Validation analysis of Global Health Security Index (GHSI) scores 2019

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ABSTRACT

Introduction The COVID-19 pandemic powerfully demonstrates the consequences of biothreats. Countries will want to know how to better prepare for future events. The Global Health Security Index (GHSI) is a broad, independent assessment of 195 countries’ preparedness for biothreats that may aid this endeavour. However, to be useful, the GHSI’s external validity must be demonstrated. We aimed to validate the GHSI against a range of external metrics to assess how it could be utilised by countries.

Methods Global aggregate communicable disease outcomes were correlated with GHSI scores and linear regression models were examined to determine associations while controlling for a number of global macromeasures. GHSI scores for countries previously exposed to severe acute respiratory syndrome (SARS), Middle East respiratory syndrome and Ebola and recipients of US Global Health Security Agenda (GHSA) investment were compared with matched control countries. Possible content omissions in light of the progressing COVID-19 pandemic were assessed.

Results GHSI scores for countries had strong criterion validity against the Joint External Evaluation ReadyScore (rho=0.82, p<0.0001), and moderate external validity against deaths from communicable diseases (r=−0.56, p<0.0001). GHSI scores were associated with reduced deaths from communicable diseases (F3, 172=22.75, p<0.0001). The proportion of deaths from communicable diseases decreased 4.8% per 10-point rise in GHSI. Recipient countries of the GHSA (n=31) and SARS-affected countries (n=26), had GHSI scores 6.0 (p=0.0011) and 8.2 (p=0.0010) points higher than matched controls, respectively. Biosecurity and biosafety appear weak globally including in high-income countries, and health systems, particularly in Africa, are not prepared. Notably, the GHSI does not account for all factors important for health security.

Conclusion The GHSI shows promise as a valid tool to guide action on biosecurity, biosafety and systems preparedness. However, countries need to look beyond existing metrics to other factors moderating the impact of future pandemics and other biothreats. Consideration of anthropogenic and large catastrophic scenarios is also needed.

INTRODUCTION

International efforts to mitigate biothreats are grounded in the 2005 International Health Regulations (IHR), which require countries to prevent, detect and respond to emerging threats. Nations self-report their IHR compliance annually through a monitoring tool.

Key questions

What is already known?

- The report on the Global Health Security Index (GHSI) was published in October 2019 to benchmark preparedness for biothreats and showed that the world is not prepared.
- A number of global organisations have described health security weaknesses and called for action, including the United Nations, World Bank, WHO and Global Preparedness Monitoring Board.
- Few studies have attempted to validate metrics of global health security and no studies have linked GHSI scores to global health security investments or previous experience with outbreaks, and there is little published critical appraisal of the GHSI to date.

What are the new findings?

- This study determined the association of GHSI scores with outcomes of communicable diseases, therefore providing some degree of concurrent and external validation of the tool.
- Results reveal associations between GHSI scores and general education, Global Health Security Agenda investment and previous experience with severe acute respiratory syndrome.
- The study highlights the breadth of the GHSI in comparison to Joint External Evaluations (JEE), but reveals some factors relevant to mitigating high-consequence biothreats yet to be addressed by the GHSI.

What do the new findings imply?

- The GHSI is the most comprehensive tool released to date for benchmarking countries’ capability to prevent and manage communicable disease and exhibits some validity against related tools and common disease outcomes.
- Given the clear lack of health security capability, countries (especially those who have not completed a JEE) should look to the GHSI, which goes beyond the requirements of the International Health Regulations and JEE, for actionable steps they can take to reduce the impact of future biothreats.
- However, action also needs to move beyond the GHSI to successfully anticipate and mitigate potentially very high consequence and as yet unprecedented events.
(International Health Regulations Monitoring Tool, IHRMT) developed by the WHO and can voluntarily undertake a Joint External Evaluation (JEE) to evaluate their level of compliance. The JEE is a multisectoral process and consists of a country self-assessment, which is shared with an external team of WHO and non-WHO experts, who then visit and make a week-long independent assessment.2

The Global Health Security Agenda (GHSA) was established in 2014 to stimulate better IHR compliance and improve epidemic detection, preparedness and response. A number of countries have additional programmes focused on global health security capabilities, such as Public Health England’s IHR Strengthening Project. However, reports from the United Nations, World Bank, Global Preparedness Monitoring Board and US National Academy of Sciences have criticised ongoing lack of preparedness globally.3–6 GHSA investment has built capacity equivalent to raising JEE scores in some countries,7 and was renewed to 2024.8

Given the large self-assessment component and the facilitation of JEE by discussions, the JEE process may be subject to self-assessment bias. There may also be selection bias in which countries have so far requested a JEE. As of 31 July 2020, 110 countries had completed such an assessment.10 Furthermore, many factors contribute to the emergence and mitigation of biothreats beyond those measured by the JEE. Prior to 2019, there existed no objective, sufficiently broad, universal metric assessed independently. This led to the development of the Global Health Security Index (GHSI) by the Nuclear Threat Initiative, Johns Hopkins Centre for Health Security and the Economist Intelligence Unit.11–13 A similar metric is the Epidemic Preparedness Index tool, also published in 2019 but with fewer countries and indicators included.14 This present paper focuses on the GHSI.

