0.0001	-0.13 (-0.19, -0.06)	0.0002
6.2.4) Public confidence in government	-0.10 (-0.15, -0.06)	<0.0001	-0.08 (-0.12, -0.03)	0.0008
6.2.6) Inequality	-0.11 (-0.19, -0.03)	0.0056	-0.11 (-0.18, -0.04)	0.0035
6.3) Infrastructure adequacy	-0.16 (-0.20, -0.11)	<0.0001	-0.11 (-0.18, -0.03)	0.0049
6.4) Environmental risks	-0.08 (-0.23, 0.07)	0.3244	-0.04 (-0.19, 0.10)	0.5659
6.5) Public health vulnerabilities	-0.30 (-0.39, -0.22)	<0.0001	-0.21 (-0.32, -0.10)	0.0003
6.5.1) Access to quality healthcare	-0.23 (-0.49, 0.02)	0.0710	-0.27 (-0.51, -0.03)	0.0306
6.5.4) Trust in medical and health advice	-0.06 (-0.10, -0.01)	0.0150	-0.01 (-0.06, 0.04)	0.5972
6.5.4a) Trust medical and health advice from the government	-0.02 (-0.06, 0.02)	0.3892	0.01 (-0.02, 0.05)	0.5280
6.5.4b) Trust medical and health advice from medical workers	-0.08 (-0.13, -0.03)	0.0038	-0.04 (-0.09, 0.02)	0.1918

Effect sizes compare a 5-score difference in each index; separate regressions were implemented for each Global Health Security Index measure to assess the effect of the measure independent of other indicators. The unadjusted analysis does not include any covariates while the adjusted analysis includes 2019 gross domestic product per capita as a covariate in each regression. The 95% confidence intervals (Cis) and p-values constructed based on robust covariance matrix estimation from model parameters. Some risk environment category capacities including political and security risk, inequality, environmental risks, public health vulnerabilities are reverse coded such that higher levels indicate lower risks. IHR, International Health Regulations; JEE, Joint External Evaluation; PVS, Performance Veterinary Services.

Table S3. One-way sensitivity analyses of the primary analysis using the 2019 iteration of the Global Health Security index.

	2021 GHS Index				2019 GHS Index			
	Unadjusted analysis		Income adjusted analysis		Unadjusted analysis		Income adjusted analysis	
	Coefficient	p-value	Coefficient	p-value	Coefficient	p-value	Coefficient	p-value
Global Health Security Index Score	-0.29 (-0.39, -0.19)	<0.0001	-0.21 (-0.33, -0.10)	0.0004	-0.28 (-0.37, -0.18)	<0.0001	-0.19 (-0.30, -0.07)	0.0014
Prevention score	-0.19 (-0.26, -0.11)	<0.0001	-0.11 (-0.20, -0.03)	0.0086	-0.17 (-0.24, -0.09)	<0.0001	-0.09 (-0.18, -0.01)	0.0331
Detection score	-0.14 (-0.21, -0.07)	<0.0001	-0.09 (-0.17, -0.02)	0.0140	-0.14 (-0.21, -0.06)	0.0003	-0.08 (-0.16, 0.00)	0.0525
Response score	-0.27 (-0.39, -0.15)	<0.0001	-0.19 (-0.32, -0.05)	0.0072	-0.24 (-0.34, -0.14)	<0.0001	-0.16 (-0.27, -0.05)	0.0060
Health system score	-0.18 (-0.26, -0.09)	<0.0001	-0.10 (-0.20, -0.01)	0.0366	-0.18 (-0.27, -0.09)	0.0001	-0.10 (-0.20, 0.00)	0.0526
International norms score	-0.21 (-0.34, -0.08)	0.0021	-0.17 (-0.30, -0.04)	0.0127	-0.21 (-0.33, -0.09)	0.0008	-0.16 (-0.29, -0.03)	0.0143
Risk environment score	-0.33 (-0.41, -0.25)	<0.0001	-0.30 (-0.42, -0.18)	<0.0001	-0.35 (-0.43, -0.26)	<0.0001	-0.32 (-0.44, -0.19)	<0.0001

Note: Effect sizes compare a 5-score difference in each index; Separate regressions were implemented for each GHS index measure to assess the effect of the measure independent of other indicators. The unadjusted analysis does not include any covariates while the adjusted analysis includes 2019 gross domestic product (GDP) per capita as a covariate in each regression. 95% Confidence interval constructed using robust standard errors.

