

Supplementary material for

Socioeconomic determinants of global distribution of multiple sclerosis: an ecological investigation based on Global Burden of Disease data

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The definition of Human Development Index (HDI) and its components based on information of the United Nations Development Programme (UNDP) database (<http://hdr.undp.org/en/data>)

HDI is a complex index measuring development of countries not only by economic growth but also by three variables include: having a decent standard of living (income index: gross national income (GNI) per capita), long and healthy life (health index: life expectancy at birth) and being knowledgeable (education index: mean and expected years of schooling).

Method for calculating HDI. The following three indices are used(1):

- Health index: Life expectancy at birth (LEB)
- Education index: Mean and Expected years of schooling (MYS and EYS)
- income index: GNI per capita (PPP US\$)

A. Life Expectancy Index (LEI) = $\frac{LE-20}{85-20}$

LEI is 1 when LEB is 85 and 0 when LEB is 20.

B. Education Index (EI) = $\frac{MYSI+EYSI}{2}$

Mean Years of Schooling (MYS) Index = $\frac{MYS}{15}$

15 is the projected maximum of this indicator for 2025.

Expected Years of Schooling (EYSI) Index = $\frac{EYS}{18}$

18 is equivalent to achieving a master's degree in most countries.

C. Income Index (II) = $\frac{\ln(GNIpc)-\ln(100)}{\ln(75000)-\ln(100)}$

II is 1 when GNI per capita is \$75,000 and 0 when GNI per capita is \$100.

HDI is the geometric mean of the previous three normalized indices:

$$HDI = \sqrt[3]{LEI.EI.II.}$$

LE: Life expectancy at birth

MYS: Mean years of schooling (i.e. years that a person aged 25 or older has spent in formal education)

EYS: Expected years of schooling (i.e. total expected years of schooling for children under 18 years of age)

GNIpc: Gross national income at purchasing power parity per capita

The definition of Prosperity Index components based on information of The Legatum Prosperity Index™ 2018(2)

1. The Economic Quality pillar ranks countries on the openness of their economy, macro-economic indicators, and foundations for growth, economic opportunity and financial sector efficiency.
2. The Business Environment pillar measures a country's entrepreneurial environment, its business infrastructure, barriers to innovation and labour market flexibility.
3. The Governance pillar measures a country's performance in three areas: effective governance, democracy and political participation and rule of law.
4. The Personal Freedom pillar measures national progress towards basic legal rights, individual liberties and social tolerance.
5. The Social Capital pillar measures the strength of personal relationships, social network support, social norms and civic participation in a country.
6. The Safety & Security pillar ranks countries based on national security and personal safety.
7. The Education pillar ranks countries on access to education, quality of education and human capital.
8. The Health pillar measures a country's performance in three areas: basic physical and mental health, health infrastructure and preventative care.
9. The Natural Environment pillar measures a country's performance in three areas: the quality of the natural environment, environmental pressures and preservation efforts.

The highest and lowest values were observed in Norway and Yemen, respectively (Figure 1). The lowest values for economic quality, governance, and education were observed in Yemen, Yemen, and Central African Republic, respectively. The highest values for the same parameters were recorded in Switzerland, Finland, and Switzerland, respectively.

Figure S1 shows PI with nine component value in 2017.