The GHSI is scored by examining published and publicly available evidence across six categories (prevention, detection, rapid response, health system, commitments to international norms and risk environment) with the intention of encouraging nations to document and publicise their preparations.12 The GHSI points explicitly to very high-consequence events, robust health systems, commitments to international norms, the risk environment and is therefore a much broader assessment than the JEE. By requiring published evidence, the GHSI aimed to ensure there is no suspicion that nations are not prepared and shows all nations their preparedness gaps. Like the JEE, the GHSI may be prone to certain biases, such as overlooking measures that are in place but not documented. However, to date there is no gold standard in measuring global health security and the JEE and GHSI approaches are both likely to be limited and incomplete.

Commentary on the GHSI generally laments weak preparedness,11 15 even among relatively rich countries.16 New Zealand authors identified the nation’s low scores and highlight the implications for Pacific regional health security.17 A letter has critiqued the UK and US responses to COVID-19, and calls into question the value of GHSI if these are the top scoring nations.18 Another brief commentary has critiqued the focus of the GHSI, its reliance on published data only and questions whether the GHSI offers any added value.19 However, there is as yet no in-depth critical appraisal or external validation of the GHSI tool in the literature published to date to our knowledge.

The IHRMT, JEE and GHSI are only useful if they have reasonable validity, if they cover the relevant domains, if scores bear some relationship to experience and actual health outcomes, if action can improve scores and if countries then implement what they recommend. Few attempts to validate the IHRMT and JEE have been made.20 21 and the validity of IHR compliance and JEE evaluations has been called into question.22 Therefore, the validity of the GHSI needs to be assessed.

Assessing the validity of an index requires several evaluations. These include the face validity (does it look right?), the content validity (does it include all the items it should?), the construct validity (do scores have the expected relationships with other variables?), criterion validity (do scores align with other measures of the same thing?), concurrent or predictive validity (do scores map to outcomes of interest?), as well as internal consistency and test–retest reliability.23

After the COVID-19 pandemic experience in 2020, countries will be looking for actionable steps to find weaknesses, mitigate risk and where to direct efforts to reduce any future impact of COVID-19 and other biothreats. The GHSI is the most comprehensive tool with the aim of supporting these tasks. Therefore, it was our aim to examine the content, construct, criterion and concurrent validity of the GHSI and therefore provide countries with some account of its relevance and limitations. In evaluating the validity of the GHSI we expected that GHSI scores should be positively correlated with existing measures of health security and negatively correlated with harm from communicable diseases. On the basis of our validation analyses, along with our interpretation of the GHSI scores as published, we explore how the GHSI might be used by countries.

METHODS
We evaluated the criterion validity of the GHSI by correlating GHSI with the JEE ReadyScore (as explained below). We evaluated the construct validity by comparing the GHSI scores of countries receiving US GHSA investments to those that did not, as well as the GHSI scores of countries previously exposed to severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS) and Ebola versus those that were not. We evaluated the concurrent validity by correlating aggregate measures of communicable disease outcome with GHSI scores. Finally, we evaluated the content validity by considering whether responses to the COVID-19 pandemic suggest items the GHSI has overlooked.
Criterion validation of GHSI was performed by calculating correlations between GHSI overall score and the JEE ReadyScore. The JEE ReadyScore is a single summary metric of JEE results and is derived as the average of the scores for the 19 JEE domains expressed as a score from 0 to 100.\(^2\) Given that both metrics can be interpreted as global measures of health security, we therefore expected GHSI scores to correlate with ReadyScore.

Concurrent validation was performed by calculating correlations between GHSI and the proportion of deaths in each country due to communicable disease. We obtained data for the percentage of the population in each country dying from communicable diseases.\(^3\) Given that the dataset for this metric included nutritional diseases and maternal and neonatal deaths, we also obtained more focused data for an aggregate of deaths per capita per annum from five relevant communicable diseases as reported in data from the Global Burden of Disease Study (diarrhoeal disease, HIV, lower respiratory tract infection, meningitis and tuberculosis).\(^4\)

Linear regression was performed to evaluate associations between GHSI as the independent variable and communicable disease deaths as the dependent variable. In order to control for potential major confounders in our analyses, we obtained data describing countries’ gross domestic product (GDP) per capita,\(^5\) percentage of GDP spent on health,\(^6\) population size,\(^7\) political stability (as measured by the proportion of the population over 25 years of age that was not a recipient of US GHSA aid. GDP per capita was chosen given that the GHSI report authors describe a moderate correlation between GHSI and GDP per capita. A list of all countries and controls is presented in online supplemental table S5.

