Does Access to HCQ Help to Save Lives from COVID-19? A Cross-Country Analysis

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and

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Abstract

Over the last year the world experienced the COVID-19 pandemic coupled with unprecedented policy responses. In this paper we examine the determinants of COVID-19 infections and fatalities in a cross-country analysis. We find that countries with greater obesity, less urban and more elderly populations, fewer hospital beds, less sunshine, and more freedom experienced greater fatalities. While availability of hydroxychloroquine (HCQ) reduced fatalities, we find little evidence that other policies such as lockdowns, travel restrictions, or mask requirements reduced fatalities. PCR testing is positively associated with infections but is unassociated with fatalities. Controlling for a variety of other possible determinants of COVID-19 fatalities, we find a robust negative relationship between access to HCQ and fatalities.

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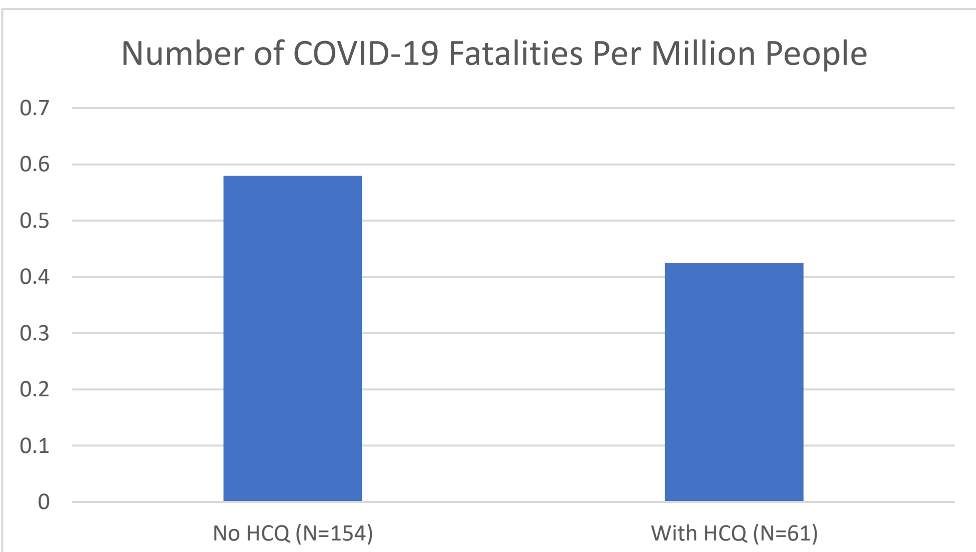
1. Introduction

The COVID-19 pandemic emerged in late 2019 spreading across the globe, but countries differed greatly in terms of infections, fatalities, and policy responses. Variability in infections and fatalities offers an opportunity for exploration---what factors are associated with lower rates of infections and fatalities? Socio-economic and political characteristics as well as pandemic policy responses vary from country to country. Some countries imposed nationwide travel restrictions, mandatory lockdowns, and mask requirements, whereas others did not. Developed countries relied heavily on PCR testing to determine infection rates, whereas generally less developed counties did not. In some countries hydroxychloroquine (HCQ) is available, which if administered early is effective and safe for most people (and inexpensive), whereas other countries discouraged and even prevented its use. Do these policy differences explain any of the variability across countries in infections and fatalities? Controlling for the underlying socio-economic, political, and geographic factors, this paper examines the degree to which different policies helped to save lives, with a particular focus on HCQ.

As the pandemic unfolded, we learned that the elderly, obese, and those with underlying health conditions are vulnerable, whereas younger healthy people are more resilient. In the United States (U.S.) the survival rate for those 70 years older is 94.6% but is 99.997% for those aged 19 and under (CDC, 2021). Our evaluation of the determinants of COVID-19 infections and fatalities follows a line of research on disaster vulnerability that has shown that developed countries tend to be safer from disaster shocks because they are able to devote greater resources to safety. (Kahn, 2005, Toya and Skidmore, 2007). Our analysis of the COVID-19 pandemic contributes to this line of research by examining the degree to which socio-economic, political, geographic, and policy-related factors help to explain variability infections and fatalities.

