

Environmental Variables Related to Life Expectancy, Ecology, Demography/Social, Economy, and Lifestyle (LEEDELS): Correlations with the Main Common illnesses in 49 WHO Selected Countries (SC)

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Received March 19, 2020; Accepted April 13, 2020; Published June 28, 2020

ABSTRACT

Background: Environmental variables may have an impact on many illnesses.

Objective: To correlate life expectancy (LE), ecological, demographical/social, economic, life style variables (overall defined as LEEDELS) with the most common illnesses in those 49 countries (49SC) considered reliable by WHO in terms of Age Standardized Death Ratio (ASDR) registry.

Material and Methods: ASDRs of 34 diseases (17 non cancer and 17 cancers), retrieved from WHO records, were correlated with LEEDELS in the years between 2000 and 2016.

Results: LE and population increase were respectively 4.5 years and 19.7 %. Most of the illnesses showed a significant decrease, a part from pancreas cancer (+7%) and Alzheimer (+ 72 %), while HIV, digestive diseases, prostate and brain cancers were not significantly modified.

In general, the modifications (positive or negative) were more correlated with those LEEDELS indicative of welfare status (GDP, cars, internet, cell phones), while social/demographical and ecological variables showed a minimal impact. The pancreatic cancer was positively correlated with cell phones.

Conclusions: In the 49 SC, the welfare variables influence positively most of the ASDRs. TBC, STD, diarrheal, peptic ulcer among non-cancer illnesses while stomach, liver and cervix among cancers were bound to a lower economic status. Pancreatic cancer was positively correlated with cells.

Keywords: Ecology, Demography, Economy, Cancers, Diseases, Pancreatic cancer

INTRODUCTION

The relationship between LE, ecology, demography/social, economy and life style (complexively reported as LEEDELS variables) has been matter of so many reports and debates that it will be very difficult to summarize all of them, a part from the common statement that humans are spoiling the earth and compromising the life of the new generations [1-3], in terms of loss of biodiversity [4,5], climate emergency [6], and CO₂ emission [7].

How has the belief come about that our ancestors have done wrong in trying to provide a better life for us.

Is it true that in bringing a steak, vegetables and fruits on the family table we have compromised the life of our grandchildren? How is it a crime to provide comfort to our

families by heating the houses in winter and providing some fresh air in hot summer?

Perhaps is necessary to focus our attention between progress and health.

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Citation: Umberto C, Giovanni B & Martino R. (2020) Environmental Variables Related to Life Expectancy, Ecology, Demography/Social, Economy, and Lifestyle (LEEDELS): Correlations with the Main Common illnesses in 49 WHO Selected Countries (SC). J Pathol Toxicol Res, 1(1): 15-30.

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The aim of the present study was to analyze, in the period between 2000 and 2016, the correlations between the Average Standard Death Ratio (ASDRs) and the most common diseases with LEEDELS, in those countries considered reliable by WHO in terms of data registration.

MATERIAL AND METHODS

Criteria of choice for the variables and time frame

The Age-Standardized Death Rate x 100,000 population (ASDRs) were considered for some diseases (non-cancer and cancers, **Table 1**) were compared to some of the LEEDELS (**Table 2**).

Table 1. ASDRs of the different diseases divided by gender: Mean values ± SD and correlations between 2000 and 2016; *r* values in *Italic characters* are statistically significant at *p*<0.01.

Diseases	GHE	Gender M/F	ASDRs values Mean ± SD			% 2016 Vs 2000	Correlation <i>r</i> 2000 Vs 2016
			2000	2010	2016		
Diabetes	800	M/F	25.29 ± 31.551	24.60 ± 34.173	23.41 ± 31.017 ^a	-7	<i>0.9461</i>
Diabetes	800	F	24.99 ± 32.686	23.20 ± 33.466	21.12 ± 28.477	-15	<i>0.9305</i>
Iron-deficiency anemia [IDA]	580	M/F	0.76 ± 1.261	0.67 ± 1.045	0.57 ± 0.857	-25	<i>0.9032</i>
Iron-deficiency anemia [IDA]	580	F	0.69 ± 1.030	0.67 ± 0.984	0.57 ± 0.836	-17	<i>0.9479</i>
Tuberculosis (TBC)	30	M/F	4.04 ± 6.339	2.17 ± 3.251	1.43 ± 2.172	-65	<i>0.9070</i>
STD	40	M/F	0.17 ± 0.207	0.10 ± 0.126	0.08 ± 0.118	-53	<i>0.7620</i>
Chlamydia	60	F	0.024 ± 0.0253	0.015 ± 0.0143	0.010 ± 0.0103	-58	<i>0.4956</i>
HIV/AIDS	100	M/F	5.00 ± 15.801	3.30 ± 8.160	3.54 ± 9.373 ^a	-29	<i>0.9691</i>
Diarrheal diseases	110	M/F	2.36 ± 6.472	1.52 ± 3.072	1.32 ± 2.133	-44	<i>0.9426</i>
Hepatitis	185	M/F	0.77 ± 0.948	0.44 ± 0.456	0.43 ± 0.316	-44	<i>0.6917</i>
Respiratory infectious	380	M/F	25.42 ± 21.866	17.63 ± 13.744	16.55 ± 11.338	-35	<i>0.7633</i>
Alzheimer	950	M/F	9.18 ± 8.25	12.80 ± 9.045	15.78 ± 11.193	+72	<i>0.7874</i>