It might be supposed that countries can learn from previous epidemics and therefore those countries that were exposed to some previous epidemic might have improved health security capability. It has been specifically suggested that countries exposed to the SARS pandemic in 2003 have managed the COVID-19 pandemic better than other countries.\(^8\) We assumed that some institutional memory exists and chose SARS as a previous major biothreat that affected a sufficiently large number, though not all, countries. If GHSI is a valid measure of health security, we expected scores would be higher in countries that had cases of SARS in 2003 compared with matched controls. For this analysis countries were matched by GDP per capita alone, rather than within WHO region, due to difficulty matching the USA and Canada to countries with near GDP per capita within WHO region. SARS exposure was obtained from the WHO summary of probable SARS cases.\(^9\) We performed the same analysis for countries that experienced MERS cases\(^10\) and those having Ebola outbreaks.\(^11\)

Content validity must be assessed by expert inspection of the items in an index. We examined the WHO COVID-19 situation reports and sought examples of responses to COVID-19 by high and low-scoring GHSI countries in order to determine whether there appeared to be factors important for health security that are not adequately captured by the GHSI. We report on a number of such factors.

Correlations and multiple regressions were performed with R (V.3.1.0). Differences between means were calculated using two-tailed paired t-tests in Microsoft Excel (V.16.37).

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This study was funded by the Strategic Priorities Fund and the Open Philanthropy Project. These funders had no input into study design, collection, analysis, or interpretation of data, written outputs or the decision to submit for publication. Patients or the public were not involved in the design, or conduct, or reporting or dissemination plans of our research.

RESULTS
Macroindices and GHSI scores
For reference, the mean GHSI scores by WHO region are reproduced in online supplemental table S2. Correlations between macroindices and GHSI scores are displayed in table 1. There is a very strong correlation between GHSI and ReadyScore. The proportion of the population that completed upper secondary school shows a moderate but highly significant correlation with GHSI score. This correlation is stronger than that for GDP, population, health spending and political stability, although all showed statistically significant correlations and were included in regression analyses. In multiple linear regression to examine any relationship between GHSI and the other macroindices (excluding ReadyScore), a significant regression equation was found ($F(5,149)=29.51$, $p<0.001$).
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Communicable diseases and GHSI scores

Table 1 shows the correlations between ReadyScore as well as GHSI scores and two measures of communicable disease deaths. We found a strong negative correlation between ReadyScore and communicable disease deaths and a moderate but significant negative correlation between GHSI overall score and communicable disease deaths.

Multiple linear regression to explore the association between GHSI and communicable disease deaths, while controlling for GDP per capita and population size, revealed a significant regression equation ($F(3, 172)=22.75, p<0.0001$), with an $R^2$ of 0.28. The proportion of the population dying from communicable diseases decreased 4.8% for each 10-point rise in GHSI (figure 1).

GDP per capita was also associated with communicable deaths, but this association was no longer significant when controlling for education, political risk and health on February 12, 2021 by guest. Protected by copyright.

### Table 1 Spearman correlations (p value) between GHSI categories and some global macroindicators

| Score/score component | ReadyScore (average of 19 JEE domains) | Education (population over 25 years that completed upper secondary) | GDP per capita (US$) | Population size | Health spend (% of GDP) | Political stability and absence of violence/terrorism index |
|-----------------------|----------------------------------------|---------------------------------------------------------------|---------------------|----------------|----------------------|----------------------------------------------------------|
| GHSI total            | 0.82 (<0.0001)                         | 0.57 (<0.0001)                                               | 0.56 (<0.0001)      | 0.36 (<0.0001) | 0.32 (<0.0001)       | 0.25 (0.00041)                                           |
| Prevent               | 0.79 (<0.0001)                         | 0.56 (<0.0001)                                               | 0.52 (<0.0001)      | 0.40 (<0.0001) | 0.35 (<0.0001)       | 0.18 (0.012)                                             |
| Detect                | 0.66 (<0.0001)                         | 0.41 (<0.0001)                                               | 0.37 (<0.0001)      | 0.42 (<0.0001) | 0.25 (0.0006)        | 0.05 (0.50)                                              |
| Respond               | 0.67 (<0.0001)                         | 0.37 (<0.0001)                                               | 0.40 (<0.0001)      | 0.35 (<0.0001) | 0.28 (0.00012)       | 0.17 (0.017)                                             |
| Health system         | 0.80 (<0.0001)                         | 0.56 (<0.0001)                                               | 0.56 (<0.0001)      | 0.34 (<0.0001) | 0.33 (<0.0001)       | 0.22 (0.0019)                                            |
| Commitments           | 0.41 (<0.0001)                         | 0.30 (<0.0001)                                               | 0.24 (0.0013)       | 0.35 (<0.0001) | 0.19 (0.0098)        | 0.10 (0.17)                                              |
| Risk environment      | 0.81 (<0.0001)                         | 0.64 (<0.0001)                                               | 0.91 (<0.0001)      | −0.24 (0.001)  | 0.32 (<0.0001)       | 0.78 (<0.0001)                                           |

Spearman’s rho reported, note that Pearson’s r differed substantially from Spearman’s rho only for population size, where correlation with GHSI overall score was $r=0.14$, $p<0.05$. GDP, gross domestic product; GHSI, Global Health Security Index; JEE, Joint External Evaluation.

