Supplementary Material

Validation Analysis of Global Health Security Index (GHSI) Scores 2019

SUPPLEMENTARY BACKGROUND

Biological threats, or biothreats, range in scale from local outbreaks that can be contained, to pandemics that could kill billions of people. These threats can emerge from nature or be the result of human actions. The category of anthropogenic threats include, but are not limited to, unintentional laboratory accidents and deliberate development and release of bioweapons. Over the last 20 years high-impact biothreats have threatened health and economies, these have included severe acute respiratory syndrome (SARS), Influenza A (H1N1), Ebola, Middle East respiratory syndrome (MERS), Zika virus disease, the 2001 anthrax attacks and now the COVID-19 pandemic. The latter is a powerful demonstration of the consequences of biothreats, compelling nations to improve capabilities for dealing with future events, whether low or high-consequence, natural or anthropogenic.

A number of previous studies have identified health security weaknesses around the world. These include the United Nations (UN),[1] the US National Academy of Sciences,[2] the Global Preparedness Monitoring Board,[3] the Global Health Centre,[4] and Rand Corporation,[5] among others. Findings of these previous analyses indicate that vulnerabilities exist in Africa and improvements are needed globally in: leadership, coordination (eg, at the UN) and monitoring, financing, national health systems capacity, functioning of institutions such as the World Health Organization (WHO), research and development, and knowledge sharing among other improvements. These reports identify that in many cases countries are still not compliant with the 2005 International Health Regulations (IHR), let alone additional global health security needs.

The 2019 GHSI assessment covers 195 States Parties to the International Health Regulations (excluding the Holy See) across 140 variables in 34 indicators and six categories. Advantages of this method, which is based on a review of published documents, are repeatability, objectivity and its aspirational nature. The GHSI emphasises the exercise of public health capabilities, transparency, functional systems, testing of systems and appropriate financing.[6] The six categories of the GHSI (full descriptions) are: Prevention of the emergence or release of pathogens (Prevent); Early detection and reporting for epidemics of potential international concern (Detect); Rapid response to and mitigation of the spread of an epidemic (Respond); Sufficient and robust health system to treat the sick and protect health workers (Health System); Commitments to improving national capacity, financing plans to address gaps, and adhering to global norms (Commitments); Overall risk environment and country vulnerability to biological threats (Risk Environment).[6]

Additional published commentary on the GHSI includes description of Mongolia's scores.[7] Additional unpublished analysis of GHSI scores includes a pre-print assessing the relationship between GHSI scores and early stage outcomes (14 April 2020) in the COVID-19 pandemic.[8] This unpublished research reported that there was little relationship between GHSI scores and COVID-19 total tests performed, recovery rate or case fatality ratio (CFR). However, the authors looked only at countries with more than 1000 cases of COVID-19 and did find some moderate positive correlation between total tests performed and GHSI for high-income countries. Future research should look at all countries, tests per capita and stratify results by country strategy employed (mitigation, suppression, or elimination).

Previous attempts to validate metrics of Global Health Security
Tsai et al compared epidemic response and outcome with self-reported international health regulations monitoring tool (IHRMT) scores and found them to have some validity.[9] Garfield et al took a qualitative approach to validation of the Joint External Evaluations (JEE) and compared JEE reports with actions taken during actual outbreaks in three countries.[10] One of the authors of the GHSI has provided an informal qualitative look at the US response to COVID-19.[11] Such qualitative validation approaches might overcome the breadth of the GHSI, which means that not all items are applicable to all situations. Also, there is some evidence in Garfield et al, that countries with low JEE scores might ask for aid more quickly and may also have improved response due to actions taken following a low-score assessment. This means that scores (for JEE and perhaps GHSI) might not reflect current capability.

SUPPLEMENTARY METHODS

Macro-indices

We acknowledge that the authors of the GHSI explored correlations with macro-indices, such as GDP and population size, as well as a range of indicators of development such as the Human Capital Index. We performed our own analyses on population and GDP per capita so that these could be included in our regression models. We also note that the Human Capital Index includes measures of life expectancy and child mortality, which may confound analysis of any relationship between education and GHSI, therefore we examined the proportion of secondary school completions in over 25-year olds.

Matching countries

We compared the GHSI scores for countries that were the recipients of US GHSA aid (n = 31) with countries matched by WHO region and GDP per capita. Countries receiving US GHSA aid were chosen for analysis because the US was by far the largest contributor to the GHSA programme. When matching countries, small island developing nations with less than one million population were excluded. The GHSI report (2019, p.49) noted that every island country with a population below 1 million scores far below the average GHSI, with the exception of Iceland and Cyprus.[6] A list of small developing island nations is provided by the UN: https://sustainabledevelopment.un.org/topics/sids/list

Sources of Data

Table S1 displays the sources of data used in this study.

Table S1: Sources of data

Data	Source
GHSI Scores	Global Health Security Index: https://www.ghsindex.org/
Population size	World Bank: Population, total (2018): https://data.worldbank.org/indicator/sp.pop.totl
GDP per capita	World Bank (2018): https://data.worldbank.org/indicator/NY.GDP.PCAP.CD
Health spend as % of GDP	World Bank (2017 - most recent year): https://data.worldbank.org/indicator/SH.XPD.CHEX.GD.ZS
Secondary school completions	World Bank: Educational attainment, at least completed upper secondary, population 25+, total (%) (cumulative), most recent year varies by country https://data.worldbank.org/indicator/SE.SEC.CUAT.UP.ZS
Political stability	World Bank: Political Stability and Absence of Violence/Terrorism percentile rank (2018) https://databank.worldbank.org/reports.aspx?source=1181&series=PV.PER.RNK
Proportion of population dying from communicable disease (including maternal, neonatal, and nutritional disease deaths)	Our World in Data: https://ourworldindata.org/causes-of-death
Infectious disease deaths per capita per annum (composite of HIV, tuberculosis, diarrhoeal disease, lower respiratory infections, meningitis)	Our World in Data: https://ourworldindata.org/causes-of-death#what-do-people-die-from [data was originally extracted from Global Burden of Disease study data: http://ghdx.healthdata.org/gbd-results-tool]
SARS cases in the 2003 pandemic	WHO summary of probable SARS cases: https://www.who.int/csr/sars/country/table2004_04_21/en/
Countries with MERS cases	WHO list of 27 countries with MERS as at January 31, 2019: https://www.who.int/csr/disease/coronavirus_infections/faq/en/
Countries with Ebola outbreaks	Centres for Disease Control and Prevention map and table of Ebola cases as at June 19, 2019: https://www.cdc.gov/vhf/ebola/history/distribution-map.html
GHSA recipients of US aid	US Centers for Disease Control and Prevention 2019[12]
Time to outbreak communication and recognition	Kluberg et al 2016[13]

GBD: Global Burden of Disease, GDP: gross domestic product, GHSI: global health security index, SARS: severe acute respiratory syndrome, WHO: World Health Organization

SUPPLEMENTARY RESULTS

GHSI previously published findings

Table S2 displays the GHSI scores extracted from the GHSI Excel worksheet and Table S3 reproduces the GHSI Report's high-level findings.

