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Multi-Drug Resistant Tuberculosis in Developing and Developed Countries: A Study of GNI per capita, Human Development Index and the incidence of Multi-Drug Resistant Tuberculosis

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Abstract

This paper explores the factors contributing to Multi-Drug Resistant Tuberculosis (MDR-TB) in developing and developed countries. Existing studies indicated that low income and low human development factors contribute to widespread antimicrobial resistance in developing countries. Such factors are examined in depth by performing statistical measures on a sample size of 171 countries from recent data provided by the World Bank and the United Nations Development Programme. First, the relationship between Gross National Income (GNI) per capita and incidence of MDR-TB was tested and a strong correlation was not found. Second, the Human Development Index and incidence of MDR-TB are researched and a strong correlation was not found. The findings of this study indicate that despite the perception that a low income and human development index are among the main causes of antimicrobial resistance, underdevelopment and poverty may not play as large of a role in antimicrobial resistance as originally thought. Thus, policies aiming to combat antimicrobial resistance cannot group countries based on their level of development or income – there are several other factors that must be accounted for. Policies tailored to individual countries and their existing antimicrobial environment is recommended to combat antimicrobial resistance.

Keywords: Antimicrobial Resistance, GNI per capita, Human Development Index, Multi-Drug Resistant Tuberculosis, Statistical Analysis

1. Introduction

In September of 2016, world leaders gathered at the United Nations General Assembly to address the recent and ever-growing threat of antimicrobial resistance (AMR) (Fleck & Humphreys, 2016). AMR has the serious potential of reversing achievements made by modern medicine by resurfacing communicable diseases that caused substantial mortality prior to the use of antibiotics (WHO, 2014). For example, in 2016 there were 600,000 new cases of Multi-Drug Resistant Tuberculosis (MDR-TB) alone, leaving a significantly large portion of the global population without the means to treat TB (WHO, 2017).The WHO is placing an increased importance on the growing issue of MDR-TB (see Figure 1).

Through the use of recent country-level data provided by the World Health Organization (WHO), the United (UN) and the World Bank (WB), this paper analyzes the issue of MDR-TB from a development economics standpoint. First, the relationship between Gross National Income (GNI) per capita of a country and its incidence of MDR-TB is researched. Second, the relationship between a nation's Human Development Index (HDI) and incidence of MDR-TB is examined to gain an extensive understanding of the factors that may affect antimicrobial resistance.

Tuberculosis (TB) is an infectious, communicable disease that causes illness in approximately 10 million people worldwide each year(WHO, 2017).TB is the ninth leading cause of worldwide death, and the WHO has placed a large emphasis on combating it (WHO, 2017). Multi-Drug Resistant TB (MDR-TB) is defined as a resistance to anti-TB drugs rifampicin and isoniazid (WHO, 2017).

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According to the Oxford Vaccine Group (2018), the bacilli Calmette-Guérin vaccine used to prevent TB is only effective 70-80% of the time in preventing severe forms of TB and is even less effective at preventing the most common form of TB (pulmonary).The WHO (2017) continues to stress the importance for a more effective TB vaccine to be developed.

2. Review of existing literature

Several works of literature discussing the relationship between antimicrobial resistance (AMR), income and human development have been compiled and grouped together by theme to provide insight into the current understanding of AMR. On the whole, it is argued that countries with lower human development and GNI per capita experience a high prevalence of AMR, largely due a high burden of disease and malnutrition, the cost and quality of antibiotics, and the types of health care systems in place (Alsan et al., 2015; Atabe, Ayukekbong & Ntemgwa, 2017; Bhutta et al., 2005; WHO, 2017).

2.1 High burden of disease and malnutrition

The high burden of disease in developing countries is one of the central reasons that underdevelopment and antibiotic misuse are linked. Those living in developing countries are exposed much more frequently to infectious diseases than those in developed countries, largely due to living conditions (Atabe et al., 2017; Okeke, 2010). This significantly affects the ability of populations to lead healthy lives and provides an explanation for the increased presence of AMR in less developed countries (Atabe et al., 2017; Byarugaba, 2004).