### Table 2 Spearman correlation (p value) between ReadyScore or GHSI metrics and indicators of disease outcome or management

| Score/score component | Proportion of deaths from communicable, maternal, neonatal and nutritional diseases (2017) | Deaths from five specified communicable diseases per capita per annum (2017) |
|-----------------------|------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| ReadyScore (n=93 countries) | −0.78 (<0.0001)                                                                                   | −0.73 (<0.0001)                                                           |
| GHSI overall (n=195 countries) | −0.56 (<0.0001)                                                                                   | −0.43 (<0.0001)                                                           |
| Prevent               | −0.57 (<0.0001)                                                                                   | −0.44 (<0.0001)                                                           |
| Detect                | −0.39 (<0.0001)                                                                                   | −0.30 (<0.0001)                                                           |
| Respond               | −0.37 (<0.0001)                                                                                   | −0.29 (<0.0001)                                                           |
| Health system         | −0.60 (<0.0001)                                                                                   | −0.49 (<0.0001)                                                           |
| Commitments           | −0.24 (0.00084)                                                                                   | −0.08 (0.31)                                                              |
| Risk environment      | −0.71 (<0.0001)                                                                                   | −0.56 (<0.0001)                                                           |

ReadyScore is the average across the 19 JEE categories; ‘Proportion of deaths from communicable, maternal, neonatal and nutritional diseases’ is the proportion of annual deaths by country due to communicable diseases derived from 2017 Global Burden of Disease study data, this category includes maternal and neonatal deaths and deaths due to nutritional disease. ‘Deaths from five specified communicable diseases’ is a composite of: diarrhoeal disease, HIV, lower respiratory infection, meningitis and tuberculosis, expressed as cases per capita per annum.

GHSI, Global Health Security Index; JEE, Joint External Evaluation.

### Figure 1 Relationship between proportion of the population dying from communicable diseases and countries’ GHSI overall score. Communicable deaths are derived from Global Burden of Disease Study and include maternal, neonatal and nutritional deaths. GHSI, Global Health Security Index.
spending. In the regression model including all five macroindices, only education and political stability had statistically significant associations with communicable disease deaths.

**GHSA investment and GHSI scores**

The GHSI scores of individual countries receiving US GHSA aid during 2014–2019, along with individual matched controls, are displayed in online supplemental table S5. Mean scores and between-group differences (cases vs controls) are displayed in table 3. The GHSI scores of countries receiving aid was six points higher than matched controls (p=0.0011). The GHSI category ‘Detect’ showed the largest difference (+9.9, p=0.0062) and ‘Risk Environment’ the smallest (+1.1, p=0.52).

**SARS, MERS and Ebola exposure and GHSI scores**

Countries that had experienced one or more SARS cases in 2003 (n=26) had a GHSI 8.2 points higher (p=0.0010) than matched controls, and those with more than one case of SARS (n=18) had a GHSI 13.8 points higher (p=0.0002), see table 4. The greatest difference was in ‘Detect’, where countries with more than one SARS case scored 26.0 points higher (p=0.0003). ‘Risk Environment’ had the smallest difference (+5.4, p=0.0089).

Countries that experienced MERS cases (n=27) had a GHSI 5.6 points higher (51.8 vs 46.2, p=0.055) than matched controls, with scores for ‘Prevent’ (+6.2, p=0.082), ‘Detect’ (+8.5, p=0.043), ‘Respond’ (+9.2, p=0.023) and ‘Health System’ (+5.8, p=0.088) all higher.

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**Table 3** Mean (SD) GHSI scores for countries receiving US GHSA investment versus GHSI scores of matched controls not receiving US GHSA investment

|                         | GHSI total  | Prevention | Detection and reporting | Rapid response | Health system | Compliance with international norms | Risk environment |
|-------------------------|-------------|------------|-------------------------|----------------|--------------|-------------------------------------|------------------|
| US GHSA recipient countries | 40.6 (10.3) | 34.9 (13.5) | 46.7 (15.7)             | 39.6 (13.2)    | 24.2 (14.7) | 55.0 (9.4)                         | 44.0 (10.9)      |
| Non-recipient countries  | 34.6 (8.3)  | 29.1 (10.5) | 36.8 (16.4)             | 34.9 (10.1)    | 20.4 (11.1) | 45.8 (8.5)                         | 42.9 (11.4)      |
| Difference in GHSI score | +6.0        | +5.8       | +9.9                    | +4.7           | +3.8         | +9.3                               | +1.1             |
| P value                  | 0.0011      | 0.0252     | 0.0062                  | 0.0477         | 0.1125       | 0.0001                             | 0.5207           |

Countries were matched within WHO region by next closest GDP per capita, with small island nations of <1 million population excluded.

GDP, gross domestic product; GHSA, Global Health Security Agenda; GHSI, Global Health Security Index.