Table S2: GHSI total and category scores by World Health Organization (WHO) Region

WHO region	GHSI 2019 overall score (out of 100)	Prevention	Detection and reporting	Rapid response	Health system	Compliance with international norms	Risk environment
Africa	31.3	24.8	31.9	31.3	14.8	46.7	40.9
Eastern Mediterranean	34.7	29.8	36.3	35.8	22.3	40.2	46.7
Western Pacific	37.7	28.9	37.0	38.5	24.4	43.6	58.7
South East Asia	40.1	34.6	43.0	41.0	27.2	47.7	49.1
Americas	40.5	34.6	40.8	38.1	25.4	50.8	58.1
Europe	51.4	48.5	56.3	45.5	39.8	54.4	67.6
Range for all countries	16.2–83.5	1.9–83.1	2.7–98.2	11.3–91.9	0.3–73.8	23.3–85.3	15.9–87.9

GHSI: Global Health Security Index, WHO: World Health Organization.
GHSI scores by WHO region, both overall and for each of the six categories, GHSI scores by WHO region were extracted from the GHSI model available at https://www.ghsindex.org/report-model/

Table S3: **High-level findings in the GHSI Report 2019**[6]

Finding	Description
1	OVERALL FINDING: National health security is fundamentally weak around the world. No country is fully prepared for epidemics or pandemics, and every country has important gaps to address.
2	Countries are not prepared for a globally catastrophic biological event, including those that could be caused by the international spread of a new or emerging pathogen or by the deliberate or accidental release of a dangerous or engineered agent or organism. Biosecurity and biosafety are under-prioritized areas of health security, and the connections between health and security-sector actors for outbreak response are weak.
3	There is little evidence that most countries have tested important health security capacities or shown that they would be functional in a crisis.
4	Most countries have not allocated funding from national budgets to fill identified preparedness gaps.
5	More than half of countries face major political and security risks that could undermine national capability to counter biological threats.
6	Most countries lack foundational health systems capacities vital for epidemic and pandemic response.
7	Coordination and training are inadequate among veterinary, wildlife, and public health professionals and policymakers.
8	Improving country compliance with international health and security norms is essential.

Lowest GHSI scores

We looked at the worst performing nations by GHSI scores. Out of 120 possible 'worst performances' on the GHSI (the bottom 20 places across 6 categories), 48 were African nations (also most at risk according to risk environment category scores)**,** 51 were island nations**,** 13 were countries at war or civil war (at the time of writing, or in the recent past)**,** and 11 other nations included North Korea and Iran, for whom the GHSI may not have complete information. Table S4 summarises the bottom 20 scores by category.

Table S4: The lowest GHSI scores by GHSI category

GHSI Category	Bottom 20 nations
Prevent	14 island nations, 5 African nations, plus Monaco
Detect	11 island nations, 5 African nations, plus Syria, Venezuela, North Korea, Yemen
Rapid response	10 African nations, 6 island nations, plus Iraq, Venezuela, North Korea, Yemen
Health system	10 island nations, 9 African nations, plus Yemen (note these all score below 10/100)
Commitments to norms	9 island nations, 4 African nations (northern), plus Brunei, Iraq, Iran, North Korea, Syria, Belarus, San Marino
Risk environment	15 African nations, plus Syria, Yemen, Afghanistan, Iraq, Haiti

We note that island nations, those without land borders to other countries, may have other strategies for mitigating a serious biothreat, such as strict border closure.[14] It is also the case that small developing island nations may never be able to attain a GHSI score of 100/100 due to resource constraints, and this has been noted in the literature.[15] Regional cooperation may be one solution to resource limitations. A 2016 report by the UN states, 'Regional or subregional groups of countries may also share key preparedness or response assets, such as laboratories, medical research and development efforts, or medical evacuation facilities for crisis responders. Whereas the significant cost of these assets may render them difficult to sustain in one country, their establishment on a cost-sharing basis at the regional or subregional levels may make them feasible for all participating countries.'[1] In contrast, however, the GHSI Report notes that, 'Although it may make sense for countries to form agreements and share resources, examining the potential limitations of this approach is also important. Countries should know that such agreements may not be operationally feasible during large public health emergencies.'[6]