While our primary objective is to evaluate the role of HCQ, it is also important to understand and control for other factors that may determine vulnerability. For example, income (Helliwell et al., 2021) are potentially important; those with limited resources may not have access essential healthcare services. Demographic factors are also important. As noted above, the elderly population is most vulnerable to the illness, and urbanicity may also play a role in the spread of COVID-19. The overall health of the population is also a factor. Controlling for geography such as degree of isolation may also be important as some countries such as island-states may be protected. We also offer and evaluation of other government policies implemented in response to the outbreak. Many countries restricted travel and imposed lockdowns of varying degrees, and many countries required masks. In some countries HCQ was readily accessible, whereas other countries restricted or prevented the use of HCQ. To help motivate our evaluation, consider Figure 1 which shows that COVID fatalities is about 38% higher in countries that did not use HCQ. It is important to note that HCQ is accessible over the counter in nearly all countries where Malaria is present. Thus, Malaria serves as a valid instrument that can be used to examine potential endogeneity of HCQ, and if present address endogeneity using appropriate econometric methods.

Figure 1
COVID-19 Fatalities in Non-HCQ and HCQ Countries



There are several very recent studies that have examined the underlying determinants of COVID-19 fatalities in a cross-country analysis. .This research focused on factors such as the role of contact tracing (Yalaman et al., 2021), air pollution, obesity, and strategies aimed at achieving herd immunity (Bretschger et al., 2020), and intergenerational residence patterns (Fenoll and Grossbard, 2020). However, to our knowledge there are no cross-country studies that have examined the role access to HCQ has had in potentially reducing COVID-19 fatalities. .While there is past and ongoing medical research on the efficacy of HCQ for the treatment of COVID-19[1], we note that the present study is not formal medical research but rather an examination of whether access to HCQ helped reduce COVID-19 fatalities in those countries where HCQ was readily available over the counter.

2. Empirical Analysis

COVID-19 infection and fatality data come from the World Health Organization (WHO) (https://covid19.who.int/table). .We merge these data with socio-economic, political, geographic, and policy information, which are available from several sources as shown in Appendix Table A. The country is the unit of analysis, where we examine recorded COVID-19 infections per 10 million population and fatalities per one hundred thousand population for 128 to 137 countries, depending on data availability.

To evaluate the role of HCQ in reducing infections and fatalities, we control for socio-economic, political, and geographic factors (real GDP per capita, obesity, urbanization, proportion of population aged 65 or older, number of hospital beds, degree of freedom, amount of sunshine[2], and island and OECD country indicator variables) as well as other policy tools (PCR testing, travel restrictions, lockdowns, and mask wearing). .We expect countries with lower income, fewer hospital beds, higher urbanicity and proportions of elderly, more freedom, and less sunshine to have more infections and fatalities. .Controlling for other policy measures helps to isolate the role HCQ may have in reducing infections and fatalities. Each of these measures are prominent alternative policies that have been used differentially across countries.

HCQ is used in many African countries for the treatment of Malaria and thus the medication was known to be safe for most people and was widely available. .In contrast, North American and European countries discouraged and even prevented HCQ use. .Appendix Table B provides summary statistics for all variables and Appendix Table C provides a list of countries included in the evaluation.