For example, developing countries (predominantly in Africa), are currently facing an AIDS epidemic, and due to a weakened immune state, HIV-positive populations are extremely vulnerable to acquiring TB (WHO, 2017). 1.0 million of the 10.3 million cases of TB reported globally in 2016 occurred in HIV-positive populations (WHO, 2017). Such patients require an increased use of antimicrobials to fight disease, increasing the risk for developing drug resistant strains. Further, HIV positive patients in hospitalized settings often face a high rate of exposure to drug resistant pathogens as a result of poor infection control, largely increasing the incidence of antimicrobial resistance in countries with large HIV/AIDS-positive populations (Bhutta et al., 2005; WHO, 2017).

Additionally, it is argued that MDR-TB is more common in countries with lower income and human development due to the high prevalence of malnutrition in these countries (WHO, 2017). Malnutrition weakens the body's immune defense against infection and has been labeled by the WHO (2017) as a leading risk factor for acquiring TB. Due to the large undernourished population in low-income/less developed countries, malnutrition is responsible for nearly twice as many TB cases as HIV – 1.9 million of the 10.4 million globally reported cases of TB in 2016 were due to malnutrition (WHO, 2017). Those unable to afford proper nutrition are at an income level with low access to antibiotics, resulting in the misuse of the limited antibiotics available and an increased number of MDR-TB strains(Alsan et al., 2015; WHO, 2017).

2.2 Antibiotic cost and quality

The high prevalence of MDR-TB in developing countries is largely due tothe economic implications of receiving antibiotics and the resulting quality of antibiotics received (Atabe et al., 2017; WHO, 2017). In many developing countries, access to suitable medical care is often costly and inaccessible, resulting in inexperienced individuals practicing self-medication, or seeking medical care from less regulated private health care providers(Alsan et al., 2015; WHO, 2017).

Additionally, those living in poverty often receive weakened doses of antibiotics, shorten treatment cycles, and/or use lower quality and expired antimicrobials, due to the high cost of these drugs (Atabe et al., 2017). Byarugaba (2004) argues, "Economic hardships in developing countries lead to premature cessation of treatment or sharing one single dose of treatment by a whole family." Such practices increase the incidence of MDR-TB in developing countries. Due to this high prevalence of AMR in developing countries, more toxic and costly forms of antimicrobials must be produced, deepening the cycle of unaffordability and resistance (Byarugaba, 2004).

Further, low doctor-to-patient ratios are common in developing countries and result in doctors having insufficient time to properly diagnose illnesses or communicate with patients how to properly use antibiotics (Atabe et al., 2017). For example, in a Lebanese study it was found that 52% of prescriptions provided by doctors for antimicrobials were not appropriate and 63.7% of physicians prescribed antibiotics with the wrong length of treatment (Atabe et al., 2017).

2.3 Health care system

The coexistence of public and private healthcare system options in many developing countries also contributes to an increased incidence of antimicrobial resistance, including MDR-TB (Alsan et al., 2015; WHO, 2017). It was found in a study published by The Lancet Infectious Disease in 2015 that out-of-pocket health expenditures are strongly related to antimicrobial resistance in developing countries (Alsan et al., 2015). This data was retrieved from 47 developing countries requiring fixed payment amounts for specific services, called co-payments, on antimicrobials in the public sector (Alsan et al., 2015).