**Table 4** Mean (SD) GHSI scores of countries exposed to one or more SARS cases in 2003 and matched control countries with no SARS cases

|                              | GHSI total  | Prevention | Detection and reporting | Rapid response | Health system | Compliance with international norms | Risk environment |
|------------------------------|-------------|------------|-------------------------|----------------|--------------|-------------------------------------|------------------|
| Countries that had any SARS cases (n=26) | 60.5 (11.7) | 56.0 (13.6) | 70.7 (19.1)             | 58.5 (13.8)    | 48.6 (13.2) | 60.5 (12.0)                         | 69.6 (11.7)      |
| Matched countries that had no SARS cases | 52.3 (12.0) | 48.5 (14.3) | 56.3 (16.7)             | 47.6 (12.9)    | 42.0 (16.7) | 56.8 (11.5)                         | 66.1 (13.8)      |
| Difference in GHSI score     | +8.2        | +7.5       | +14.5                   | +10.9          | +6.6         | +3.7                               | +3.5             |
| P value                      | 0.0010      | 0.0122     | 0.0025                  | 0.0016         | 0.0281       | 0.2454                             | 0.0205           |
| Countries that had more than one SARS case (n=18) | 63.1 (12.0) | 58.5 (15.1) | 76.5 (15.8)             | 60.1 (14.2)    | 50.7 (13.8) | 63.4 (12.6)                         | 69.5 (12.1)      |
| Matched countries that had no SARS cases | 49.3 (13.0) | 46.8 (15.3) | 50.5 (22.0)             | 47.3 (13.3)    | 39.2 (17.7) | 51.6 (10.0)                         | 64.1 (14.7)      |
| Difference in GHSI score     | +13.8       | +11.7      | +26.0                   | +12.8          | +11.5        | +11.7                              | +5.4             |
| P value                      | 0.0002      | 0.0070     | 0.0003                  | 0.0003         | 0.0075       | 0.0073                             | 0.0089           |

Countries were matched globally by GDP per capita.

GDP, gross domestic product; GHSI, Global Health Security Index; SARS, severe acute respiratory syndrome.
in MERS-exposed countries than controls. However, only ‘Detect’ and ‘Respond’ reached statistical significance at the p<0.05 level. Results are displayed in online supplemental tables S7 and S8.

Countries that experienced Ebola outbreaks in the period 1976–2020 (n=13) had similar overall GHSI scores to matched controls (33.6 vs 32.4, difference +1.2, p=0.69). Category differences were not statistically significant but were greatest in ‘Respond’ (+5.3), ‘Norms’ (+5.2) and ‘Risk Environment’ (−3.9), see online supplemental tables S9 and S10.

With regard to content validity, we found that the WHO situation reports on the COVID-19 pandemic up to 31 July 2020 indicated that a number of countries with high GHSI scores have had large numbers of cases and deaths from COVID-19, while some others with modest GHSI scores appear to have successfully contained or suppressed pandemic spread. We found a number of items in the content of the GHSI that might account for this finding. For example, GHSI item-level scores show that the UK scores half-marks or less for: number of field epidemiologists, number of doctors, nurses and hospital beds per capita, access to care, ability to receive foreign health personnel, evidence of a plan for vulnerable populations or plan to prioritise healthcare for health workers, plan for personal protective equipment supply issues, domestic spending on health per capita, public–private healthcare communication, public confidence in government, international tensions. Additionally, the US exhibits low scores for political and security risks, socioeconomic resilience and public confidence in government, all of which can impact pandemic response. However, given the COVID-19 responses, the content of the GHSI may not fully capture health security and we explore this further in the Discussion section below.

**DISCUSSION**

Individual GHSI scores for countries (and the average global score of 40.2/100) led the GHSI authors to conclude that collective international preparedness and health security are weak and that, political, socioeconomic and environmental vulnerabilities can amplify these deficiencies.12

Our results suggest that the GHSI shows some validity as a measure of health security but may not fully suffice as a stand-alone metric. The GHSI has face validity, being the culmination of a programme of work that began with a systematic search for factors that underpin health security.13 The GHSI correlates with the ReadyScore as well as aggregate outcomes for communicable diseases. GHSI scores are typically higher for countries with past domestic cases of SARS and those that received US investment through the GHSA programme. This latter finding may imply that investment in health security more generally (other countries and other programmes) might be associated with improving GHSI scores.

Our results also suggest other factors associated with higher GHSI scores including GDP per capita and the proportion of the population over 25 who have completed secondary education. Although there is likely collinearity among the variables evaluated, the relationship between education and GHGI is interesting. It might merely reflect that education is a proxy for other factors that could be causally related to GHSI scores, such as human and workforce capital, a welfare state, beliefs about the determinants of health, or many other variables. These relationships should be investigated in future work.

The strong correlation between the ReadyScore and GHSI overall score is important. This more than likely reflects the substantial overlap in the design of these two metrics. Two further points should be made. First, the GHSI exists for a further 85 countries that at the time of writing had not yet completed a JEE. This makes GHSI a potentially very useful reference for these countries. Second, the fact that GHSI measures many factors that JEE does not, and yet still correlates strongly with JEE, suggests that the additional domains of health system, commitments to international norms and features of the risk environment are all aspects of a stable overarching construct, namely ‘health security’.

ReadyScore is more strongly associated with deaths from communicable disease than the GHSI. This is not surprising given that the JEE approach is more specific to preventing, detecting and responding to known communicable diseases, whereas the GHSI has a substantial focus on commitments to norms, the risk environment and planning for unknown catastrophic risks such as emerging anthropogenic threats. That said, only one country with a GHSI overall score greater than 50 has a proportion of deaths from communicable disease greater than 20% (figure 1).