A challenge with any policy evaluation is in identifying causal relationships. In the context of the COVID-19 crisis, rising infections and fatalities spur countries to implement policies, thus potentially confounding coefficient estimates generated from standard regression analysis. What is required to evaluate and properly address potential endogeneity are valid instruments. A valid instrument must be a significant determinant of the policy instrument but be unassociated with COVID-19 fatalities. In this analysis, we are not able to examine the potential endogeneity of all the policy variables we consider. However, we are able to examine the potential endogeneity of HCQ availability using a valid instrument. HCQ is available over the counter and used to treat Malaria in countries where Malaria is prevalent. Detailed data on countries where Malaria is present is available from the U.S. Center for Disease Control and Prevention (https://www.cdc.gov/malaria/travelers/country_table/a.html). In regression estimates that are available from the author upon request, a Malaria indicator variable is a positive and highly significant determinant of HCQ availability[3], but not a significant predictor of COVID-19 fatalities. Thus, a Malaria indicator is a valid instrument. We also conduct a Hausman specification test to examine the potential endogeneity HCQ. In the first stage of the Hausman specification test we estimate a model where HCQ is the dependent variable that is a function of the Malaria indicator and the other control variables in the model. The residual from the HCQ regression is then included as a regressor in a COVID-19 fatality regression. If the residual from the HCQ regression is a significant determinant in the fatality regression,

[1] See https://c19hcq.com/ for a real-time database and meta-analysis of 280 HCQ studies of which 208 are peer reviewed. These studies show that early treatment with HCQ consistently has positive effects. In the U.S., HCQ was discouraged and even prohibited, even though the U.S. National Institute of Allergy and Infectious Diseases (NIAID) published an article in 2005 (Vincent et al.,2005) in its Virology Journal, which showed that HCQ was an effective treatment for coronavirus.

[2] We include degree of sunshine as a proxy for vitamin D in the population. Research shows that those with insufficient vitamin D are more susceptible to COVID-19. Skin needs adequate exposure to the sun to produce vitamin D. Otherwise, supplements may be required, especially in the winter months in the far northern and southern hemispheres.

[3] The coefficient and t-value of on the Malaria variable in the first-stage HCQ regression is 0.38 and 2.51, respectively. These full set of estimates are available from the author upon request.

then endogeneity is present.[4] In estimates that are available from the author upon request, the residual from HCQ regression is statistically insignificant in the fatality regression. Thus, there is no evidence of endogeneity; a two-stage least squares (2SLS) estimation is unnecessary.[5] However, for comparison we report a 2SLS regression using a generalized method of moments estimator.

In an effort to address concerns about endogeneity of the other policies, the policy variables measure status before April 2020 so that they can be interpreted as predetermined. For example, travel restrictions may be adopted in places where COVID-19 infections/fatalities are growing. Further, policies adopted later are less likely to have been implemented on time to have had a large effect on COVID-19 infections and fatalities during the period of analysis (December 8, 2019 – May 8, 2021). For example, several countries began to administer Ivermectin and Remdesivir in late 2020, but approval and subsequent dissemination across a given nation takes time and thus may not have had large impacts during the period of analysis. Though this approach is imperfect, note that the primary focus of this paper is in evaluating the role of HCQ, which to our knowledge has not been systematically examined in a cross-country framework.

We estimate multivariate regressions to determine the relationship between the policy variables with controls and COVID-19 infections and fatalities in a robust regression estimation. The regressions are characterized by the following equations:

$$\text{Infections}_i = \alpha_1(\text{HCQ}) + \alpha_m(\text{Controls}_{ji}) + \alpha_n(\text{Policies}_{ki}) + e_i$$

$$\text{Deaths}_i = \beta_1(\text{HCQ}) + \beta_m(\text{Controls}_{ji}) + \beta_n(\text{Policies}_{ki}) + e_i$$

where infections and fatalities are the total number of COVID-19 infections per ten million population and deaths per one hundred thousand population in country i between December 8, 2019 and May 8, 2021, respectively. Policy_{ki} is vector of k policy variables including PCR testing, travel restrictions (complete and partial), lockdowns (mandatory national, mandatory local, recommended national, recommended local), and mask recommended. Controls_{ji} represents a vector of j control variables that determine infections and fatalities as presented above. Finally, HCQ is an indicator variable that is equal to 1 if a HCQ is easily accessible in a country over the counter, and 0 otherwise.