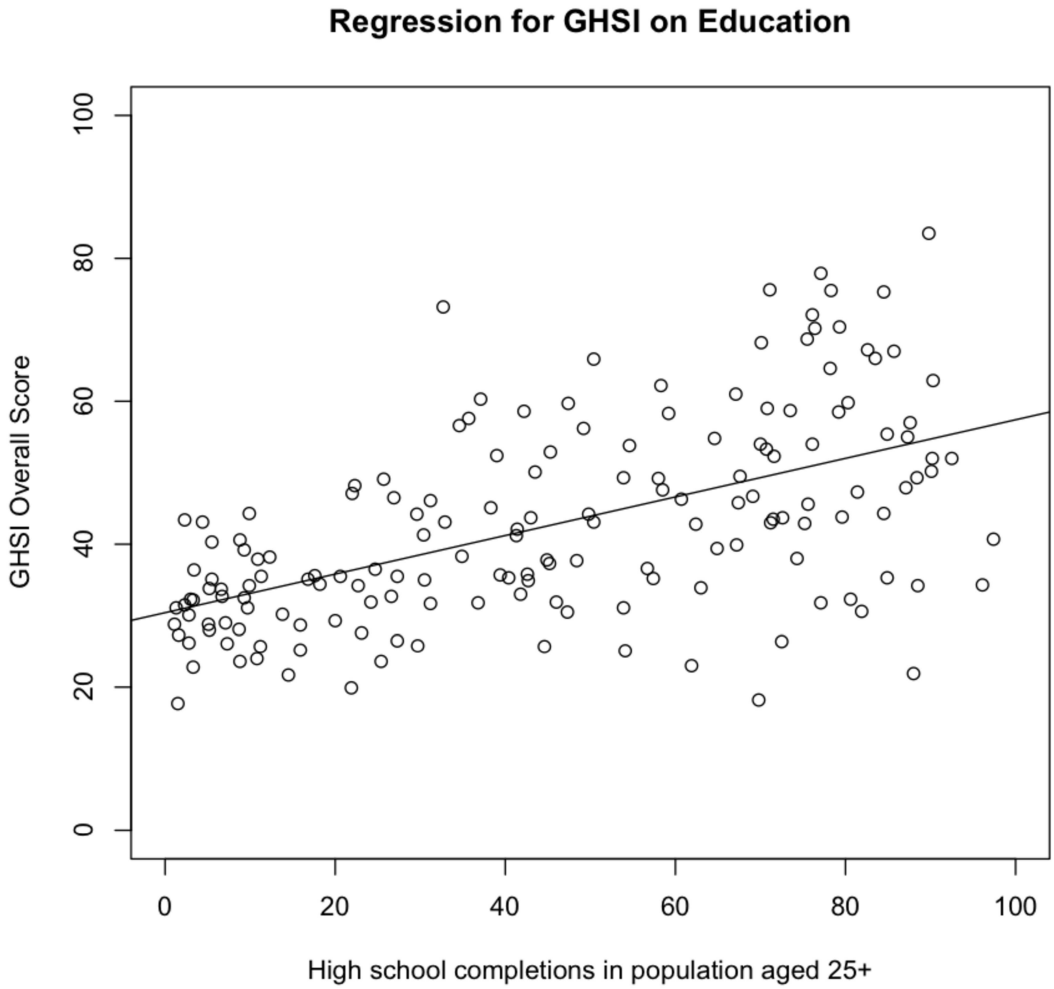
ReadyScore vs GHSI

As we report in the body of the paper there is very strong correlation between GHSI and ReadyScore (see Figure S1). However, we suspect that given that GHSI depends on published information, there will be instances where preparations have been made, but not published, this important fact may explain higher variance where the GHSI score is moderate (eg, 40–60), yet ReadyScore is high. As more countries provide published evidence of their preparations, these data points may show a rightward shift.

Figure S1: GHSI overall score vs ReadyScore

Macro-indices and GHSI

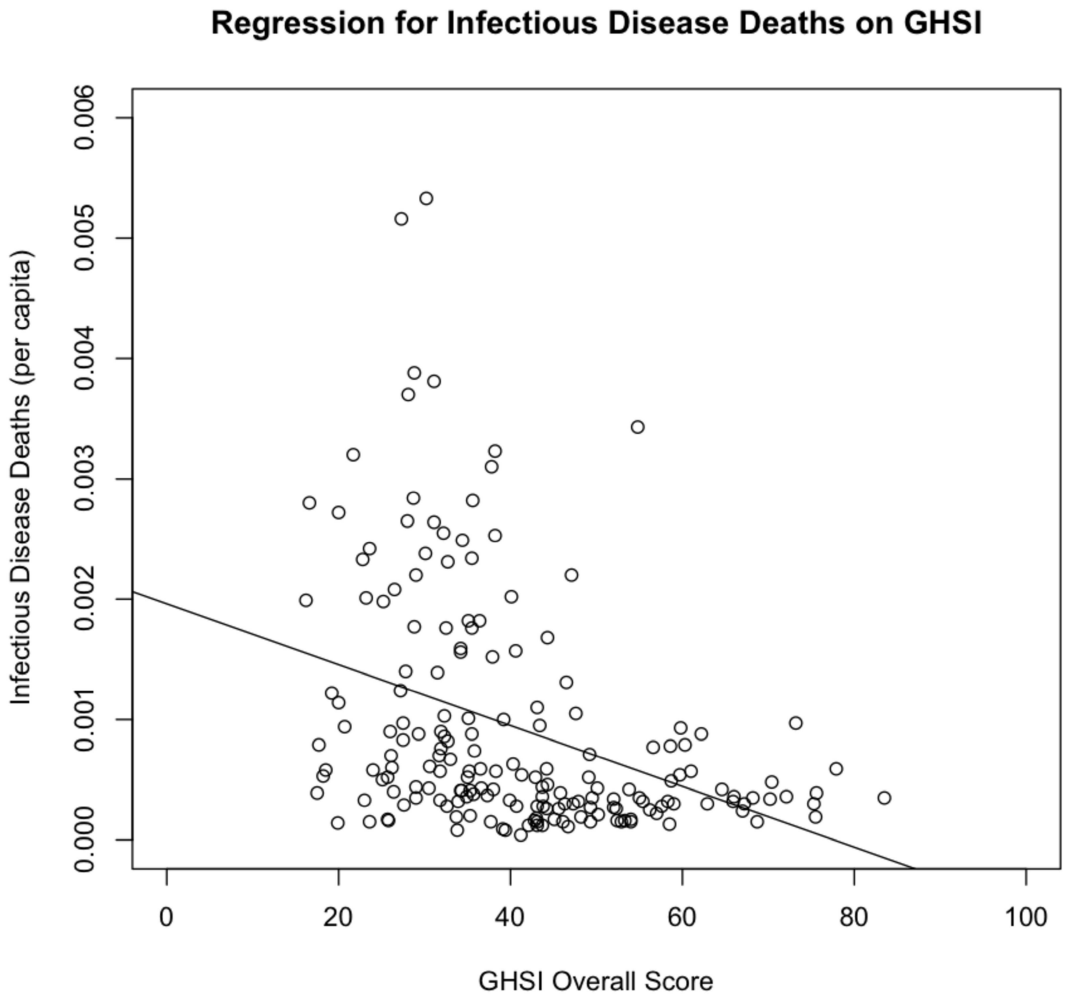
Figure S2: Education achievement (upper secondary completions in the population aged 25 and over vs GHSI overall score), with linear regression plotted.