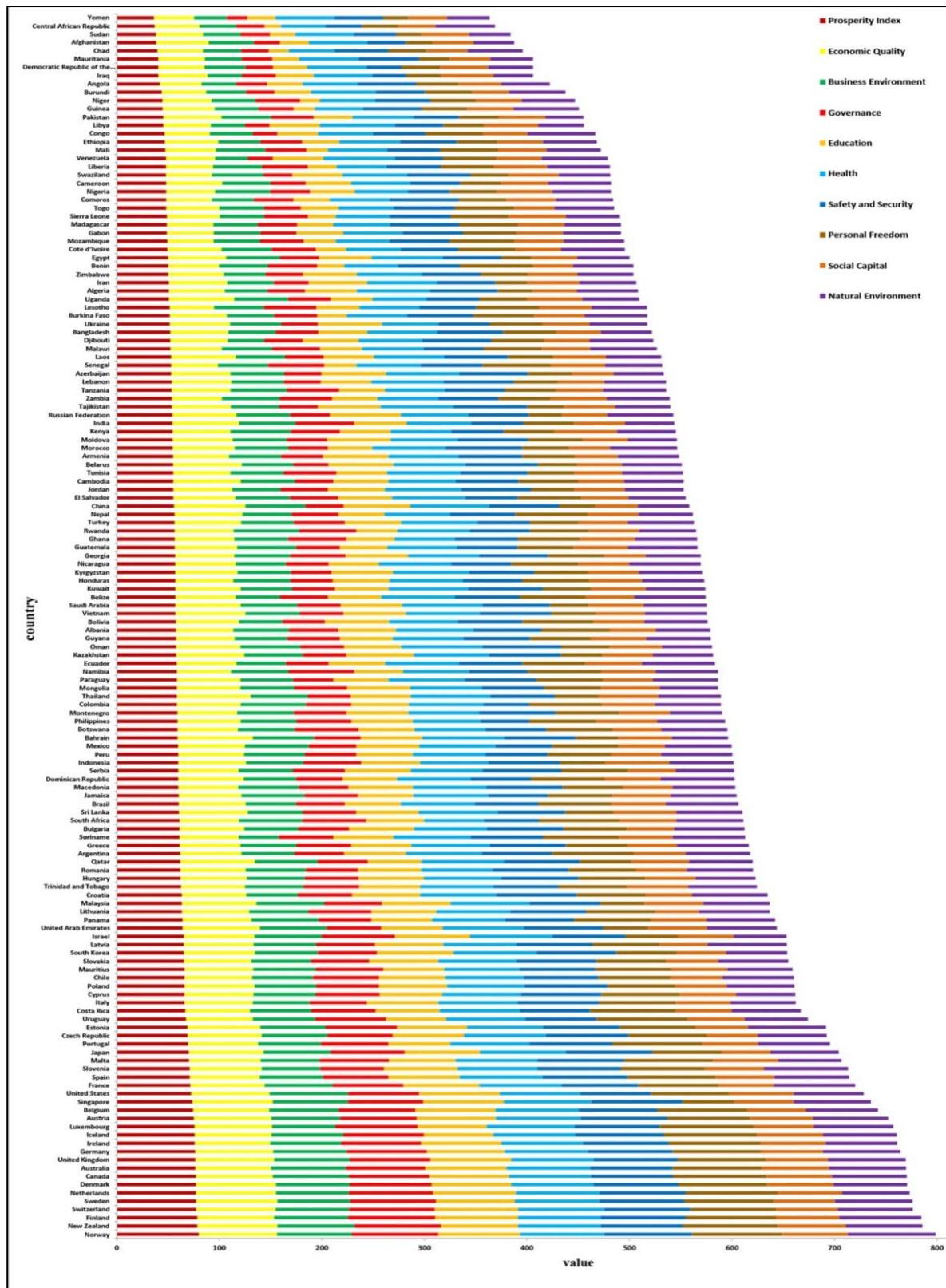


Fig.S1 The value of PI and its subgroups in countries 2017 (3)