Tables 1 and 2 present five infection and fatality regressions, respectively. As shown in Table 1, the adjusted R^2 ranges from 0.582 to 0.630, signifying that the regressions capture a significant proportion of the cross-country variation in infections. The control variables show that countries with greater obesity, older populations, fewer beds, more freedom, and less sunshine had higher rates of infection. Though not shown in the regression, we also find that the more isolated island countries also experienced fewer infections. Turning to the policy variables, countries with recommended local lockdowns experienced fewer infections, but the other lockdown measures, travel restrictions, and mask wearing were unassociated with infections. However, PCR testing is a positive and significant determinant of infections; this finding will be discussed in more detail later. Last, note that HCQ was unassociated with infection rates.

Turning to Table 2, the regressions again capture a significant portion of the cross-country variation in fatalities. As with infections, countries with greater obesity, fewer beds, more freedom, more elderly, and less sunshine experienced more fatalities. Higher income and more urbanized countries experienced fewer fatalities. Island countries also experienced fewer fatalities, though not shown in Table 2. With the

[4] See Kennedy (1992) for a description of the Hausman specification test.

[5] We also examine endogeneity by including several other weak instruments in addition to Malaria as the strong instrument. These weak instruments include a tropics indicator variable and indicator variables for primary religion: (Christian, Muslim, Buddhist, and Hindu). Again, we find no evidence of endogeneity. In the two-stage least squares estimates presented in the paper, we use these variables as instruments: HCQ, Tropics, Christian, Muslim, Buddhist, and Hindu).

exception of HCQ, none of the policy variables were statistically significant, though there is some evidence that recommended local lockdowns were helpful as shown in column 4. However, the availability of HCQ is consistently associated with lower fatalities in all regressions. According to the coefficient estimate on HCQ in column 2, if the U.S. had made HCQ widely available (as opposed to restricting use), recorded COVID-19 fatalities would have been reduced from 515,000 to about 429,000.[6] Extending this calculation to all countries where HCQ was not readily available, we estimate that 4,000 lives could have been saved had HCQ been made accessible. The 2SLS estimation in column 3 and 5 has a statistically significant coefficient on HCQ that is roughly twice as large. Recall, however, that we do not find evidence endogeneity; we present the 2SLS estimation for comparison but think the column 2 or 4 estimations are more appropriate. The 2SLS estimate suggests that the columns 2 and 4 estimates are a lower bound.

[6] The magnitude of this effect is generally consistent with COVID-19 patient-based studies examining HCQ effectiveness in reducing fatalities.

Table 1
Determinants of COVID-19 Infections (December 8, 2019 – May 8, 2021)

Dependent variable: Total confirmed cases per 10 million population of May 8, 2021

	OLS 1	OLS 2	GMM 3	OLS 4	GMM 5
Log GDP per capita	0.011	0.009	0.046	-0.036	-0.037
	(0.218)	(0.172)	(1.007)	(-0.580)	(-0.692)
Obesity	0.009	0.009	0.009	0.009	0.010
	(4.926)	(4.903)	(4.985)	(4.005)	(5.243)
Aged 65 and above	0.030	0.030	0.031	0.028	0.024
	(4.390)	(4.374)	(4.793)	(3.655)	(3.459)
Beds per 1000 people	-0.023	-0.023	-0.028	-0.018	-0.014
	(-2.439)	(-2.360)	(-3.193)	(-1.572)	(-1.230)
Urbanization	0.004	0.004	-0.037	-0.118	-0.142
	(0.028)	(0.026)	(-0.292)	(-0.760)	(-1.037)
Not free	-0.096	-0.099	-0.102	-0.096	-0.131
	(-2.669)	(-2.751)	(-2.998)	(-2.591)	(-3.295)
Sunshine high	-0.069	-0.068	-0.131	-0.118	-0.132
	(-1.024)	(-1.007)	(-2.208)	(-1.636)	(-2.178)
Sunshine middle-high	-0.138	-0.138	-0.147	-0.143	-0.121
	(-2.206)	(-2.196)	(-2.610)	(-2.184)	(-2.218)
Sunshine middle-low	-0.108	-0.107	-0.154	-0.139	-0.150
	(-1.730)	(-1.718)	(-2.814)	(-2.045)	(-2.529)
HCQ		0.012	-0.052	0.018	0.021
		(0.348)	(-0.628)	(0.456)	(0.292)
PCR test				0.147	0.202
				(1.756)	(2.553)
Mandatory national lockdown				-0.024	0.062
				(-0.469)	(1.094)
Mandatory local lockdown				-0.065	0.000
				(-1.232)	(0.005)
Recommended national lockdown				-0.061	0.037
				(-0.640)	(0.480)
Recommended local lockdown				-0.288	0.523
				(-3.350)	(0.721)
Travel closed				0.046	0.075
				(0.765)	(1.439)
Travel partial				-0.021	-0.035
				(-0.486)	(-0.947)
Mask				0.067	0.022
				(0.490)	(0.197)
Number of Countries	137	137	136	129	128
adj.R^2	0.630	0.628	0.610	0.638	0.582