It is argued that high co-payment costs for public sector antibiotics in developing countries causes large portions of populations to seek less expensive private-sector care (Alsan et al., 2015). This is due to private healthcare systems existing alongside public health care systems in developing countries, to the extent by which an increase in price in one sector increases demand, or use, in the other sector for antibiotics (Alsan et al., 2015). Consequently, incentives are often created for informal private suppliers to overprescribe antibiotics (which are often low-quality), resulting in increased incidences of AMR in developing countries (Alsan et al., 2015). For example, Nigeria has one of the highest global incidences of MDR-TB (WHO, 2017), and it was found that 78% of low-quality drugs prescribed in Nigeria were from private health care providers who shortened treatments and/or provided drugs at weakened strengths (Alsan et al., 2015). Thus, co-payments in the public sector may lead to a problematic increase in less regulated private-sector drug prescriptions, and in turn, resistance to drugs used to treat TB and other diseases.

3. Data collection and results

MDR-TB data, GNI per capita data, and HDI data have been gathered using a sample size of 171 countries. The sampled countries used in this study are listed in Appendix A& B of this report, and represent all countries with available MDR-TB, GNI per capita, and HDI data.

First, we explore a possible correlation between a country's GNI per capita in 2016 (World Bank Atlas method) and its incidence of MDR-TB in 2016. A negative relationship between GNI per capita and MDR-TB is hypothesized, by which an increase in GNI per capita will denote a decrease in the incidence of MDR-TB. This hypothesis arose based on the literature cited in the previous section, which qualitatively explains that low human development and low incomes create widespread antibiotic resistance in less developed countries.

Second, we explore the relationship between the level of human development and incidence of MDR-TB. HDI and incidence of MDR-TB will be correlated such that an increase in a nation's HDI will denote a decrease in its incidence of MDR-TB. This hypothesis comes from the understanding in the cited literature that less developed countries (in terms of income and education/health) will have a very high prevalence of antimicrobial resistance.

3.1. GNI per capita and MDR-TB

Based on the World Bank (2017) income classifications, the 171 observed countries have been divided into four categories; low-income countries (GNI per capita $1,005 or less), lower-middle income countries (GNI per capita between $1,006 and $3,955), upper-middle income countries (GNI per capita between $3,956 and $12,235) and high-income countries (GNI per capita of $12,236 or more). Country classifications by income level are listed in Appendix A. GNI per capita has been determined using the World Bank Atlas method, which is among the only available methods of calculating GNI per capita provided by the World Bank with clearly defined income groups. MDR-TB and GNI per capita statistics were gathered using the WHO Global Tuberculosis Report 2017 and the World Development Indicators Data Bank (WB, 2018a). Descriptive statistics and regression information can be found in Table 1.

Table 1. Statistical results – GNI per capita &Incidence of MDR-TB

	Low-Income (n=26)	***Lower-Middle Income*** (n=46)	***Upper-Middle Income*** (n=48)	***High-Income*** (n=51)
Descriptive Statistics (GNI per capita)				
Mean	592.8	2377.778	7180.851	34469.38776
Standard Deviation	188.5364686	954.4534	2378.444	18387.45014
Minimum	280	1100	4060	12330
Maximum	950	3920	12140	82090
(Incidence MDR-TB)				
Mean	1345.28	7723.978	4010.106	168.2857143
Standard Deviation	2210.896095	22812.52	14000.63	810.4112639
Minimum	45	10	0	0
Maximum	7600	46	73000	5700
Regression Results (Variable: MDR-TB)				
Coefficient	1877.108676	13877.49393	-1494.53	257.9086
Standard Error	1513.794	9269.661615	6574.413	250.1526
Multiple R	0.076505	0.108276329	0.130226	0.058993
R Square	0.005853	0.011723763	0.016959	0.00348
P Value	0.227476845	0.141675484	0.8212	0.307815

When observing the relationship between the GNI-per capita and the prevalence of MDR-TB and in low-income countries, the correlation coefficient is 0.077 and the coefficient of determination is 0.006. These low r and R2 values indicate that there is not a strong correlation between GNI per capita and MDR-TB in low-income countries. This contradicts the overall perception that the lower the level of income is, the higher the prevalence of MDR-TB will be. However, the p-value is 0.227, which indicates that the null hypothesis should not be completely rejected.