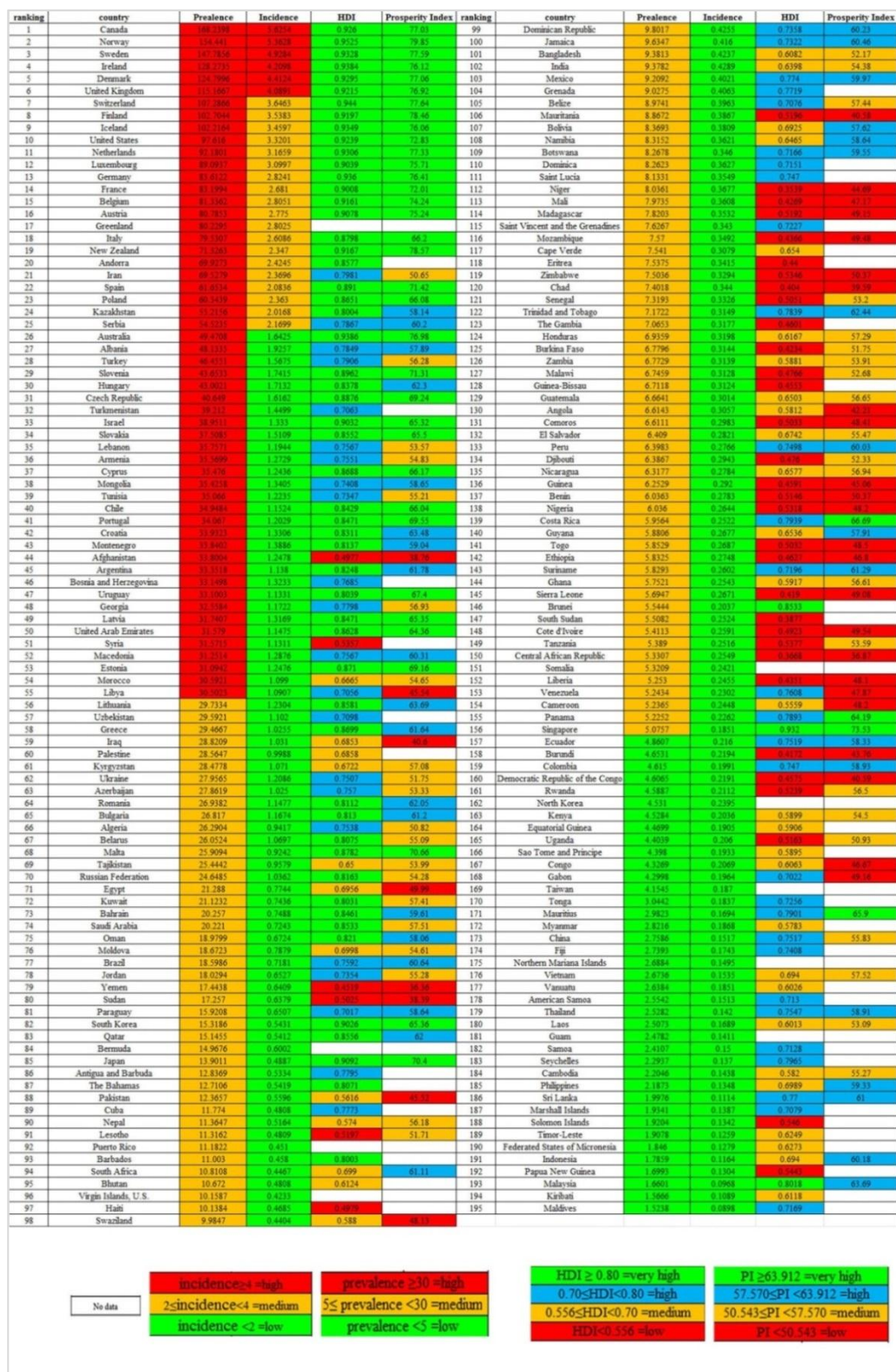


Fig. S2 The MS prevalence and incidence, PI and HDI in 195 countries in our study

Table S1 Unstandardized regression coefficients for multivariable associations between MS indices and HDI subgroups in 2017

Variables	Incidence ^a	Prevalence ^a	DALY ^a	Mortality ^a
	B (SE)	B (SE)	B (SE)	B (SE)
Expected Years of Schooling	0.12 (0.03)**	3.59 (0.81)**	1.94 (0.37)**	0.03 (0.01)**
Mean Years of Schooling	0.04 (0.02)	1.16 (0.65)	0.59 (0.29)*	0.01 (0.01)
Gross National Income	1.84x10 ⁻⁵ (<0.01)**	0.001 (<0.01)**	<0.01 (<0.01)**	2.82x10 ⁻⁶ (<0.01)**

** P< 0.01; * P<0.05; , a: unit of measure is per 100,000 persons-years

Multivariable regression showed that there are associations between PI subgroups and MS variables. Governance and Education had significant associations with MS variables. Incidence and prevalence were affected mostly by Governance; while, mortality and DALY were influenced mostly by Education.