We also suspect that given that GHSI depends on public and published information, there will be instances where preparations have been made, but not published. This means that the GHSI might systematically underestimate countries’ health security capabilities. We also note the correlation with ReadyScore is not perfect and there is high variance in ReadyScore, for example where the GHSI score is moderate (see online supplemental figure S1). This variance may help explain why some countries have low GHSI and low communicable disease deaths (figure 1). The fact that default GHSI scoring weights all six categories approximately equally (12.8%–19.2% of overall score depending on the category) means that a significant contribution to the overall score comes from aspects that JEE does not measure. These contributions are largely derived from the ‘Norms’ and ‘Risk environment’ categories. Adjusting the weighting of various GHSI categories up and down would likely produce stronger and weaker correlation with JEE.

We found that countries previously exposed to SARS had higher overall and category GHSI scores than those that did not have SARS cases. SARS largely occurred in Asian countries and possible regional biases in factors...
such as national leadership and history of other region-specific outbreaks could bias results. However, a similar pattern was seen with MERS, although the findings were not as statistically robust. No trend was observed among countries having Ebola outbreaks, however the sample size of n=13 is small.

The GHSI has been criticised given that some high-scoring nations appear to have performed poorly in their initial 6-month response to the COVID-19 pandemic. We believe it is premature to dwell on this and at some future point a thorough analysis of GHSI scores and COVID-19 response will be needed.

A list of reasons why GHSI may not correlate with COVID-19 outcomes at present includes: low GHSI countries may not have identified many of their cases and deaths, outcome will depend on country strategy (eg, exclusion, elimination, suppression or mitigation); countries impacted later have the advantage of learning from those impacted earlier; the pandemic as 29 July 2020 was still accelerating and far from over, perhaps still beginning, countries that have done well so far may yet be overwhelmed; and various items in the GHSI might apply to COVID-19 and others may not, meaning that subsets of items (not necessarily GHSI categories) might need to be analysed in isolation. It is possible that countries performing ‘poorly’ at one point in time may yet look successful in the future, for example, if they develop vaccines and roll out vaccination quickly.

On the one hand we found that the content of the GHSI provides some explanation for the poor performance of some high GHSI countries (namely the UK and US, see case studies in online supplemental material). High overall GHSI scores may mask many of these specific shortcomings. However, there appear to be factors that are not part of the GHSI that are important for health security capabilities. In particular, it appears that the GHSI indicators may not adequately measure the ability to leverage capacity at the right time. Also, the GHSI is based on national information, and cannot determine local capacity in federal systems. Issues such as trust in government, leadership challenges, health insurance coverage, undocumented immigrants, polarised news sources or rampant misinformation and disinformation on social and mainstream media and of course value trade-off between economics and health, all appear to be conspiring in some countries to subvert an optimal health response and many of these factors are not adequately covered in the content of the GHSI.

Given that the COVID-19 pandemic is still developing at the time of writing, the predictive validity of the GHSI remains to be explored. GHSI scores should eventually be compared with COVID-19 pandemic outcomes but only once the pandemic is over (or at least a 2-year review point is analysed) and using strong evidence such as excess deaths stratified by country strategy, for example, elimination, suppression or mitigation. Future research should also identify subsets of GHSI items specific to particular events such as COVID-19 or laboratory accidents and validate these subsets of items against prospective external data.

Overall the GHSI is very heterogeneous and more like a maturity model than an index of one concept (eg, pandemic response). In fact, a single and highly valid universal index encompassing all aspects of health security, and applying to all countries, may not be possible. In the GHSI, some items may be very important for some countries such as screening all DNA sequence orders (and customer vetting) and others not important for some nations (eg, dual-use research oversight in Tuvalu). What the GHSI appears to show is where countries may have weaknesses and where the world might need to cooperate to bolster gaps in preparedness.

Many of these gaps can be seen in the GHSI 2019 Report, which provides a heat map of global GHSI scores (p18–19). The main weaknesses in health security appear to lie in Africa where scores for ‘health system’ are particularly low (mean 14.8/100). Low scores for small island nations are also noted by the GHSI Report authors. The GHSI demonstrates that low scores in the WHO Africa region are in areas of biosecurity, biosafety, dual-use research oversight, zoonotic disease, data integration, emergency preparedness, linking public health and security agencies, health system capacity, medical countermeasures, communications with healthcare workers and infection control and availability of equipment. We further observed that African nations, small island nations, war-torn nations and nations isolated from the global community are over-represented in the bottom 20 scores across the six categories (see online supplemental material).

We are aware that our analyses have focused mainly on naturally occurring and endemic disease. However, important biothreats are not limited to naturally occurring human pathogens and emerging zoonoses. The risk of biothreats arising from laboratory error or failure of oversight, intentional misuse of biotechnology or deliberate attack are a major concern. This is why the GHSI is also explicitly inclusive of anthropogenic threats.