GHSI and disease outcomes

To exclude possible confounding from maternal and neonatal death and nutritional disease, which are included in the data for 'Communicable disease deaths' as reported in the main body of the paper, we calculated the death per capita due to five infectious diseases tracked by the GBD project (HIV, tuberculosis, diarrhoeal disease, lower respiratory tract infection, and meningitis). We reported the correlation between this composite and GHSI scores in the body of the paper. Figure S3 displays this association.

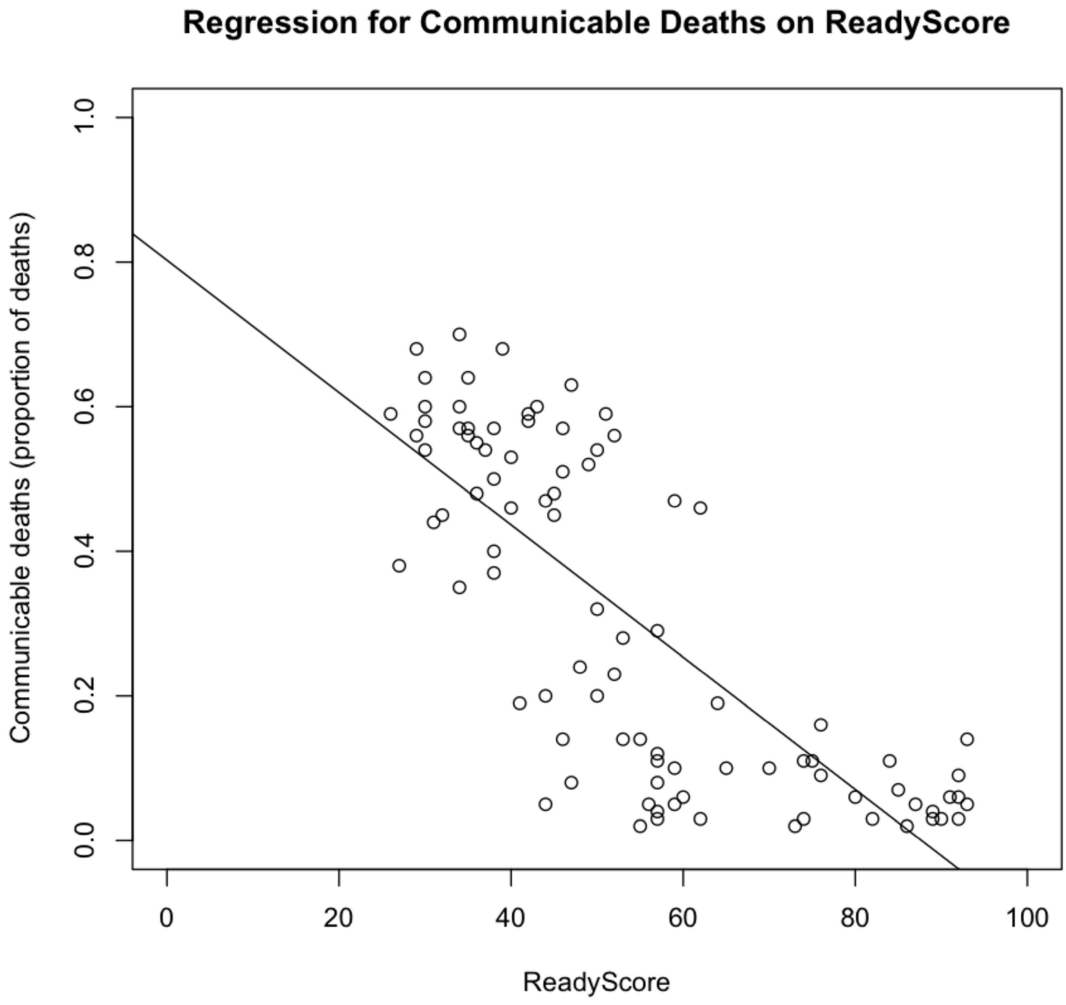
Figure S3: GHSI overall score vs Infectious disease deaths per capita per annum (with linear regression plotted)



ReadyScore and disease outcomes

In the main body of the paper, we report the association of GHSI scores with the proportion of deaths due to communicable diseases in each country. GHSI correlates with communicable deaths (rho = -0.56, $p < 0.0001$) and ReadyScore correlates with communicable deaths (rho = -0.78, $p < 0.0001$). Figure S4 displays the relationship between ReadyScore and communicable disease deaths.

Figure S4: ReadyScore vs proportion of population dying from communicable disease (with linear regression plotted)



Time to outbreak detection and communication

We piloted correlating GHSI scores with the time in days to outbreak detection and time to communication of an outbreak within countries. We did this by examining the mean time to outbreak detection (for those outbreaks listed in the WHO Outbreak News) as reported by Kluberg et al, aggregated by WHO region.[13] Unfortunately, this analysis was limited by there being only 6 data points (the WHO regions). However, we found that the lowest two regions by GHSI score had the longest time to communication of outbreaks. However, no further conclusions could be drawn.

GHSI and COVID-19

In a preprint, Maraghi et al report a moderate correlation on 14 April 2020 between total number of COVID-19 tests and GHSI overall score (0.43, $p = 0.007$) in high-income economies only.[8] This research suggests that there is little relationship between GHSI scores and COVID-19 total tests performed, recovery rate or case fatality ratio. However, we note that the pandemic may have been in its early stages in many countries on this date, that the authors looked only at countries with >1000 cases (countries doing well may have had far fewer), the measure of testing was total tests, not tests per capita, and as noted above not all GHSI items may be relevant to COVID-19. Finally, the strategy a country took will impact on tests and CFR.

In an exploratory analysis, we examined the number of COVID-19 tests per capita (per million) to control for population size. We also included all countries, not just those with more than 1000 cases. We found that on 28 April 2020, there was a statistically significant correlation between GHSI overall score and number of COVID-19 tests per million population (rho = 0.59, $p < 0.0001$). However, COVID-19 appears to have spread around the world by affecting higher income countries first (in Asia, Europe and North America), these countries also have higher GHSI scores (since GHSI is correlated with GDP per capita). Therefore, the number of cases may confound any association between GHSI and number of tests. We do note that by 17 May 2020, the correlation between GHSI and COVID-19 tests per million was unchanged (rho = 0.59, $p < 0.0001$). However, a complete analysis will need to wait until at least the first wave of the pandemic is over.