CVD	1100	M/F	270.3 ± 131.87	209.8 ± 129.18	179.2 ± 115.84	-34	0.9356
Ischemic stroke	1141	M/F	42.27 ± 27.07	29.94 ± 22.188	23.99 ± 18.664	-51	0.8649
Hemorrhagic stroke	1142	M/F	34.03 ± 21.692	23.92 ± 16.632	19.75 ± 14.088	-58	0.9063
Respiratory diseases	1170	M/F	34.18 ± 19.531	26.04 ± 10.172	20.02 ± 9.350	-41	0.4146
Digestive diseases	1210	M	32.61 ± 14.673	28.71 ± 13.373	25.481 ± 14.403 ^a	-21	0.8869
Peptic ulcer	1220	M/F	3.07 ± 2.199	1.95 ± 1.561	1.85 ± 1.472	-40	0.7353
Acute glomerulonephritis	1271	M/F	0.05 ± 0.163	0.03 ± 0.074	0.03 ± 0.053	-40	0.9463
Chronic kidney disease	1272	MF	3.31 ± 3.272	3.06 ± 2.673	2.78 ± 2.670 ^a	-16	0.7626
Cancers							
Mouth oropharynx	620	M/F	3.91 ± 2.051	3.65 ± 2.036	3.47 ± 1.843	-11	0.8221
Stomach	640	M/F	11.22 ± 6.236	8.37 ± 4.818	7.29 ± 3.999	-35	0.9012
Colorectal cancer	650	M/F	15.74 ± 5.933	14.57 ± 4.695	14.03 ± 4.599	-11	0.7790
Liver	660	M/F	5.40 ± 3.386	5.42 ± 3.067	5.39 ± 2.670 ^a	0	0.8659
Pancreas	670	M/F	6.72 ± 1.975	7.20 ± 2.026	7.18 ± 2.124 ^b	+7	0.9083
TBL (Trachea/bronchus/lung)	680	M/F	25.45 ± 10.158	24.11 ± 9.552	22.37 ± 8.538	-12	0.9424
Melanoma	690	M/F	2.52 ± 1.215	2.64 ± 1.352	2.56 ± 1.185	+2	0.9435
Breast	700	F	21.37 ± 7.065	18.52 ± 5.146	18.01 ± 5.937	-16	0.7364
Cervix	710	F	6.50 ± 5.339	5.74 ± 5.359	5.09 ± 4.502	-22	0.9737

Ovarian	730	F	6.10 ± 2.400	5.97 ± 2.163	5.50 ± 1.859	-11	0.7883
Prostate	740	M	23.79 ± 16.114	22.53 ± 18.254	20.26 ± 15.547 ^a	-15	0.9437
Kidney	745	M/F	3.20 ± 1.667	2.96 ± 1.269	3.01 ± 1.314	-6	0.7409
Bladder	750	M/F	3.41 ± 1.420	3.26 ± 1.350	3.05 ± 1.131	-11	0.8668
Brain	751	M/F	4.20 ± 1.567	4.10 ± 1.452	4.06 ± 1.335 ^a	-3	0.8528
Thyroid cancer	754	M/F	0.56 ± 0.207	0.48 ± 0.156	0.48 ± 0.222	-14	0.6377
Lymphoma	760	M/F	6.60 ± 2.515	5.79 ± 1.847	5.71 ± 1.700	-13	0.8451
Leukemia	770	M/F	4.79 ± 1.036	4.36 ± 0.925	4.12 ± 0.941	-14	0.5459
Life expectancy	years	M/F	74.89 ± 4.377	77.58 ± 4.115	79.16 ± 3.658	+5.7	0.9821

GHE (Global Health Estimation code)

a = Mann-Whitney U test 2000 Vs 2016 $p > 0.05$, b = 2010 Vs 2016 $p < 0.05$

Table 2. LEEDLEs variable: Mean ± SD values of the 49 SC compared to the other 142 countries.