This aspect of the GHSI will also require validation. This could be performed by analysing the incidence of, or response to, laboratory accidents for example (749 potential incidents were reported in US Federal Select Agent Programme incident data 2009–2015). Methods should be sought to correlate aspects of the GHSI with Biological Safety Level (BSL)-3 and BSL-4 laboratory incidents, with deliberate biological events, and the response to these type of events.

Such work would be valuable given that the GHSI indicates that evidence for mitigation of anthropogenic biological hazards is scant. For example, the GHSI shows insufficient evidence of oversight of dual-use research and screening requirements for genetic material (186 countries), insufficient biosafety systems, laws, agencies or standardised training (121 countries) and many scores of zero for biosecurity (89 countries).
The vast majority of all the harm due to biological events, comes from very rare catastrophic events.\textsuperscript{40, 41} The highest consequence events are catastrophic risks that threaten to permanently curtail the potential of humanity,\textsuperscript{12} and existential threats, which could eliminate humanity,\textsuperscript{45} but critically, there is no way to determine external validity of GHSI (or JEE) with respect to unprecedented events. This is where the face and content validity of tools like the GHSI is important and where the very low scores across many countries in indicators of biosecurity, biosafety and dual-use research oversight are so concerning.

Beyond the GHSI
The impact of COVID-19 makes clear that we need to address factors that the JEE and GHSI do not measure and perhaps cannot measure. Institutional knowledge, a sense of urgency, relationships established in living memory, cross-sectoral logistics and resilience, all these factors may be critical to responses, and difficult to measure. Other overlooked factors may include root cause analysis of laboratory accidents and near misses; gathering intelligence on biological threats; cyberbiosecurity practices; the capability to strictly manage borders and quarantine; the elimination of wet markets and wildlife trade; and the apparent negative impact of sanctions, federalism, the politicisation of media and misinformation and disinformation on social and mainstream media.\textsuperscript{44} Future research should examine these factors not covered by the GHSI, many of which appear to have confounded efforts to respond to the COVID-19 pandemic. Our findings suggest that the role of general education in health security should also be explored further.

Global biological catastrophe stems from high-risk environments, which the GHSI identifies. However, it is clear that countries need more than internal efforts as measured by GHSI or JEE scores. Efforts will require global leadership and strong international coordination mechanisms to overcome the failures and piecemeal responses to the COVID-19 pandemic.

To facilitate international cooperation there have been repeated calls for heads-of-state summits on global health security and to bolster the Biological Weapons Convention.\textsuperscript{5, 12, 43} Lessons learnt in global health security have been collated.\textsuperscript{45} The IHR may need to be reformed for a world where border closures, lockdowns and anthropogenic risks are the new norm. The IHR may also need to facilitate enhanced information sharing, early in an outbreak. Concern for the wellbeing of future generations may need to be written into international law, and the disagreements and grievances of present states must not be allowed to risk the flourishing of humanity's future. Given all of these potentially important factors, it seems clear that even high GHSI scores will not be enough to ensure global health security.

Study strengths and limitations
This study has the strengths of being the first analytical attempt to consider the validity of the GHSI and being able to consider the GHSI in the context of previous global outbreaks such as SARS, MERS and Ebola. Nevertheless, an ecological study like ours has a number of limitations. This includes the use of aggregate and composite data, which can introduce collection bias. We note that gaps in the available data mean that not every metric has a score for every country. We are only able to show correlation, and so cannot demonstrate causation. However, in most instances the correlation went in the a priori expected direction. Any analysis of the relationship between COVID-19 response and the GHSI is subject to many limitations where the outcome of interest is still developing. The GHSI is based on published documents and may fail to score capabilities that have not been written up or published on websites. Although we assessed a number of measures of validity, we have not specifically assessed the validity of the GHSI with respect to anthropogenic bioterror. Furthermore, the GHSI is a heterogeneous index, and it may be the case that subsets of items (not necessarily the defined six GHSI categories) are the best indicators of certain capabilities, perhaps pandemic response. The GHSI has some overlap with some of the metrics we compare it to (eg, the JEE—ReadyScore—and the GHSI ultimately share a number of items), however, the GHSI uses different methods to assess capabilities and therefore correlation remains useful.

CONCLUSION
Our results suggest that the GHSI is a somewhat valid measure of health security, but remains incomplete. The GHSI identifies considerable potential gaps in global health security capabilities and that anthropogenic threats remain neglected, although further validation of the GHSI as a measure of preparedness to mitigate these threats is desirable. It appears that US investments through GHSA and prior experience with the SARS pandemic were associated with higher GHSI scores, suggesting the importance of improved epidemic detection, preparedness and response and institutional experience.

The GHSI authors conclude that collective international preparedness and health security are weak. We conclude that all countries, particularly those with advanced biotechnology programmes, need to ensure sufficient bioscience measures, however, scoring high on the GHSI, while desirable, is likely not enough to adequately mitigate threats. It is particularly relevant that the GHSI authors identified political, socioeconomic and environmental vulnerabilities as factors that can amplify deficiencies in preparedness.\textsuperscript{12} We have suggested that some of these factors are not yet accounted for in measures of global health security.