Table S4. One-way sensitivity analyses of the primary analysis including Oxford Stringency Index as a covariate.

	Income adjusted (primary analysis)	Income & stringency adjusted
Global Health Security Index score	-0.21 (-0.41, -0.02)	-0.27 (-0.47, -0.06)
Prevention score	-0.11 (-0.26, 0.03)	-0.15 (-0.31, -0.01)
Detection score	-0.09 (-0.22, 0.03)	-0.13 (-0.27, 0.00)
Response score	-0.19 (-0.41, 0.04)	-0.21 (-0.45, 0.03)
Health system score	-0.10 (-0.27, 0.06)	-0.13 (-0.31, 0.05)
International norms score	-0.17 (-0.39, 0.05)	-0.19 (-0.42, 0.04)
Risk environment score	-0.30 (-0.50, -0.10)	-0.31 (-0.52, -0.11)

NOTE: Effect sizes compare a 5-score difference in each index. Separate regressions were implemented for each GHS index measure to assess the effect of the measure independent of other indicators. The stringency index value for each country was computed by taking the average of daily stringency index values during the observation period. 95% confidence interval constructed using robust standard errors. The 95% confidence intervals were also adjusted to take into account multiple hypotheses. The adjusted 95% confidence intervals are therefore analogous to 99.91% confidence intervals.

Table S5. One-way sensitivity analyses of the primary income-adjusted analysis using WHO and Economist excess mortality estimates.

	IHME 2020		IHME 2020-2021		WHO 2020		WHO 2020-2021		Economist 2020		Economist 2020-2021	
	Coefficient	p-value	Coefficient	p-value	Coefficient	p-value	Coefficient	p-value	Coefficient	P-value	Coefficient	p-value
Global Health Security Index Score	-0.72 (-1.07, -0.37)	<0.0001	-0.21 (-0.33, -0.10)	0.0004	0.07 (-0.04, 0.18)	0.2252	0.04 (-0.05, 0.12)	0.4060	0.06 (-0.02, 0.13)	0.1414	0.01 (-0.05, 0.08)	0.6818
Prevention score	-0.40 (-0.65, -0.14)	0.0022	-0.11 (-0.20, -0.03)	0.0086	0.11 (0.03, 0.19)	0.0076	0.06 (-0.01, 0.12)	0.0739	0.09 (0.04, 0.15)	0.0013	0.04 (-0.01, 0.09)	0.1434
Detection score	-0.31 (-0.53, -0.09)	0.0059	-0.09 (-0.17, -0.02)	0.0140	0.03 (-0.03, 0.10)	0.3266	0.03 (-0.02, 0.08)	0.3147	0.03 (-0.02, 0.08)	0.2112	0.02 (-0.02, 0.06)	0.3702
Response score	-0.63 (-1.03, -0.22)	0.0027	-0.19 (-0.32, -0.05)	0.0072	-0.02 (-0.12, 0.09)	0.7628	-0.01 (-0.09, 0.07)	0.8330	-0.03 (-0.11, 0.06)	0.5184	-0.04 (-0.11, 0.03)	0.2946
Health system score	-0.37 (-0.66, -0.08)	0.0126	-0.10 (-0.20, -0.01)	0.0366	0.12 (0.04, 0.21)	0.0043	0.07 (0.00, 0.13)	0.0398	0.10 (0.04, 0.15)	0.0007	0.04 (-0.00, 0.09)	0.0542
International norms score	-0.55 (-0.96, -0.15)	0.0080	-0.17 (-0.30, -0.04)	0.0127	0.03 (-0.08, 0.13)	0.6140	0.01 (-0.06, 0.09)	0.7361	-0.01 (-0.08, 0.07)	0.8754	-0.02 (-0.07, 0.04)	0.5818
Risk environment score	-0.99 (-1.36, -0.62)	<0.0001	-0.30 (-0.42, -0.18)	<0.0001	-0.21 (-0.29, -0.12)	<0.0001	-0.13 (-0.18, -0.07)	<0.0001	-0.10 (-0.17, -0.03)	0.0084	-0.10 (-0.15, -0.04)	0.0018

Note: Effect sizes compare a 5-score difference in each index; Separate regressions were implemented for each GHS index measure to assess the effect of the measure independent of other indicators. Gross domestic product (GDP) per capita in 2019 included as covariate in each regression. 95% Confidence interval constructed using robust standard errors.