Variable ^a	Measure	49 SC	Other 142 countries
		Mean ± SD	Mean ± SD
Life expectancy (LE) M/F	Years	79.2 ± 3.66	68.5 ± 4.12 ^b
Life expectancy (LE) F	Years	80.9 ± 3.67	69.9 ^c ± 4.59 ^b
Life expectancy (LE) M	years	78.1 ± 3.57	67.3 ± 3.97 ^b
Population density	Subjects/km ²	165.7 ± 222.35	153.3 ± 482.45
Urban population	% of the total	70.7 ± 19.22	50.1 ± 21.75 ^b
GDP/inhabitants	USD	32253 ± 25339.2	6845 ± 11308.6 ^b
Unemployment	% people	8.8 ± 6.18	10.2 ± 8.31 ^b
GDP 1	% of total GDP	8.4 ± 9.34	33.1 ± 25.01 ^b
GDP 2	% of total GDP	23.3 ± 6.88	20.0 ± 9.69
GDP 3	% of total GDP	68.3 ± 11.53	48.9 ± 21.12 ^b
GDP 2+3	% of total GDP	91.7 ± 9.03	66.9 ± 25.11 ^b

Education	% of total GDP	5.3 ± 1.71	4.4 ± 2.40 ^b
Hospital beds	Number/1000 inhabitants	4.7 ± 2.28	2.3 ± 2.13 ^b
Forests	% of country surface	33.0 ± 20.38	29.8 ± 23.40
Forests Km²	Square kilometers/1000 inhabitants	10 ± 16.70	13.06 ± 35.00
Particulate matter	mcg/m ³	29.1 ± 16.2	50.6 ± 39.83 ^b
Cars	Number/1000 inhabitants	361.7 ± 187.98	86.5 ± 124.74 ^b
Cells	Number/1000 inhabitants	1173.2 ± 239.51	993 ± 436.96
Internet	Number of people with connection/1000 inhabitants	722.2 ± 198.77	319.4 ± 241.54 ^b

a = see material and methods for details; b = Mann-Whitney U test 49 SC vs other 142 countries p < 0.05

ASDRs are free of the bias related to age distribution unlike crude data or prevalence/incidence measures. The ASDRs data listed as Global Health Estimates 2016 and published in 2018 were used [8].

The ASDRs do not consider the number of inhabitants in the country with the consequence that values in small countries (e.g., Bahamas- about 0.4 million inhabitants) have the same weight as for larger countries (e.g. USA-about 322 million inhabitants), which can create a bias in the average values of the 49 SC.

However, despite the increase of the population, ASDRs remain significantly correlated (as reported in **Table 1**; r > 0.3772; p < 0.005). For this reason, ASDRs values were considered sufficiently reliable.

For all the variables the values were relative to both genders, a part from prostate cancer which was in relation to males, and breast and cervix cancers concerning females only. Seventeen ecological, environmental and demographic variables limited to 2016 were also taken into consideration [8-10] for the correlation with the different illnesses.

The list and the criteria of choice for the countries

In total, the countries listed by WHO in terms of ASDRs are 191. The data used for correlations were relative only to those 49 countries (selected countries or SC) considered by WHO “with high completeness and quality of cause-of-death assignment” that “may be compared and time series may be used for priority setting and policy evaluation” [7].

List of the countries

The following 49 SC countries were considered: Armenia, Australia, Austria, Bahamas, Belgium, Brazil, Brunei, Canada, Chile, Croatia, Cuba, Czechia, Denmark, Estonia, Finland, France, Germany, Grenada, Guatemala, Hungary, Iceland, Ireland, Israel, Italy, Japan, Kyrgyzstan,

Latvia, Lithuania, Luxembourg, Malta, Macedonia, Mauritius, Mexico, Moldova, Netherlands, New Zealand, Norway, Romania, Saint Vincent & Grenadinas, South Korea, Trinidad & Tobago, United Kingdom, USA, Uzbekistan.

Data collection

The values up to the fourth decimal place were taken from the WHO records. For LEEDELS only the values of 2016 were considered because of very high correlation (r > 0.9) with previous years (2000 and 2010).

For LEEDELS the variables were taken from the Atlante Geografico DE Agostini 2016 Ed De Agostini Novara Italy [9] and by CIA World Factbook 2016 [10].