Table S2 Unstandardized regression coefficients for multivariable associations between MS indices and PI subgroups in 2017

variables	Incidence ^a		Prevalence ^a		DALY ^a		Mortality ^a	
	B (SE)	P	B (SE)	P	B (SE)	P	B (SE)	P
Economic Quality	<0.001 (0.018)	0.98	-0.041 (0.542)	0.94	0.032 (0.244)	0.90	0.001 (0.004)	0.86
Business Environment	-0.007 (0.016)	0.69	-0.194 (0.489)	0.69	-0.094 (0.220)	0.67	-0.001 (0.004)	0.79
Governance	0.030 (0.013)	0.02	0.920 (0.381)	0.02	0.343 (0.171)	<0.05	0.004 (0.003)	0.15
Education	0.029 (0.010)	0.01	0.788 (0.311)	0.01	0.495 (0.140)	<0.01	0.008 (0.002)	<0.01
Health	-0.016 (0.016)	0.32	-0.336 (0.481)	0.49	-0.346 (0.216)	0.11	-0.007 (0.004)	0.06
Safety and Security	0.013 (0.010)	0.21	0.335 (0.309)	0.28	0.190 (0.140)	0.18	0.003 (0.002)	0.16
Personal Freedom	0.006 (0.008)	0.46	0.149 (0.232)	0.52	0.134 (0.104)	0.20	0.003 (0.002)	0.06
Social Capital	0.004 (0.015)	0.80	0.227 (0.460)	0.62	-0.096 (0.207)	0.64	-0.003 (0.003)	0.39
Natural Environment	-0.013 (0.012)	0.29	-0.348 (0.350)	0.32	-0.131 (0.158)	0.41	-0.002 (0.003)	0.51

a: unit of measure is per 100,000 persons-years

MS and countries classification (developed vs developing)

Pearson correlation analysis showed that the subgroups of HDI and PI were significantly associated with MS variables in both developed and developing countries. The relationship in developed countries was stronger.

Table S3 Correlation (r) between MS variables and HDI, PI in Developing and Developed countries

category	Variables	Prevalence ^a	Incidence ^a	DALY ^a	Mortality ^a
Developing	HDI	0.351**	0.346**	0.400**	0.382**
	PI	0.052	0.067	0.091	0.130
Developed	HDI	0.706**	0.694**	0.673**	0.605**
	PI	0.675**	0.664**	0.662**	0.627**

HDI= Human Development Index, PI= Prosperity Index, ** P<0.01, * P<0.05, ; a: unit of measure is per 100,000 persons-years

Multivariable regression between HDI and PI and MS variables showed that controlling for PI, there is an association between HDI and incidence in both developed and developing countries. Associations with HDI were stronger than PI in both groups of countries. PI in developing countries was inversely associated with MS variables. In developed countries, HDI only significant for incidence and prevalence of MS.

Table S4 Unstandardized regression coefficients for multivariable associations between MS indices and HDI and PI in 2017

Dependent variables	Independent variables	Developing	Developed
		B (SE)	B (SE)
Incidence ^a	HDI	2.38 (0.44)**	11.11 (5.10)**
	PI	-0.03 (0.01)**	0.06 (0.04)
Prevalence ^a	HDI	69.11 (11.95)**	341.53 (150.59)*
	PI	-0.82 (0.22)**	1.72 (1.02)
DALY ^a	HDI	38.00 (7.23)**	130.65 (66.06)
	PI	-0.41 (0.14)**	0.80 (0.45)
Mortality ^a	HDI	0.58 (0.14)**	1.60 (1.17)
	PI	-0.01 (0.00)**	0.02 (0.01)

** P<0.01, * P<0.05. HDI= Human Development Index, PI= Prosperity Index, ; a: unit of measure is per 100,000 persons-years

Multiple regressions showed that there are significant positive relationships between the PI subgroups in developed and developing countries and MS variables.

Table S5 Unstandardized regression coefficients for multivariable associations between MS indices and PI subgroups in developed and developing countries