The GHSI anticipates and calls on the world to mitigate the greatest of threats. Countries need to overcome the failure of imagination demonstrated by lack of
preparedness ahead of the COVID-19 pandemic and the complacency that strong JEE assessments were sufficient. The world is in a challenging situation, clearly needing to do more, but many countries are still not compliant with the 15-years-old IHR. This highlights the magnitude of what is needed. Countries need a new scale of thinking that is focused on high-consequence future threats, with coordinated, well-financed and qualitatively different approaches to preparedness.

GHSI assessments have gone where JEEs have not, to 195 States Parties to the IHR to highlight the many risks and preparedness gaps. Biological catastrophe could strike soon and suddenly, and the world should consider the vision of the GHSI alongside lessons learnt from COVID-19 and institutional knowledge and trialled experience.

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**Contributors** ON conceived the project, contributed to interpreting the data and writing the manuscript and provided important intellectual content. MBJ performed literature reviews, compiled the data, analysed the data and wrote the manuscript. NW advised on the methodology, contributed to interpreting the data and writing the manuscript and provided important intellectual content.

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**Data availability statement** All data analysed in this study are publicly available and links to the data sources are presented in online supplemental table S1. Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

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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).

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. 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.

| 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 (%)           |
| Political stability                       | Political Stability and Absence of Violence/Terrorism percentile rank (2018)                             |
| Proportion of population dying from       | Our World in Data: https://ourworldindata.org/causes-of-death                                             |
| communicable disease                      | (including maternal, neonatal, and nutritional disease deaths)                                             |
| Infectious disease deaths per capita per   | Our World in Data: https://ourworldindata.org/causes-of-death                                             |
| annum (composite of HIV, tuberculosis,    | [data was originally extracted from Global Burden of Disease study data: http://ghdx.healthdata.org/gbd-results-tool] |
| diarrheal disease, lower respiratory      |                                                                                                             |
| infections, meningitis)                   |                                                                                                             |
| SARS cases in the 2003 pandemic           | WHO summary of probable SARS cases: https://www.who.int/en/sars/country/table2004_04_21/en/                 |
| Countries with MERS cases                 | WHO list of 27 countries with MERS as at January 31, 2019:                                               |
| Countries with Ebola outbreaks            | Centres for Disease Control and Prevention map and table of Ebola cases as at June 19, 2019:             |
| GHSA recipients of US aid                 | US Centers for Disease Control and Prevention 2019                                                       |
| Time to outbreak communication and        | Kluberg et al 2016                                                                                         |
| recognition                               | GBD: Global Burden of Disease, GDP: gross domestic product, GHSI: global health security index, SARS:     |
|                                           | severe acute respiratory syndrome, WHO: World Health Organization                                        |

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/](https://www.ghsindex.org/report-model/).

Table S3: High-level findings in the GHSI Report 2019

| 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. Biosafety and biosecurity 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. 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. 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.’ 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.’
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 (e.g., 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

Regression for Ready Score Derived from JEE on GHSI
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. 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. 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   | 50.47         | 63.59 |                  |
| MERS countries       | 51.8       | 47.7    | 58.1   | 50.8    | 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. 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 (e.g., 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 ‘zeros’ 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’.

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. 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’. 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
1.3.1d) 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
5.4.2a) 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         | 0            |
| [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] |              |
| 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 | 0            |
| [Note, overarching indicator (5.5) scores exactly 66.7, so these weaknesses were included] |              |
| 5.5.1b) National budget to address gaps identified in PVS assessment or gap analysis | 0            |
| [Note, as item above]                                                      |              |
| 6.3.2a) Adequacy of airports                                                | 50           |
| [Note, overarching indicator (6.3) scores exactly 66.7, so these weaknesses were included] |              |
| 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.\textsuperscript{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.\textsuperscript{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                                                        | 30%                                         | $311b        | 1672%                         |

Costs are in billions of US dollars. The $622b figure is anchored by $570b reported by Fan et al.\textsuperscript{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.\textsuperscript{18} The GDP loss of the 1918 influenza pandemic in the UK was estimated at 17%.\textsuperscript{19} There is at least one serious pandemic per century and a 20% chance of four or more.\textsuperscript{3} 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).\textsuperscript{19,21} According to Fan et al the annualised cost of non-seasonal influenza pandemics is comparable to the projected impact of climate change.\textsuperscript{20} Factors such as increasing globalisation may even magnify these impacts,\textsuperscript{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).\textsuperscript{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.\textsuperscript{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 SARS + MERS $10b, 2015 Ebola $53b, 2014 + Zika $7b, 2016–19), not to mention the severe demand and supply shocks of COVID-19,\textsuperscript{22} 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),33 which were doubled in a 2019 World Bank update of pandemic preparedness financing.34 The WHO estimated $100b over five years in 67 low and middle-income countries,35 and the US National Academy of Sciences estimated $4.5b per year as a minimum.36 Costing tools exist to estimate the cost of bringing countries up to compliance with the IHR,37 for example a case study calculation for Nigeria resulted in 5-year cost estimates from $66m–612m across three costing methods.38

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,39 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%.40 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.34

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,41 and the ways in which catastrophe can change probabilities, risk appetite, and therefore calculus of risk.42 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.43 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,44 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.

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.

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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