Life expectancy, ecological, demographic/social, economic, life style variables (LEEDELS)

The following variables were chosen:

- Life expectancy (LE): years
- Population density: as number of subjects/km²
- Urban population: as % in comparison to the total population
- GDP/inhabitant (Gross Domestic Product/inhabitant) as total values/inhabitants (USD) of goods and final services related to economic activities, capital investments
- Unemployment: as % of people looking for a job in relation to the labor force
- GDP 1: GDP rate as % in relation to primary industry bound to agriculture, forests, livestock, fishing
- GDP 2: GDP rate as % in relation to industry, mining and construction
- GDP 3: GDP rate as % in relation to commerce, transportation, communication, tourism, and insurance
- GDP 2+3: sum of the rates as % related to GDP 2 + GDP 3
- Education: as % of the investments in public and private instruction in relation to GDP
- Hospital beds: number of hospital beds/1000 inhabitants
- PM: particulate matter (PM_{2.5} and PM₁₀) in mcg/m³ measured in cities with > 100,000 inhabitants

Forests: rate as % of the country surface covered by forests
 Forests Km²: square kilometers of forest/1000 inhabitants.
 Cars: number of cars/1000 inhabitants
 Cell: number of cell phones/1000 inhabitants
 Internet: number of people with internet connection/1000 inhabitants.

Statistical evaluation

For all the variables the mean values and dispersion indexes were calculated.

The level of p <0.05 was considered as the cut off. The Mann-Whitney U test was used to calculate the difference in

ASDRs among the periods (2000-2016), while for the correlations ASDRs/LEEDELs the cut off was p <0.01.

In terms of correlations among variables, following a linear Pairwise Correlation analysis, the presence of some or more out outlier may compromise the r values. The impact of the outlier was minimized using the Robust fit [11] further adjusted following the method M of Huber [12].

The JMP14 Pro of SAS Institute was used for the analysis.

RESULTS

The data concerning the population increase for both genders were reported in **Table 3**.

Table 3. Population: males and females in 2000 and 2016.

Year	Population males 10 ⁶			Population females 10 ⁶			Total population 10 ⁶		
	191 countries	49 SC	% of 49 SC	191 countries	49 SC	% of 49 SC	191 countries	49 SC	% of 49 SC
2000	3063.097	640.490	20.9	3024.847	662.603	21.9	6087.944	1303.093	21.4
2016	3717.324	719.690	19.4	3673.749	737.667	20.1	7391.073	1457.366	19.7

The 49 SC represented between 19.4 % and 20.1 % of the world population. In the 191 SC between 2000 and 2016 the population increased by 21.4 %, whereas in the 49 SC the increase was 11.8 % only.

The modifications of the ASDRs for the selected diseases were reported in **Table 1**. The significant correlations between 2000 and 2016 indicate that the values of the different diseases are constant over time. This condition allows to consider the values of 2016 as a reliable mirror for all the previous years. In the period 2000 Vs 2016 LE increase of 5.7 % while the other LEEDLEs variables showed very different trends (**Table 2**).

Most of the common illnesses were significantly reduced, a part from Alzheimer which increased by 72%.

The average reductions of HIV, diarrheal diseases, and chronic kidney diseases were not statistically significant due to the large variance. In relation to cancers, a statistically significant reduction was found for all cancers with the exception of liver, and brain cancers showing almost identical ASDRs during the entire period. The only cancer showing a significant increase was the pancreatic cancer (+7 %).

Limited to year 2016, the LEEDLEs variable list comparing the 49 SC with the rest of the 142 countries was reported in **Table 2**.

The differences between the two blocks of countries are consistent for most of the variables, and not significant only for some of the ecological variables (forests) and cell phones.

The correlations between illnesses (non-cancer and cancers) and the LEEDLEs variables were reported in **Table 4**.

The negative correlation indicates that the increase of the disease corresponds to a lower value of the variable, at the opposite a positive correlation corresponds to the increase of the variable. As an example: Alzheimer’s disease increases with the increase of LE, GP/inhab and GP2+3 (high profit), internet connections and cars, while it decreases in case of GP1 (low profit) and PM (particulate matter).

For a more readable evaluation, the correlations between LEEDLEs Vs different illnesses, were reported in **Table 5**, according to the number of variables showing statistically significant r correlation (0.338 as cut off for p<0.01), starting from diseases showing the highest number of correlations (9) to the lowest (0) .

A block of 8 illnesses showed an almost identical tendency with negative correlations for LE, % of urban population, GDP/inhabitants, % GDP 3, % GDP 2+3, internet connections/inhabitant and positive correlation for % GP1. The only diseases with a completely different pattern was Alzheimer, characterized by specular/opposite correlations

for all the variables compared to the rest of the block, with the addition of PM which showed to be negative. Lymphoma also showed a pattern similar to Alzheimer a part from LE which was not significant.