	Covariates	Incidence ^a	Prevalence ^a	DALY ^a	Mortality ^a
		B (SE)	B (SE)	B (SE)	B (SE)
Developing	Economic Quality	-0.015 (0.009)	-0.440 (0.235)	-0.176 (0.144)	-0.003 (0.003)
	Business Environment	0.003 (0.008)	0.068 (0.222)	0.068 (0.136)	0.002 (0.003)
	Governance	0.002 (0.007)	0.100 (0.201)	-0.058 (0.124)	-0.002 (0.002)
	Education	0.014 (0.005)*	0.355 (0.151)*	0.270 (0.093)**	0.004 (0.002)*
	Health	0.008 (0.008)	0.294 (0.220)	0.024 (0.135)	<0.001 (0.003)
	Safety and Security	0.008 (0.005)	0.185 (0.149)	0.076 (0.092)	0.001 (0.002)
	Personal Freedom	0.001 (0.005)	-0.034 (0.132)	0.091 (0.081)	0.003 (0.002)*
	Social Capital	-0.016 (0.008)	-0.447 (0.228)	-0.229 (0.139)	-0.004 (0.003)
	Natural Environment	-0.020 (0.007)**	-0.488 (0.190)*	-0.316 (0.117)**	-0.006 (0.002)**
Developed	Economic Quality	0.068 (0.060)	1.779 (1.779)	0.932 (0.756)	0.016 (0.013)
	Business Environment	-0.067 (0.047)	-1.888 (1.398)	-0.854 (0.594)	-0.012 (0.010)
	Governance	0.010 (0.032)	0.269 (0.949)	0.221 (0.403)	0.003 (0.007)
	Education	0.082 (0.028)**	2.439 (0.846)**	0.964 (0.360)**	0.014 (0.006)*
	Health	-0.081 (0.055)	-1.823 (1.623)	-1.711 (0.690)*	-0.035 (0.012)**
	Safety and Security	-0.012 (0.028)	-0.593 (0.837)	0.106 (0.356)	0.007 (0.006)
	Personal Freedom	0.014 (0.017)	0.451 (0.505)	0.187 (0.215)	0.003 (0.004)
	Social Capital	0.087 (0.038)*	2.737 (1.130)*	0.871 (0.480)	0.010 (0.008)
	Natural Environment	0.004 (0.024)	0.068 (0.706)	0.188 (0.300)	0.004 (0.005)
** $P < 0.01$, * $P < 0.05$, ; a: unit of measure is per 100,000 persons-years					

Regression model in developed countries showed positive associations of EYS on all MS variables. Additionally, incidence and prevalence of MS were positively associated with LE. The other variables was not statistical significant with HDI subgroups in developed country and all variables in developing country.

Table S6 Unstandardized regression coefficients for multivariable associations between MS indices and HDI subgroups in developed and developing countries

MS variables	covariate	Developing		Developed	
		B (SE)	P	B (SE)	P
Incidence ^a	Expected Years of Schooling	0.013 (0.022)	0.55	0.293 (0.082)	<0.01
	Mean Years of Schooling	0.013 (0.013)	0.33	0.030 (0.057)	0.60
	Life Expectancy	0.011 (0.007)	0.11	0.072 (0.034)	0.04
	Gross National Income	5.343x10 ⁻⁶ (<0.001)	0.53	1.131x10 ⁻⁵ (<0.001)	0.14
Prevalence ^a	Expected Years of Schooling	0.300 (0.608)	0.62	8.929 (2.407)	<0.01
	Mean Years of Schooling	0.335 (0.355)	0.35	0.714 (1.675)	0.67
	Life Expectancy	0.335 (0.196)	0.09	2.321 (0.985)	0.02
	Gross National Income	<0.001 (<0.001)	0.46	<0.001 (<0.001)	0.10
DALY	Expected Years of Schooling	0.391 (0.340)	0.25	3.789 (1.090)	<0.01
	Mean Years of Schooling	0.222 (0.199)	0.27	0.544 (0.758)	0.48
	Life Expectancy	0.181 (0.110)	0.10	0.760 (0.446)	0.09
	Gross National Income	8.678x10 ⁻⁵ (<0.001)	0.51	9.091x10 ⁻⁵ (<0.001)	0.38
Mortality ^a	Expected Years of Schooling	0.009 (0.006)	0.17	0.057 (0.019)	<0.01
	Mean Years of Schooling	0.004 (0.004)	0.32	0.008 (0.013)	0.54
	Life Expectancy	0.003 (0.002)	0.15	0.008 (0.008)	0.28
	Gross National Income	1.293x10 ⁻⁶ (<0.001)	0.60	8.445x10 ⁻⁷ (<0.001)	0.64

a: unit of measure is per 100,000 persons-years

MS and HDI classification

Based on the data of United Nations Development Programme (UNDP) and the Legatum Institute's data of MS, 186 (out of 195) countries were placed into four groups, including low (N = 39), medium (N = 39), high (N = 51), and very high HDI countries (N = 57). One-way ANOVA test demonstrated that all MS variables differed significantly among countries in different HDI levels ($p < 0.01$). The results of post hoc tests demonstrated that difference between group means of MS variables in the countries with very high HDI was significantly lower than other categories ($p < 0.01$) (Figure 3), but there was no significant difference between high, medium and low HDI categories (with Graph pad prism software).