Similarly, the correlation coefficient is 0.108 and the coefficient of determination is 0.012 when studying a correlation between GNI per capita and MDR-TB in lower-middle income countries. The p-value is also relatively high in this relationship, with a value of 0.142.In upper-middle income countries, the correlation coefficient and coefficient of determination are also low, respectively, 0.130 and 0.017. The p-value is highest in this income group, with a value of 0.821, indicating that the null hypothesis should not be rejected.

The regression results in regards to high income countries produced a relatively low correlation coefficient of 0.059 and a coefficient of determination of 0.003. The p-value is 0.308, again indicating that the null hypothesis should not be entirely rejected. Upon observing the descriptive statistics in the relationship between GNI per capita and MDR-TB, interesting findings can also be observed. Most notably, the mean incidence of MDR-TB does not consistently decrease as income increases. Instead, the order from the highest to lowest mean incidence of MDR-TB is: lower-middle income countries, upper-middle income countries, low-income countries, and then high income countries. In regards to the average incidence of MDR-TB, as income increases, MDR-TB does not necessarily decrease. This questions some of the qualitative information discussed in the existing literature section of this paper that heavily credits income-related factors to antimicrobial resistance.

3.2. Human Development Index and MDR-TB

The most recent HDI formulations have been gathered from the United Nations Development Programme (UNDP, 2016). The HDI is calculated based on several nation-level statistics – life expectancy at birth, expected years of schooling, mean years of schooling, and GNI per capita (UNDP, 2016). This provides a more multidimensional measure of poverty and development, instead of simply observing income. The 171 countries observed in this study have been divided into four categories, pre-determined by the United Countries Development Programme (UNDP, 2016): low human development, medium human development, high human development, and very high human development. The 171 countries used in this study are categorized by their HDI in Appendix B.

Table 2 shows descriptive statistics as well as a regression analysis performed on the relationship between HDI and the incidence of MDR-TB. Among low HDI groups, human development and incidence of MDR-TB produced a correlation coefficient of 0.15478 and a coefficient of determination of 0.024, which indicate a relatively weak correlation between HDI and MDR-TB. The p-value is 0.563, demonstrating that the null hypothesis should not be rejected.

Table 2. Statistical results– HDI & Incidence of MDR-TB

	Low HDI (n=36)	***Medium HDI*** (n=38)	***High HDI*** (n=50)	***Very High HDI*** (n=47)
Descriptive Statistics (HDI)				
Mean	0.467	0.628789474	0.753897959	0.881
Standard Deviation	0.050395495	0.047612262	0.028302124	0.040690703
Minimum	0.352	0.55	0.701	0.8
Maximum	0.541	0.698	0.796	0.949
(MDR-TB)				
Mean	1872.028571	8159	2731.306122	1567.695652
Standard Deviation	3717.828236	24974.05495	10815.30943	9297.133988
Minimum	29	10	0	0
Maximum	20000	147000	73000	63000
Regression Results (Variable: MDR-TB)				
Coefficient	-3431.5	5746.324	34406.78	55377.12
Standard Error	5881.084	54372	41341.5	28328.87
Multiple R	0.15478	0.007468	0.11018	0.272823
R Square	0.023957	5.58E-05	0.01214	0.074433
P Value	0.56342	0.916419	0.409385	0.056836

When observing the relationship between HDI and the incidence of MDR-TB in countries with medium human development, we found extremely low correlation and the coefficient of determination. Consistent with the previous findings in this report, the p-value when analyzing HDI and MDR-TB in countries with medium human development was high (0.916).