PM showed a positive impact for ischemic stroke and stomach cancer only. All the other diseases with a number of significant correlations between 7 to 1 each seemed to a different pattern for some of the variables (see discussion). A block of 6 illnesses had no correlation with any of the LEEDLEs, meaning they seemed to develop independently from the environmental variables.

For a more comprehensive overview, the different LEEDLEs was also summarized separately and reported in **Tables 5-9**.

Life expectancy

In term of LE dependence the results are reported in **Table 6**.

All the correlations for the listed illness with LE were negative, with the exception of Alzheimer’s disease.

Ecological variables

The classical ecological variables, such as population density, forests % in the country, and forests km²/1000 inhabitants, did not reach the cut off correlation of p < 0.01 with the listed illnesses, and were not reported in the table. The only correlated variable was PM as reported in **Table 7**.

Table 4. Correlations between LEEDLEs and different illnesses.

Diseases	LE	% urb pop	GDP/ inhab	% GDP1	% GDP3	PM	Cars 10 ³	Cells 10 ³	Inter 10 ³	% GDP 2+3
2DM M/F	- <i>0.5144</i>	- <i>0.4483</i>	- <i>0.3102</i>	0.1753	- <i>0.2962</i>	- <i>0.0191</i>	- <i>0.4609</i>	0.0270	- <i>0.4206</i>	- <i>0.1672</i>
2DM F	- <i>0.5463</i>	- <i>0.4568</i>	- <i>0.3370</i>	0.2248	- <i>0.3333</i>	- <i>0.0029</i>	- <i>0.4412</i>	- <i>0.0570</i>	- <i>0.4557</i>	- <i>0.2257</i>
IDA M/F	- <i>0.2590</i>	- <i>0.3446</i>	- <i>0.1595</i>	0.1582	- <i>0.2425</i>	- <i>0.0227</i>	- <i>0.3078</i>	0.0331	- <i>0.3231</i>	- <i>0.1574</i>
IDA F	0.0982	- <i>0.4653</i>	- <i>0.2316</i>	0.2294	- <i>0.3837</i>	0.0219	- <i>0.4063</i>	0.0517	- <i>0.4333</i>	- <i>0.2287</i>
TBC	- <i>0.4794</i>	- <i>0.4020</i>	- <i>0.4388</i>	<i>0.5093</i>	- <i>0.4579</i>	0.0020	- <i>0.5121</i>	- <i>0.0631</i>	- <i>0.5087</i>	- <i>0.5115</i>
STD	- <i>0.4354</i>	- <i>0.1642</i>	- <i>0.3275</i>	<i>0.4050</i>	- <i>0.4022</i>	0.2201	- <i>0.4945</i>	- <i>0.2569</i>	- <i>0.4358</i>	- <i>0.4062</i>
Chlamydia F	- <i>0.1716</i>	0.1821	0.1623	0.0348	0.0155	0.1966	- <i>0.2590</i>	<i>0.3772</i>	- <i>0.1796</i>	- <i>0.0360</i>
HIV	- <i>0.4732</i>	- <i>0.1369</i>	- <i>0.2014</i>	0.0592	- <i>0.0026</i>	0.1101	- <i>0.2490</i>	- <i>0.2410</i>	- <i>0.1612</i>	- <i>0.0609</i>
Diarrheal diseases	- <i>0.2702</i>	- <i>0.1884</i>	- <i>0.2386</i>	<i>0.4021</i>	- <i>0.3104</i>	- <i>0.0060</i>	- <i>0.4093</i>	- <i>0.1697</i>	- <i>0.4626</i>	- <i>0.4210</i>
Isch stroke	- <i>0.6358</i>	- <i>0.5285</i>	- <i>0.5887</i>	<i>0.5434</i>	- <i>0.5925</i>	<i>0.4351</i>	- <i>0.5100</i>	0.0047	- <i>0.4416</i>	- <i>0.5362</i>
Hem stroke	- <i>0.6371</i>	- <i>0.6472</i>	- <i>0.5583</i>	<i>0.5643</i>	- <i>0.6119</i>	<i>0.3467</i>	- <i>0.6261</i>	- <i>0.1470</i>	- <i>0.5809</i>	- <i>0.5668</i>
Hepatitis	-	-	-	0.2793	-	-	-	-	-	-