US GHSA investment and GHSI

Table S5: List of countries receiving US GHSA aid during 2014–2018 and their GHSI scores along with the GHSI scores of controls matched by WHO region and GDP per capita

Country receiving US GHSA investment	GHSI overall score	Matched country not receiving US GHSA investment	GHSI overall score
Bangladesh	35	Nepal	35.1
Burkina Faso	30.1	Togo	32.5
Cameroon	34.4	Zambia	28.7
Côte d'Ivoire	35.5	Zimbabwe	38.2
Guinea	32.7	Guinea-Bissau	20
Ethiopia	40.6	Gambia	34.2
India	46.5	Myanmar	43.4
Indonesia	56.6	Sri Lanka	33.9
Kenya	47.1	Nigeria	37.8
Liberia	35.1	Madagascar	40.1
Mali	29	Benin	28.8
Pakistan	35.5	Sudan	26.2
Senegal	37.9	Lesotho	30.2
Sierra Leone	38.2	Malawi	28
Tanzania	36.4	Mauritania	27.5
Uganda	44.3	Central African Republic	27.3
Vietnam	49.1	Mongolia	49.5
Cambodia	39.2	Papua New Guinea	27.8
Congo (Democratic Republic)	26.5	Niger	32.2
Georgia	52	Azerbaijan	34.2
Ghana	35.5	Angola	25.2
Haiti	31.5	Belize	31.8
Jordan	42.1	Tunisia	33.7
Kazakhstan	40.7	Turkey	52.4
Laos	43.1	Philippines	47.6
Malaysia	62.2	China	48.2
Mozambique	28.1	Burundi	22.8
Peru	49.2	Colombia	44.2
Rwanda	34.2	Chad	28.8
Thailand	73.2	Bhutan	40.3
Ukraine	38	Moldova	42.9
Mean	40.6		34.6

GHSA: global health security agenda, GHSI: global health security index.
Matching by GDP per capita was performed by matching to nearest GDP per capita country, within same WHO region, that was not a recipient of US GHSA investment.

SARS and GHSI

Table S6: **List of countries with one or more SARS cases in the 2003 pandemic and control countries matched by GDP per capita (globally)**

Country with SARS cases (2003)	GHSI Score (2019)	Matched country without SARS cases	GHSI Score (2019)
Malaysia	62.2	Argentina	58.6
Germany	66.0	Austria	58.5
Kuwait	46.1	Bahrain	39.4
Canada	75.3	Belgium	61.0
South Africa	54.8	Colombia	44.2
Romania	45.8	Croatia	53.3
New Zealand	54.0	Cyprus	43.0
Spain	65.9	Czechia	52.0
Singapore	58.7	Denmark	70.4
Vietnam	49.1	Egypt	39,9
Mongolia	49.5	eSwatini (Swaziland)	31.1
Sweden	72.1	Finland	68.7
Ireland	59.0	Iceland	46.3
United Kingdom	77.9	Israel	47.3
United States	83.5	Japan	59.8
China	48.2	Mexico	57.6
Australia	75.5	Netherlands	75.6
India	46.5	Nigeria	37.8
Switzerland	67.0	Norway	64.6
Thailand	73.2	Peru	49.2
Italy	56.2	Portugal	60.3
South Korea	70.2	Saudi Arabia	49.3
France	68.2	Slovenia	67.2
Indonesia	56.6	Sri Lanka	33.9
Russia	44.3	Turkey	52.4
Philippines	47.6	Ukraine	38.0
Mean	60.5		52.3

GHSI: global health security index

Note that matching by GDP per capita was performed globally, rather than by WHO region, because high income SARS affected countries such as Canada and the United States lack closely matched peers by GDP per capita in their WHO region.

MERS and GHSI

Table S7: **List of countries with one or more MERS cases and control countries matched by GDP per capita and WHO region**

Country with MERS cases	GHSI (2019)	Matched country with no MERS cases	GHSI (2019)
Algeria	23.6	eSwatini (Swaziland)	31.1
Yemen	18.5	Sudan	26.2
Egypt	39.9	Djibouti	23.2
Tunisia	33.7	Pakistan	35.5
Jordan	42.1	Morocco	43.7
Lebanon	43.1	Libya	25.7
Oman	43.1	Hungary	54
Saudi Arabia	49.3	Estonia	57
Bahrain	39.4	Portugal	60.3
Kuwait	46.1	Malta	37.3
United Arab Emirates	46.7	Andorra	30.5
Qatar	41.2	Iceland	46.3
Iran	37.7	Syria	19.9
Turkey	52.4	Bulgaria	45.6
Greece	53.8	Slovakia	47.9
Italy	56.2	Spain	65.9
France	68.2	Israel	47.3
United Kingdom	77.9	Sweden	72.1
Germany	66.0	Belgium	61
Austria	58.5	Finland	68.7
Netherlands	75.6	Denmark	70.4
United States	83.5	Canada	75.3
Thailand	73.2	Sri Lanka	33.9
Philippines	47.6	Papua New Guinea	27.8
China	48.2	Mongolia	49.5
Malaysia	62.2	Argentina	58.6
South Korea	70.2	Brunei	32.6
Mean	**51.8**	**Mean**	**46.2**

GHSI: global health security index

Note that matching by GDP per capita was performed by WHO region where possible, but the number of countries exposed to MERS in the Middle East meant that some matching by GDP outside of WHO region was required.

Table S8: Mean GHSI scores by category for countries with previous MERS cases vs matched countries without MERS cases.