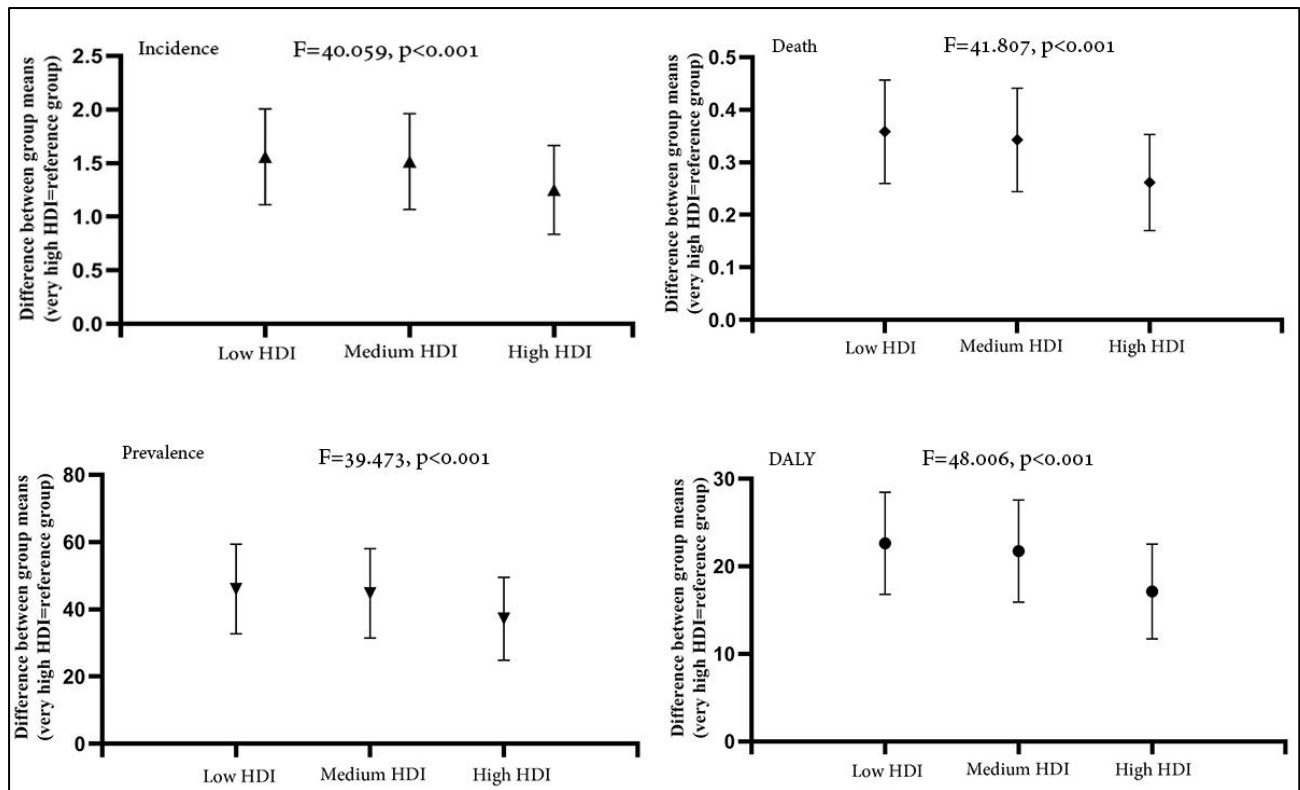


Fig. S3 Differences between group means of MS variables in four HDI groups with ANOVA tests. Differences between group means of MS variables in low, medium and high HDI countries is significantly higher than that of very high HDI countries. Vertical lines represent differences between group means.

References

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