	0.2047	0.3198	0.3546		0.2584	0.0575	0.3788	0.0338	0.4047	0.2383
Peptic ulcer	-	-	-	0.5199	-	-	-	-	-	-
	0.7026	0.4031	0.4465		0.4825	0.0952	0.3811	0.0429	0.3850	0.5211
Res infections	-	-	0.3317	0.2698	-	0.1343	-	-	-	-
	0.4747	0.1531			0.2879		0.4574	0.2445	0.3870	0.2704
CVD	-	-	-	0.4422	-	-	-	-	-	-
	0.7137	0.6516	0.6141		0.6402	0.1715	0.5721	0.0705	0.5428	0.6435
Digestive diseases	-	-	-	0.6667	-	0.1469	-	-	-	-
	0.7050	0.4884	0.5904		0.6015		0.5886	0.0756	0.6295	0.6691
Acute glomerulonephritis	-	-	-	0.3241	-	-0-	-	-	-	0.3151
	0.1923	0.2665	0.2002		0.1819	0.733	0.2887	0.1813	0.2790	
Chronic Kidney diseases	-	-	-	0.2337	-	0.1282	-	-	0.3795	-
	0.3668	0.1673	0.2631		0.2022		0.4319	0.1933		0.2354
Alzheimer	0.5238	0.5195	0.5796	-	0.5726	-	0.4710	-	0.5607	0.4362
				0.4306		0.4605		0.0319		
Cancers										
Mouth oropharinx	-	-	-	-	-	-	-	-	-	0.0053
	0.4033	0.2727	0.3128	0.0103	0.2513	0.1262	0.1005	0.0045	0.1205	
Stomach	-	-	-	0.5790	-	0.5552	-	0.0696	-	-
	0.4567	0.3289	0.6216		0.6142		0.5875		0.4892	0.6006
Colorectal	-	0.0714	0.0309	-	0.1287	-	0.2519	0.0366	0.3439	0.3916
	0.0029			0.3927		0.2318				
Liver	-	-	-	0.5050	-	0.4029	-	-	-	-
	0.2441	0.1582	0.3210		0.4081		0.4260	0.1137	0.3772	0.5081
Pancreas	0.3503	0.2755	0.2362	0.3398	0.1644	-	0.4545	0.3995	0.4868	0.3363
						0.2507				
TBL	0.3248	0.2965	0.2063	-	0.2199	-	-	0.0070	0.3849	0.2947
				0.2940		0.2086	0.3394			
Melanoma	0.2319	0.2469	0.3048	-	0.1754	0.1253	0.3428	0.0733	0.3264	0.2247
				0.2210						
Breast	-	-	0.0238	-	0.0047	-	0.0152	-	0.1337	0.1837
	0.2911	0.1039		0.1780		0.3192		0.0093		
Cervix	-	-	-	0.3746	-	0.0984	-	-	-	-
	0.7160	0.4769	0.4800		0.5279		0.5414	0.1512	0.4603	0.3746
Ovarian	-	-	0.1835	-	0.1308	-	-	0.2498	0.2899	0.3848
	0.0592	0.0199		0.3745		0.3842	0.3055			
Prostate	-	-	-	-	-	-	-	0.0628	0.0304	0.0591
	0.4206	0.1877	0.0082	0.0594	0.1051	0.1606	0.0872			
Kidney	0.0458	-	-	-	0.0876	-	0.3484	0.2814	0.3997	0.2116
		0.1367	0.0266	0.2135		0.1398				

Bladder	0.0059	0.1171	0.0651	- 0.1905	0.1198	- 0.0945	0.2674	0.1376	0.2927	0.1894
Brain	0.1319	0.1337	0.0735	0.0270	0.0111	- 0.0371	0.2178	0.0750	0.2096	0.0296
Thyroid	- 0.2613	0.0331	- 0.2086	0.2456	- 0.1725	- 0.0577	- 0.1564	0.0480	- 0.1686	- 0.0246
Lymphoma	0.1836	0.2734	0.3897	- 0.6576	0.4876	- 0.4700	0.5246	0.0659	0.5198	0.6606
Leukemia	- 0.0178	0.0920	0.1698	- 0.3047	0.1458	0.0779	0.3229	0.2705	0.2698	0.3030

The significant correlations ($r < 0.01$) were reported in bold Italic characters

Table 5. The correlations between LEEDLEs Vs different diseases from the highest number of correlations (9) to the lowest (0). Significant correlations ($r < 0.01$) were reported in Italics characters.