	GHSI total	Prevent	Detect	Respond	Health system	Norms	Risk environment
Control countries	46.20	41.52	49.60	41.66	34.69	50.47	63.59
MERS countries	51.8	47.7	58.1	50.8	40.5	52.1	63.2
Difference	+5.58	+6.20	+8.54	+9.17	+5.77	+1.61	-0.38
p	0.055	0.082	0.043	0.023	0.088	0.634	0.859

Ebola and GHSI

Table S9: **List of countries with one or more Ebola outbreaks since 1976 and control countries matched by GDP per capita and WHO region**

Country with Ebola outbreak	GHSI	Matched control	GHSI
Sierra Leone	38.2	Mozambique	28.1
Congo (Democratic Republic)	26.5	Madagascar	40.1
Uganda	44.3	Togo	32.5
Liberia	35.1	Burkina Faso	30.1
Guinea	32.7	Guinea-Bissau	20
Mali	29.0	Benin	28.8
Senegal	37.9	Cameroon	34.4
Côte d'Ivoire	35.5	Kenya	47.1
Nigeria	37.8	Zimbabwe	38.2
South Africa	54.8	Namibia	35.6
Gabon	20.0	Botswana	31.1
South Sudan	21.7	Syria	19.9
Congo (Brazzaville)	23.6	Ghana	35.5
Mean	**33.62**	**Mean**	**32.42**

Table S10: Mean GHSI scores by category for countries with previous Ebola outbreaks vs matched countries without Ebola outbreaks

	GHSI Total	Prevent	Detect	Respond	Health system	Norms	Risk environment
Control countries	32.42	26.07	37.39	30.95	14.62	46.85	40.70
Countries with Ebola outbreaks	33.62	25.48	35.98	36.21	16.09	52.01	36.82
difference	+1.21	-0.59	-1.42	+5.26	+1.48	+5.16	-3.88
p	0.69	0.85	0.82	0.26	0.63	0.16	0.17

GHSI and COVID-19 Response: Case studies of the United States and United Kingdom

The COVID-19 pandemic has raised important questions about the GHSI and whether it tracks response capability to communicable disease.[16] The US and UK response has appeared poor during the early stages of the pandemic given their GHSI scores, although it is possible that countries performing 'poorly' at one point in time may yet look successful in the future (eg, if they develop vaccines and roll out vaccination quickly). However, there is much more to the story than raw GHSI score. We must look to gaps in GHSI scores by country. No country is fully prepared, critical 'zeroes' might make all the difference, and capability does not equal execution. We must look also to gaps in the GHSI itself to see what is important but not measured in the index. The GHSI emphasises that no country is fully prepared for epidemics or pandemics and every country has gaps. The responses to COVID-19 have underscored that, 'capacity alone is insufficient if that capacity isn't fully leveraged'.[11]

The US has the highest 2019 GHSI score but does not appear to have optimally responded to COVID-19, having the highest number of deaths of any country as at 26 May 2020 and the 12th most deaths per million population. However, one of the authors of the GHSI has noted that the US still had important gaps including in 'health system', where access to care is ranked only 175th out of 195 countries, and that additionally the WHO ranked the US only 75th for number of hospital beds per capita in 2013. This commentary also noted that the US also scores well down the rankings for political and security risks, socio-economic resilience, and public confidence in government, all of which can impact response.[11] Also, the GHSI is based on national information, and cannot determine local capacity in a federal system. The US also actively subverted the global response (by not endorsing WHO test kits and withdrawing funding from WHO). Furthermore the 2019 'Clade X' biothreat simulation exercise found 'leadership challenges were hardwired into the American system'.[17] The US is also home to many undocumented migrants who might avoid seeking medical contact, many US citizens have no health insurance (worsened through unemployment during a pandemic), and there is also a polarised media and rampant misinformation and disinformation on social and mainstream media.

A priori the GHSI score in 2019 would predict that the UK's overall response to COVID-19 would be good (overall score 77.9/100) but will be limited by: A lack of field epidemiologists, few doctors, nurses, and hospital beds per capita, no ability to receive foreign health personnel, no plan for vulnerable populations, no plan to prioritise healthcare for health workers, no plan for personal protective equipment (PPE) supply issues, not enough domestic spending on health per capita, limited public-private healthcare communication, low public confidence in government, and international tensions. The UK scores less than 50 for these indicators and zero for many. In fact there are 19 GHSI indicators where the UK scores zero, these are:
1.2.1c) Cross-ministerial department/agency/unit for zoonotic disease
1.2.3a) Annual reporting to OIE on zoonotic disease incidence
1.3.1d) Consolidation of especially dangerous pathogens into minimum # of facilities
1.3.2a) Biosecurity training using a standardised, required approach
1.4.2a) Biosafety training using a standardised, required approach
1.5.1a) Evidence of national assessment of dual use research
1.5.2a) Requirement to screen synthesised DNA against list prior to sale
2.3.2a) Evidence of at least 1 trained field epidemiologist per 200,000 people
3.1.1c) Vulnerable populations in national public health emergency response plan
3.3.1c) EOC activation within 120 minutes of identification of emergency/scenario
4.2.3a) Plan to receive foreign health personnel during a public health emergency
4.3.2a) Government prioritisation of care for healthcare workers during response
4.4.1b) Inclusion of public and private sector in healthcare communication system
4.5.1a) Plan to address routine and public health emergency PPE supply issues
5.4.1b) Completion and publication of a NAPHS or GHSA roadmap
5.4.2a) Completion and publication of PVS report (past five years)
5.4.2b) Completion and publication of PVS gap analysis (past five years)
5.5.1a) National budget to address gaps identified in JEE, NAPHS or GHSA roadmap
5.5.1b) National budget to address gaps identified in PVS assessment or gap analysis

A look at all the indicators where the UK scores less than two-thirds (outside of the GHSI tertile of 'most-prepared'), suggests that priority issues for UK health security include a need for: more focus on zoonotic disease and veterinary capability, standardising biosecurity and biosafety training, assessing dual use research and screening synthesised DNA, investment in more epidemiologists, doctors, nurses, hospital beds, formulation of a plan to prioritise healthcare worker care during an event, improve communication with private sector health care workers, ensure PPE supplies, completion of a health security roadmap (NAPHS) and performance of

veterinary services (PVS) gap analysis, and budget to implement these plans, and improve air transport services (Table S11).