For countries with high human development, low coefficients of correlation and determination and relatively high p-values were found when analyzing the relationship between HDI and MDR-TB. High human development countries have a correlation coefficient of 0.110, a coefficient of determination of 0.012 and a p-value of 0.409. The coefficient of correlation, determination and p-value for countries classified as very high human development are, respectively, 0.273, 0.074 and 0.057. The p-value for countries with very-high human development thus drops from the p-value seen in high human development countries. The regression findings are significant, as they do not completely support the current understanding of AMR in the existing literature section of this paper, which states that underdevelopment and poverty are among the leading causes of antimicrobial resistance. By considering health, education and income factors, the regression in regards to HDI and MDR-TB revealed that underdevelopment and poverty may not play as large of a role in antimicrobial resistance as originally thought.

Descriptive statistics performed on the data collected further support this idea, as it was found that the mean incidence of MDR-TB does not consistently decrease as human development level increases. The order from the highest to lowest mean incidence of MDR-TB was found to be: medium human development (8159), high human development (2731.3), low human development (1872) and very high human development (1567.7). Among one of the most notable observations is that countries will low human development and high human development do not differ significantly in regards to their incidence of MDR-TB. These findings question the idea that lower levels of human development and high incidences MDR-TB are strongly related.

4. Policy implications and concluding remarks

Based on the findings of this paper, it is evident that GNI per capita and the incidence of MDR-TB, and HDI and the incidence of MDR-TB, are not strongly correlated. Existing literature largely discusses that socioeconomic factors present in developing countries such as the high burden of disease, as well as the cost and quality of antibiotics received in developing countries, are largely responsible for the issue of antibiotic resistance in developing countries (Alsan et al., 2015; Atabe, Ayukekbong & Ntemgwa, 2017; Bhutta et al., 2005; WHO, 2017).

Byarugaba (2004) summarizes this standpoint by stating that, "the problem of antimicrobial resistance is greatly influenced by poverty and the factors related to it." The results from the statistical measures performed on nation-level data in regards to GNI per capita, HDI and MDR-TB indicate that the issue of antimicrobial resistance is complex and the root causes of this issue are much deeper than just a low incomeor low human development index. This contradicts the general understanding that poverty and underdevelopment are among the leading factors contributing to MDR-TB. There is still evidence, however, to place importance on the fact that a low GNI per capita and a low HDI are contributing factors to MDR-TB.

Thus, in order to address the complex global issue of antimicrobial resistance, this study argues in favour of approaches that break down this global issue to the individual nation-level. The statistical evidence produced in this study shows that when determining the causes of antimicrobial resistance, we cannot group countries based on their level of development or income – there is ample variation that must be accounted for. This variation, and a specific country's root causes of AMR, could be explained and combated by working with individual governments and organizations to create national AMR frameworks. By working with individual countries, policies would be appropriate to and tailored for the specific environment they are being implemented in.

For example, in India the incidence of MDR-TB is extremely high (147,000 cases reported in 2016), despite the nation being considered a lower-middle income nation and holding medium human development. Studies just observing AMR in India indicate that resistance is seriously prevalent due to over-the-counter sales making antibiotics accessible to populations at large (Chaundry & Laxminarayan, 2016; Divyapriya, Nambi, Sivagami, Srinivasan, & Vignesh, 2018). Similarly, Chaundry & Laxminarayan (2016) argue that rapid economic growth combined with poor public health infrastructure, rising incomes, high burdens of disease, as well as low-cost and low-regulated antibiotic sales account for the high rates of drug resistant strains in India. Therefore, policies aiming to combat antimicrobial resistance in India could be more tailored to antibiotic accessibility and regulation, rather than just income or development level.

In many ways, the World Health Organization and its partner agencies have developed action plans and key policy recommendations to combat AMR, including: national plans and accountability, surveillance and laboratory capacity, access to essential medicines, regulation of medicines, education and awareness, infection prevention and control, and innovation and research (WHO, 2015). The results of this study support such measures and would argue for the increased use of national plans.

Additionally, individual countries should ensure that policies are appropriate for their unique regions, rather just implementing policies based the success of another country. This can be done through pilot projects, developing national annual indicators to track the incidence of MDR-TB and creating programs to ensure that the public is well informed about the risks and causes of AMR (Dar et al., 2016; WB, 2017).