Notes: Numbers in parentheses are t-values. Other independent variables not reported here are Constant, Dummy for OECD, Low-income economies, Lower-middle-income economies, Upper-middle-income economies, and Island countries.

Table 2
Determinants of COVID-19 Fatalities (December 8, 2019 - May 8, 2021)

Dependent variable: Total confirmed deaths per 100000 population of May 8, 2021

	OLS 1	OLS 2	GMM 3	OLS 4	GMM 5
Log GDP per capita	-0.218	-0.189	-0.136	-0.244	-0.172
	(-1.986)	(-1.758)	(-1.438)	(-1.977)	(-1.668)
Obesity	0.021	0.021	0.020	0.022	0.020
	(6.293)	(6.648)	(7.474)	(5.283)	(5.522)
Aged 65 and above	0.069	0.070	0.072	0.067	0.060
	(4.185)	(4.232)	(5.102)	(3.746)	(4.347)
Beds per 1000 people	-0.047	-0.050	-0.060	-0.043	-0.043
	(-2.052)	(-2.338)	(-3.535)	(-1.910)	(-2.419)
Urbanization	-0.633	-0.629	-0.609	-0.722	-0.649
	(-1.907)	(-1.883)	(-2.001)	(-1.933)	(-1.810)
Not free	-0.391	-0.359	-0.325	-0.306	-0.290
	(-5.129)	(-5.183)	(-5.394)	(-3.627)	(-4.130)
Sunshine high	-0.312	-0.330	-0.412	-0.368	-0.433
	(-2.277)	(-2.415)	(-3.075)	(-2.287)	(-2.970)
Sunshine middle-high	-0.325	-0.334	-0.416	-0.336	-0.396
	(-2.372)	(-2.435)	(-3.214)	(-2.219)	(-2.926)
Sunshine middle-low	-0.248	-0.268	-0.386	-0.305	-0.406
	(-1.727)	(-1.865)	(-2.851)	(-1.813)	(-2.745)
HCQ		-0.184	-0.323	-0.152	-0.346
		(-2.570)	(-2.010)	(-1.891)	(-2.343)
PCR test				0.018	0.017
				(0.179)	(0.179)
Mandatory national lockdown				0.113	0.132
				(1.001)	(1.019)
Mandatory local lockdown				0.040	0.009
				(0.365)	(0.070)
Recommended national lockdown				0.147	0.010
				(0.864)	(0.072)
Recommended local lockdown				-0.470	-0.285
				(-2.516)	(-0.299)
Travel closed				-0.002	0.023
				(-0.015)	(0.191)
Travel partial				-0.084	0.002
				(-0.754)	(0.020)
Mask				0.302	0.278
				(1.335)	(1.485)
Number of Countries	137	137	136	129	128
adj.R^2	0.630	0.642	0.631	0.625	0.603

Notes: Numbers in parentheses are t-values. Other independent variables not reported here are Constant, Dummy for OECD, Low-income economies, Lower-middle-income economies, Upper-middle-income economies, and Island countries.