Table S11: **GHSI sub-indicators where the UK scores < 66.7/100, for all indicators where the UK scores < 66.7/100. Exceptions noted.**

Sub-indicator	Score (/100)
1.2.1c) Cross-ministerial department/agency/unit for zoonotic disease	0
1.2.3a) Annual reporting to OIE on zoonotic disease incidence	0
1.2.4a) Number of veterinarians per 100,000 people	20.1
1.2.4b) Number of veterinary para-professionals per 100,000 people	2.2
1.3.2a) Biosecurity training using a standardised, required approach [*note overarching indicator (1.3) score is 69.3/100, so not technically below 66.7, but included as very similar issue to next item*]	0
1.4.2a) Biosafety training using a standardised, required approach	0
1.5.1a) Evidence of national assessment of dual use research	0
1.5.2a) Requirement to screen synthesised DNA against list prior to sale	0
2.3.2a) Evidence of at least 1 trained field epidemiologist per 200,000 people	0
4.1.1a) Doctors per 100,000 people	37.4
4.1.1b) Nurses and midwives per 100,000 people	40.8
4.1.2a) Hospital beds per 100,000 people	19.7
4.3.2a) Government prioritisation of care for healthcare workers during response	0
4.4.1b) Inclusion of public and private sector healthcare workers in healthcare communication system	0
4.5.1a) Plan to address routine and public health emergency PPE supply issues	0
5.4.1b) Completion and publication of a NAPHS or GHSA roadmap	0
5.4.2a) Completion and publication of PVS report (past five years)	0
5.4.2b) Completion and publication of PVS gap analysis (past five years)	0
5.5.1a) National budget to address gaps identified in JEE, NAPHS or GHSA roadmap [*Note, overarching indicator (5.5) scores exactly 66.7, so these weaknesses were included*]	0
5.5.1b) National budget to address gaps identified in PVS assessment or gap analysis [*Note, as item above*]	0
6.3.2a) Adequacy of airports *Note, overarching indicator (6.3) scores exactly 66.7, so these weaknesses were included*	50
6.4.1a) Urban population (% of total population)	19.4
6.4.2a) Change in forest area (percentage points)	59.6

GHSA: global health security agenda, JEE: joint external evaluation, NAPHS: national action plan for health security, OIE: World Organization for Animal Health, PPE: personal protective equipment, PVS: performance of veterinary services

These case studies of the two highest scoring countries by GHSI merely reiterate the overall GHSI Report finding that no country is fully prepared for significant biothreats and the world must do more.

Provisional analysis around cost-effectiveness

In association with the main study we performed a coarse exploratory cost-effectiveness analysis on increasing GHSI scores.

A crude cost-effectiveness estimate using data obtained for this study
According to the CDC's GHSA Annual Report 2019, the US obligated $850 million (m) 2014–2018.[12] We estimated ongoing global investment need from the difference in GHSI scores between GHSA recipient and non-GHSA recipient nations. The 31 recipient nations score a total of 186 points higher in GHSI overall score equating to $4.6m per GHSI point difference. Extrapolating, it would cost $31 billion (b) to bring all 195 countries up to GHSI of 75/100. Assuming 50% annual maintenance costs, this is $93b over five years, or $18.6b per annum. The difference between a GHSI score of 75 and the current global mean of 40.2 is 34.8 points. The regression model that included just GHSI, GDP per capita and population, suggests that this would equate to a 16.7% reduction in the proportion of deaths due to communicable diseases.

The annualised cost of influenza pandemics has been estimated at $570b including mortality.[20,21] Inflating this figure to 2020, and adding the estimated costs of SARS, MERS, Zika virus, and Ebola (annualised for the 20-year period 2001–2020), this figure reaches $622b per annum, and plausibly could be increased much further since COVID-19 is not yet included. Supplementary Table S12 shows these costs and potential cost-effectiveness of investment in preparedness. The return on investment ranges from 334% to 1672% for reductions to the impact of biothreats of 10% to 50%.

Table S12: Global costs (all US$) of biothreats, preparedness investment needs, and estimated return on investment (excluding spill-over benefits to antimicrobial resistance control, control of tuberculosis, and other endemic diseases, the costs of COVID-19, and the potential costs of existential risks)

Annualised cost of biothreats	Investment in preparedness per annum (based on GHSI shortfall)	Reduction in impact of bio-threats (assumed)	Costs averted	Return on investment per annum
$622b	$18.6b	10%	$62.2b	334%
$622b	$18.6b	20%	$124.4b	669%
$622b	$18.6b	50%	$311b	1672%

Costs are in billions of US dollars. The $622b figure is anchored by $570b reported by Fan et al.[20,21] but adjusted up for inflation and annualised costs of outbreaks in the last 20 years other than pandemic influenza (including SARS, MERS, Ebola, Zika, but excluding COVID-19, which all total at least a further $5.5b per annum) as described below. Accounting for COVID-19, as a once-in-a-century non-influenza pandemic, then likely actual costs are substantially higher. The $18.6b annual investment needed is based on the cost per GHSI point difference between US GHSA aid recipient nations and matched controls as reported in Table 3 (main text).

Justification for cost-estimates of biological threats
One published estimate suggests an influenza pandemic could cost 4.8% of global GDP.[18] The GDP loss of the 1918 influenza pandemic in the UK was estimated at 17%.[19] There is at least one serious pandemic per century and a 20% chance of four or more.[2] Costing papers by Fan et al are widely cited and estimate economic costs and monetised life lost for influenza pandemics across time and annualise this to a figure of US$570b ($616.6b in 2020), including an average of $80b economic losses and $490b mortality costs per year (note this is a lower bound, because revealed preference – through government actions – shows mortality costs were valued extremely highly during COVID-19).[20 21] According to Fan et al the annualised cost of non-seasonal influenza pandemics is comparable to the projected impact of climate change.[20] Factors such as increasing globalisation may even magnify these impacts,[22] and the COVID-19 pandemic could cost even more than models of pandemic influenza suggest, with the IMF estimating $9 trillion (approximately 10% of global GDP in 2020).[23]

However, to this we must add non-influenza pandemics (eg SARS, Zika), costly non-pandemic outbreaks (eg MERS, Ebola), as yet unknown outbreaks (laboratory accidents, deliberate biological events), as well as rare but extreme events in the long distributional tail, as predicted by power laws, for which there is no precedent and which likely contain most of the deaths and therefore most of the cost.[24 25] We can estimate some of the costs of these by adding the impact of the events of 2000–2020 (ie, SARS $18–40 billion (b), 2003 [26] + MERS $10b, 2015 [27] + Ebola $53b, 2014 [28] + Zika $7b, 2016 [19]), not to mention the severe demand and supply shocks of COVID-19,[29] and divide by 20 years. Even excluding COVID-19 this could add more than $5.5b per annum in

present day expected costs and we still need to consider the economic impact of diseases such as tuberculosis ($12b per year) and antimicrobial resistance, which is projected to be measured in trillions by mid-century.[30] All these costs could be mitigated by effective health security measures. Therefore, the expected costs of biological threats are vast and conservatively surpasses $100b per year in direct costs, and considerably more than $600b when including mortality. Important for equity, the percentage of GDP lost to pandemics varies regionally and is greatest in Africa and South Asia,[31] and productivity loss is greatest in low- and middle-income countries.[32]