Diseases	LE	% urb pop	GDP/ inhab	% GDP1	% GDP3	PM	Cars 10 ³	Cells 10 ³	Inter 10 ³	% GDP 2+3
				9-8 variables						
Alzheimer	0.5238	0.5195	0.5796	- 0.4306	0.5726	- 0.4605	0.4710	- 0.0319	0.5607	0.4362
TBC	- 0.4794	- 0.4020	- 0.4388	0.5093	- 0.4579	0.0020	- 0.5121	- 0.0631	- 0.5087	- 0.5115
Isch stroke	- 0.6358	- 0.5285	- 0.5887	0.5434	- 0.5925	0.4351	- 0.5100	0.0047	- 0.4416	- 0.5362
Hem stroke	- 0.6371	- 0.6472	- 0.5583	0.5643	- 0.6119	0.3467	- 0.6261	- 0.1470	- 0.5809	- 0.5668
Peptic ulcer	- 0.7026	- 0.4031	- 0.4465	0.5199	- 0.4825	- 0.0952	- 0.3811	- 0.0429	- 0.3850	- 0.5211
CVD	- 0.7137	- 0.6516	- 0.6141	0.4422	- 0.6402	- 0.1715	- 0.5721	- 0.0705	- 0.5428	- 0.6435
Digestive diseases	- 0.7050	- 0.4884	- 0.5904	0.6667	- 0.6015	0.1469	- 0.5886	- 0.0756	- 0.6295	- 0.6691
Cancers										
Stomach	- 0.4567	- 0.3289	- 0.6216	0.5790	- 0.6142	0.5552	- 0.5875	0.0696	- 0.4892	- 0.6006
Cervix	- 0.7160	- 0.4769	- 0.4800	0.3746	- 0.5279	0.0984	- 0.5414	- 0.1512	- 0.4603	- 0.3746
				7-6 variables						
STD	- 0.4354	- 0.1642	- 0.3275	0.4050	- 0.4022	0.2201	- 0.4945	- 0.2569	- 0.4358	- 0.4062

Cancers										
Lymphoma	0.1836	0.2734	0.3897	-	0.4876	-	0.5246	0.0659	0.5198	0.6606
				0.6576		0.4700				
				<i>4-5 variables</i>						
2DM M/F	-	-	-	0.1753	-	-	-	0.0270	-	-
	0.5144	0.4483	0.3102		0.2962	0.0191	0.4609		0.4206	0.1672
IDA F	0.0982	-	-	0.2294	-	0.0219	-	0.0517	-	-
		0.4653	0.2316		0.3837		0.4063		0.4333	0.2287
Diarrheal diseases	-	-	-	0.4021	-	-	-	-	-	-
	0.2702	0.1884	0.2386		0.3104	0.0060	0.4093	0.1697	0.4626	0.4210
Cancers										
Liver	-	-	-	0.5050	-	0.4029	-	-	-	-
	0.2441	0.1582	0.3210		0.4081		0.4260	0.1137	0.3772	0.5081
Pancreas	0.3503	0.2755	0.2362	0.3398	0.1644	-	0.4545	0.3995	0.4868	0.3363
						0.2507				
				<i>3-1 variables</i>						
IDA M/F	-	-	-	0.1582	-	-	-	0.0331	-	-
	0.2590	0.3446	0.1595		0.2425	0.0227	0.3078		0.3231	0.1574
Hepatitis	-	-	-	0.2793	-	-	-	-	-	-
	0.2047	0.3198	0.3546		0.2584	0.0575	0.3788	0.0338	0.4047	0.2383
Chlamydia Females	-	0.1821	0.1623	0.0348	0.0155	0.1966	-	0.3772	-	-
	0.1716						0.2590		0.1796	0.0360
HIV	-	-	-	0.0592	-	0.1101	-	-	-	-
	0.4732	0.1369	0.2014		0.0026		0.2490	0.2410	0.1612	0.0609
Cancers										
Colorectal	-	0.0714	0.0309	-	0.1287	-	0.2519	0.0366	0.3439	0.3916
	0.0029			0.3927		0.2318				
Ovarian	-	-	0.1835	-	0.1308	-	-	0.2498	0.2899	0.3848
	0.0592	0.0199		0.3745		0.3842	0.3055			
Prostate	-	-	-	-	-	-	-	0.0628	0.0304	0.0591
	0.4206	0.1877	0.0082	0.0594	0.1051	0.1606	0.0872			
Kidney	0.0458	-	-	-	0.0876	-	0.3484	0.2814	0.3997	0.2116
		0.1367	0.0266	0.2135		0.1398				
Melanoma	0.2319	0.2469	0.3048	-	0.1754	0.1253	0.3428	0.0733	0.3264	0.2247
				0.2210						
				<i>0 variables</i>						
Acute glomerulonephritis	-	-	-	0.3241	-	-0-	-	-	-	0.3151
	0.1923	0.2665	0.2002		0.1819	0.0733	0.2887	0.1813	0.2790	
Cancers										
Breast	-	-	0.0238	-	0.0047	-	0.0152	-	0.1337	0.1837