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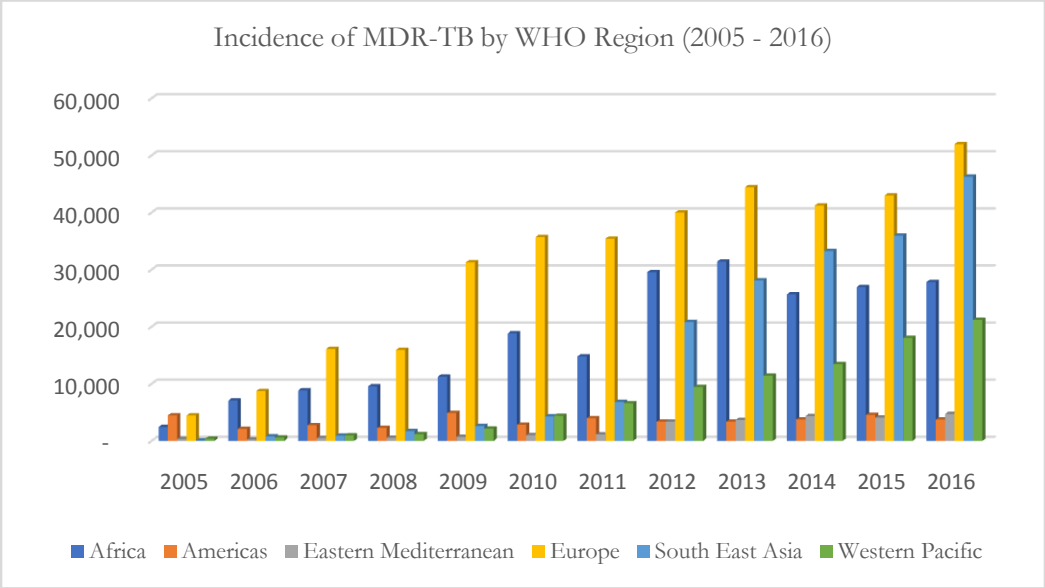
Figure 1. MDR-TB by Region



Data Source: World Health Organization (2018)

Appendix A: Country classification by National Income

Low-Income:

Afghanistan
Benin
Burkina Faso
Burundi
Central African Republic
Chad
Comoros
Congo (Democratic Republic of the)
Ethiopia
Gambia
Guinea
Guinea-Bissau
Haiti
Liberia
Madagascar
Malawi
Mali
Mozambique
Nepal
Niger
Rwanda
Senegal
Sierra Leone
Togo
Uganda
Zimbabwe

Lower-Middle Income:

Angola
Armenia
Bangladesh
Bhutan
Bolivia (Plurinational State of)
Cabo Verde
Cambodia
Cameroon
Congo
Côte d'Ivoire
Egypt
El Salvador
Georgia
Ghana
Guatemala
Honduras
India
Indonesia
Jordan
Kenya
Kiribati
Kyrgyzstan
Lao (People's Democratic Republic)
Lesotho
Mauritania
Micronesia (Federated States of)
Mongolia
Morocco
Myanmar
Nicaragua
Nigeria
Pakistan
Papua New Guinea
Philippines
Sao Tome and Principe
Solomon Islands
Sri Lanka
Sudan
Swaziland
Tajikistan
Timor-Leste
Tunisia
Ukraine
Uzbekistan
Viet Nam
Zambia

Upper-Middle Income:

Albania
Algeria
Argentina
Azerbaijan
Belarus
Belize
Bosnia and Herzegovina
Botswana
Brazil
Bulgaria
China
Colombia
Costa Rica
Croatia
Dominica
Dominican Republic
Equatorial Guinea
Ecuador
Fiji
Gabon
Grenada
Guyana
Iran (Islamic Republic of)
Iraq
Jamaica
Kazakhstan
Lebanon
Malaysia
Maldives
Mauritius
Mexico
Montenegro
Namibia
Panama
Paraguay
Peru
Romania
Russian Federation
Samoa
Serbia
South Africa
Saint Lucia
Saint Vincent and the Grenadines
Suriname
Thailand
Tonga
Turkey
Turkmenistan