In contrast to the significant positive coefficient on PCR testing in the infection regressions, the PCR testing variable was insignificant in the fatality regressions. This seeming inconsistency may be due to the high rate of false positives generated by PCR test.[7] These estimates are also robust to the inclusion of continent indicator variables. Note again that while the coefficient estimates on the policy variables may be biased due to potential endogeneity, we include these factors help to isolate the HCQ effect.

3. Conclusions

This paper offers a cross-country analysis of factors associated with COVID-19 infections and fatalities. Our evaluation generates high adjusted R^2s and thus we capture a significant portion of the cross-country variability in both infections and fatalities. We find that countries with greater obesity, fewer hospital beds, more freedom, more elderly, and less sunshine experienced greater fatalities. Turning to the policy variables, we find that greater use of PCR testing resulted in more recorded infections but was unassociated with fatalities, and we find some evidence that recommended local lockdown may have been helpful in reducing infections and fatalities. After providing evidence that HCQ is an exogenous determinant of fatalities, our regression analysis also shows that the availability of HCQ is consistently negatively associated with fatalities.[8] In summary, this evaluation offers a useful contribution to the body of research evaluation the COVID-19 pandemic policy responses.

[7] Mandavilli (2021) offers a discussion of PCR test false positives, referring to studies indicating that up to 90% of PCR tests generate false positives where "infected" individuals are neither sick nor contagious. See also Wernike et al. (2020).

[8] Emerging evidence suggests that Ivermectin and vitamin D are also effective treatments for COVID-19. See Real-time Database and Meta Analysis of 541 COVID-19 Studies, https://c19early.com/.

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Appendix Table A: Definitions and Sources of Variables

Variables	Definition	Source
Deaths	Total confirmed deaths per 100000 population of April 1, 2021	WHO
Cases	Total confirmed cases per 10 million population of April 1, 2021	WHO
Log GDP per capita	Logarithm of real GDP per capita in 2010	WDI
Obesity	Share of adults that are overweight or obese in 2015	OWD
Aged 65 and above	Population aged 65 and above of 2010 (% of total population)	WDI
Beds per 1000 people	Hospital beds per 1,000 people in 2015	WDI
Urbanization	Population in the largest city (% of total population) in 2015	WDI
Not free	Dummy for not free country	FH
OECD	Dummy for OECD country	
Island	Dummy for island country/area/territory	
Sunshine high	Dummy for high sunshine duration	WIKI SD
Sunshine middle-high	Dummy for middle-high sunshine duration	WIKI SD
Sunshine middle-low	Dummy for middle-low sunshine duration	WIKI SD
HCQ	Dummy for HCQ used widely	@CovidAnalysis
PCR test	The number of tests performed for the country/area/territory per 1 trillion people	WHO
Mandatory national lockdown	Dummy for nationwide mandatory lockdown on April 1, 2020	BBC, WIKI
Mandatory local lockdown	Dummy for mandatory local lockdown on April 1, 2020	BBC, WIKI
Recommended national lockdown	Dummy for recommended national lockdown on April 1, 2020	BBC, WIKI
Recommended local lockdown	Dummy for recommended local lockdown on April 1, 2020	BBC, WIKI
Travel closed	Dummy for travel only for citizens, residents returning home, or people in other special circumstances may enter the country.	KAYAK
Travel partial	Dummy for entrance into a country may depend on the traveler’s citizenship, point of origin, or other specific regulations.	KAYAK
Mask	Dummy for mask recommended	MASKS

Sources:

WHO: World Health Organization https://covid19.who.int/table
WDI: World Bank Indicators https://databank.worldbank.org/reports.aspx?source=world-development-indicators#
OWD: Our World in Data https://ourworldindata.org/grapher/share-of-adults-who-are-overweight
FH: Freedom House https://freedomhouse.org/report/freedom-world
WIKI SD: https://en.wikipedia.org/wiki/List_of_cities_by_sunshine_duration
@CovidAnalysis: https://c19hcq.com/countries.html
BBC: https://www.bbc.com/news/world-52103747
WIKI: https://en.wikipedia.org/wiki/COVID-19_pandemic_by_country_and_territory#Timeline_of_first_confirmed_case_by_country
KAYAK: https://www.kayak.com/travel-restrictions
MASKS: https://masks4all.co/what-countries-require-masks-in-public/

Appendix Table B: Summary of Statistics Variables

	Mean	Standard Deviation	Number of Observations
Deaths	0.315	0.335	137
Cases	0.609	0.733	137
Log GDP per capita	8.467	1.510	137
Obesity	46.90	17.56	137
Aged 65 and above	8.581	6.239	137
Beds per 1000 people	2.839	2.487	137
Urbanization	0.191	0.133	137
Not free	0.314	0.466	137
OECD	0.146	0.354	137
Island	0.109	0.313	137
Sunshine high	0.161	0.368	137
Sunshine middle-high	0.350	0.479	137
Sunshine middle-low	0.292	0.456	137
HCQ	0.409	0.493	137
PCR test	0.347	0.515	129
Mandatory national lockdown	0.473	0.501	129
Mandatory local lockdown	0.287	0.454	129
Recommended national lockdown	0.109	0.312	129
Recommended local lockdown	0.008	0.088	129
Travel closed	0.178	0.384	129
Travel partial	0.581	0.495	129
Mask	0.961	0.194	129

Appendix Table C: List of Countries Included in the Study

Afghanistan	Dominican Republic	Kuwait	Qatar
Albania	Ecuador	Kyrgyz Republic	Romania
Algeria*	Egypt, Arab Rep.	Lao PDR	Russian Federation
Argentina	El Salvador	Latvia	Saudi Arabia
Armenia	Equatorial Guinea	Lebanon	Senegal
Australia	Estonia	Liberia	Serbia
Austria	Ethiopia	Libya	Sierra Leone
Azerbaijan	Finland	Lithuania	Singapore
Bahrain	France	Madagascar	Slovak Republic
Bangladesh	Gabon	Malawi	South Africa
Belarus	Gambia, The	Malaysia	Spain
Belgium	Georgia	Mali	Sri Lanka
Benin	Germany	Mauritania	Sudan*
Bolivia	Ghana	Mexico	Sweden
Bosnia and Herzegovina	Greece	Moldova	Switzerland
Brazil	Guatemala	Mongolia	Tajikistan*
Bulgaria	Guinea	Morocco	Tanzania*
Burkina Faso*	Guinea-Bissau	Mozambique	Thailand
Burundi	Haiti	Myanmar	Togo
Cambodia	Honduras	Namibia	Trinidad and Tobago
Cameroon	Hungary	Nepal	Tunisia
Canada	India	New Zealand	Turkey
Central African Republic	Indonesia	Nicaragua*	Turkmenistan*
Chile	Iran, Islamic Rep.	Niger	Uganda
China	Iraq	North Macedonia	Ukraine
Colombia	Ireland	Norway	United Arab Emirates
Congo, Dem. Rep. *	Israel	Oman	United Kingdom
Costa Rica	Italy	Pakistan	United States
Cote d'Ivoire	Jamaica	Panama	Uruguay
Croatia	Japan	Paraguay	Uzbekistan
Cuba	Jordan	Peru	Venezuela, RB
Czech Republic	Kazakhstan	Philippines	Vietnam
Denmark	Kenya	Poland	Yemen, Rep.
Djibouti	Korea, Rep.	Portugal	Zambia
			Zimbabwe

Notes: * indicates not included in 137 sample.