The cost of mitigation

Published estimates of the investment needed to bring the world up to a minimum appropriate level of health security include those initially estimated by the World Bank ($1.9–3.4b per year over 5 years),[31] which were doubled in a 2019 World Bank update of pandemic preparedness financing.[33] The WHO estimated $100b over five years in 67 low and middle-income countries,[29] and the US National Academy of Sciences estimated $4.5b per year as a minimum.[2] Costing tools exist to estimate the cost of bringing countries up to compliance with the IHR,[34] for example a case study calculation for Nigeria resulted in 5-year cost estimates from $66m–612m across three costing methods.[35]

In this study we estimated the investment needed based on the association of US GHSA investments with GHSI scores by making the assumption that the US investment was responsible for any difference in scores between recipient countries and matched controls, and then extrapolating this globally. The 31 recipient nations score a total of 186 GHSI points higher. The CDC reports that the US has invested $850m,[12] which equates to $4.6m per additional point.

The cost-effectiveness of mitigation

Several reviews have examined the cost-effectiveness of pandemic interventions.[36 37] However, less studied is the cost-effectiveness of pre-emptive health security. Knowing the costs of biothreats and the investment needed to implement mitigation (as detailed above), we can estimate this cost-effectiveness. Cost-effectiveness can be based on direct economic costs, or inclusive costs (with mortality monetised). Some previous estimates of the cost-effectiveness of pandemic preparation, biothreat mitigation or existential risk aversion have assumed reduction in impact of biothreats of 1, 20, 50 or 100%.[24 38] An analysis of the cost-effectiveness of reducing the probability of existential biothreats by 1% reported a result ranging from 13 cents to $1600 per life year saved.[24]

Further discussion of cost-effectiveness

The estimate of cost-effectiveness that we report is likely a large underestimate because it excludes spill-over benefits for mitigating antimicrobial resistance, tuberculosis and other infectious diseases, it also excludes the expected cost of existential risk. Additional, more nuanced cost-effectiveness analysis is needed with a particular focus on the return on investment for donor countries due to improvements in health security in recipient countries. Additional factors also warrant consideration, including time-to-pandemic analysis,[39] and the ways in which catastrophe can change probabilities, risk appetite, and therefore calculus of risk.[40] Also, regional cooperation and sharing of specialist facilities might deliver better preparedness and be more cost-effective.[31]

Our results suggest a limited correlation between percentage of GDP spent on health and GHSI scores. This is important because the 2001 Abuja Agreement pushed for 15% of GDP to be spent on healthcare in African nations.[41] This limited correlation coupled with our additional finding that GHSA investment is associated with higher GHSI scores, may suggest that investments through the GHSA (or related programmes, and by many other countries other than just the US) could be a more effective avenue for improving health security than spending more and more of GDP on health. This possibility should be explored further.

SUPPLEMENTARY NOTES ON RISK AND RESPONSE

Ultimately, the world needs capability to test for all pathogens, perhaps through metagenomic sequencing, to rapidly develop vaccines, and produce broad-spectrum antivirals. We should determine criteria for when travel restrictions or lock-downs are effective,[42] national pandemic plans need to be tailored to all pandemics not just influenza and should include qualitatively different approaches for unprecedented situations (tested through simulation exercises).

It will be necessary to clearly assign responsibility for these novel measures to particular national and international organisations. One option for high-income nations are health security institutions with a clear vision on biodefence and advanced high-potential research. Such institutions should be capable of prioritising

action based on risk assessment and cost-effectiveness, not neglecting lower probability, high consequence threats. This could help national governments increase their preparedness and ensure their capability is fully realised in a crisis. Investments in the GHSA and similar programmes look worthwhile, perhaps focusing on the weakest GHSI categories (health systems, and prevention, particularly in the WHO Africa Region) as well as the very neglected indicators such as biosecurity, biosafety, dual use research oversight, and linking public health with security agencies, both at home and abroad.

Our discussion in the main body of the paper suggests on the one hand that the GHSI doesn't go far enough and there are factors that will need addressing beyond the 140 items of the GHSI. There is clearly yet more to be done. On the other hand, many countries are still not compliant with the IHR and there is an argument that this must be the focus for health security efforts. High-income nations could aim to elevate their GHSI scores to 100/100, whilst also addressing those aspects of preparedness that are important but lie beyond the scope of GHSI (including: intelligence services, cyber-biosecurity, performing root cause analysis of laboratory incidents, developing the biotechnology sector (which must form part of the solution to biothreats), or addressing misinformation.

High-income countries should also use their leadership and convening power to ensure cooperation rather than a patchwork of national and regional responses. There is a serious risk in the present geopolitical climate that countries act too autonomously and miss opportunities for cost-effective collective action. Work towards a heads of state summit with a special focus on anthropogenic risks and deliberate biological events seems highly desirable. National health systems must be strengthened around the world and partnerships will be crucial.[43]

An outbreak anywhere can potentially impact everywhere. It is in all nations' self-interest to support prevention, detection and response globally. Every person needs access to healthcare and there must be secure funding and sustainable financing plans, with appropriate authority to spend and act. The GHSI Report states that health security preparedness financing should be treated as a top priority for global health and international defence, peace, and security.[6]

The GHSA is renewed until 2024 and has 67 members, covering 6 billion people. The GHSA calls for tangible commitments at the highest level, the use of tools (action packages, metrics) and mobilising of funding. The $1b US investment correlated with higher GHSI scores and GHSI correlated with less death from communicable disease. Leverage of these existing institutions and mechanisms provides an immediate path forward. But new ones are likely to be needed. We have suggested that some countries could look to establish biosecurity institutes that can fast-track fresh thinking, innovative technologies and deduce priorities for action.

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