High-Income:

Antigua and Barbuda
Australia
Austria
Bahamas
Barbados
Belgium
Brunei Darussalam
Canada
Chile
Cyprus
Czech Republic
Denmark
Estonia
Finland
France
Germany
Greece
Hong Kong, China (SAR)
Hungary
Iceland
Ireland
Israel
Italy
Japan
Korea (Republic of)
Kuwait
Latvia
Lithuania
Luxembourg
Malta
Netherlands
New Zealand
Norway
Palau
Poland
Portugal
Saudi Arabia
Seychelles
Singapore
Slovakia
Slovenia
Spain
Saint Kitts and Nevis
Sweden
Switzerland
Trinidad and Tobago
United Arab Emirates
United Kingdom of Great Britain
United States of America
Uruguay

Appendix B: Country classification by Level of Human Development

Low Human Development:

Afghanistan
Angola
Benin
Burkina Faso
Burundi
Cameroon
Central African Republic
Chad
Comoros
Congo (Democratic Republic of the)
Côte d'Ivoire
Ethiopia
Gambia
Guinea
Guinea-Bissau
Haiti
Lesotho
Liberia
Madagascar
Malawi
Mali
Mauritania
Mozambique
Niger
Nigeria
Papua New Guinea
Rwanda
Senegal
Sierra Leone
Solomon Islands
Sudan
Swaziland
Togo
Uganda
Zimbabwe

Medium Human Development:

Bangladesh
Bhutan
Bolivia (Plurinational State of)
Botswana
Cabo Verde
Cambodia
Congo
Egypt
El Salvador
Equatorial Guinea
Gabon
Ghana
Guatemala
Guyana
Honduras
India
Indonesia
Iraq
Kenya
Kiribati
Kyrgyzstan
Lao (People's Democratic Republic)
Micronesia (Federated States of)
Morocco
Myanmar
Namibia
Nepal
Nicaragua
Pakistan
Paraguay
Philippines
Sao Tome and Principe
South Africa
Tajikistan
Timor-Leste
Turkmenistan
Viet Nam
Zambia

High Human Development:

Albania
Algeria
Antigua and Barbuda
Armenia
Azerbaijan
Bahamas
Barbados
Belarus
Belize
Bosnia and Herzegovina
Brazil
Bulgaria
China
Colombia
Costa Rica
Dominica
Dominican Republic
Ecuador
Fiji
Georgia
Grenada
Iran (Islamic Republic of)
Jamaica
Jordan
Kazakhstan
Lebanon
Malaysia
Maldives
Mauritius
Mexico
Mongolia
Palau
Panama
Peru
Saint Kitts and Nevis
Saint Lucia
Saint Vincent and the Grenadines
Samoa
Serbia
Seychelles
Sri Lanka
Suriname
Thailand
Tonga
Trinidad and Tobago
Tunisia
Turkey
Ukraine
Uruguay
Uzbekistan

Very High Human Development:

Argentina
Australia
Austria
Belgium
Brunei Darussalam
Canada
Chile
Croatia
Cyprus
Czech Republic
Denmark
Estonia
Finland
France
Germany
Greece
Hong Kong, China (SAR)
Hungary
Iceland
Ireland
Israel
Italy
Japan
Korea (Republic of)
Kuwait
Latvia
Lithuania
Luxembourg
Malta
Montenegro
Netherlands
New Zealand
Norway
Poland
Portugal
Romania
Russian Federation
Saudi Arabia
Singapore
Slovakia
Slovenia
Spain
Sweden
Switzerland
United Arab Emirates
United Kingdom of Great Britain
United States of America