	0.2911	0.1039		0.1780		0.3192		0.0093		
Bladder	0.0059	0.1171	0.0651	- 0.1905	0.1198	- 0.0945	0.2674	0.1376	0.2927	0.1894
Brain	0.1319	0.1337	0.0735	0.0270	0.0111	- 0.0371	0.2178	0.0750	0.2096	0.0296
Thyroid	- 0.2613	0.0331	- 0.02086	0.2456	- 0.1725	- 0.0577	- 0.1564	0.0480	- 0.1686	- 0.0246
Leukemia	- 0.0178	0.0920	0.1698	- 0.3047	0.1458	0.0779	0.3229	0.2705	0.2698	0.3030

Table 6. Correlation between diseases/cancers Vs LE: significant correlations only ($r < 0.01$) were reported in *Italics* characters

. Diseases	r Vs LE
2DM M/F	<i>-0.5144</i>
TBC	<i>-0.4794</i>
STD	<i>-0.4354</i>
HIV	<i>-0.4732</i>
Isch stroke	<i>-0.6358</i>
Hem stroke	<i>-0.6371</i>
Peptic ulcer	<i>-0.7026</i>
Respiratory infections	<i>-0.4747</i>
CVD	<i>-0.7137</i>
Digestive diseases	<i>-0.7050</i>
Alzheimer	<i>0.5238</i>
Cancers	
Mouth oropharinx	<i>-0.4033</i>
Stomach	<i>-0.4567</i>
Cervix	<i>-0.7160</i>
Prostate	<i>-0.4206</i>

Table 7. Correlation of non-cancer and cancers diseases Vs PM: significant correlations only ($r < 0.01$) were reported in *Italics* characters.

Diseases	r Vs PM
Isch stroke	<i>0.4351</i>
Alzheimer	<i>-0.4605</i>
Cancers	
Stomach	<i>0.5552</i>
Ovarian	<i>-0.3842</i>
Lymphoma	<i>-0.4700</i>

It seemed that PM increases the ASDRs in the case of ischemic stroke and stomach cancer, while an opposite effect was found for Alzheimer’s disease, ovarian cancer and lymphoma.

Demographic/social variables

The % of urban population was the only demographic variable showing some significant correlation, while all the others, hospital beds, and education investments were found inconsistent.

Data were reported in **Table 8**.

Table 8. Correlation of diseases/cancers Vs % of urban population: significant correlations only ($r < 0.01$) were reported in *Italics* characters.

Diseases	r Vs % urban population
2DM M/F	<i>-0.4483</i>
2DM F	<i>-0.4568</i>
IDA F	<i>-0.4653</i>
TBC	<i>-0.4020</i>
Isch stroke	<i>-0.5285</i>

Hem stroke	-0.6472
Peptic ulcer	-0.4031
CVD	-0.6516
Digestive diseases	-0.4884
Alzheimer	0.5195
Cancers	
Cervix	-0.4769

A part from Alzheimer’s disease, the ASDRs correlation with all the other illnesses were negative.

Economic variables

GDP/inhabitant and % of GPI, GDP 3 were the variables showing some significant negative correlation.

GDP 2 was not significantly correlated and was summed up with GDP 3. This last variable is complementary to % GPI. Data were summarized in **Table 9**.

A block of 8 illnesses (TBC, STD, ischemic stroke, peptic ulcer, digestive diseases, liver, stomach, and cervix cancers were showing a similar correlation pattern: negative for GDP/inhabitants and % GPD 3, and positive for the other GDPs (1 % and 2+3 %). Lymphoma and Alzheimer’s disease were the only diseases with ASDRs specular to the other. Colorectal cancer seemed influenced by GDPs only (positive for 1% GDP and negative for % GDP 2+3).

Life style variables

These variables seemed to be the most discriminant for non-cancer and cancer diseases accounting for 21 different illnesses as reported in **Table 10**.

Table 9. Correlation between non cancer/cancers diseases Vs economic variables: significant correlations only (*r* <0.01) were reported in *Italics* characters

Diseases	<i>r</i> Vs GDP/inhab	<i>r</i> Vs %GDP1	<i>r</i> Vs %GDP3	<i>r</i> Vs %GDP 2+3
IDA F	-0.2316	0.2294	-0.3837	-0.2287
TBC	-0.4388	0.5093	-0.4579	-0.5115
STD	-0.3275	0.4050	-0.4022	-0.4062
Diarrheal diseases	-0.2386	0.4021	-0.3104	-0.4210

Isch stroke	-0.5887	0.5434	-0.5925	-0.5362
Hem stroke	-0.5583	0.5643	-0.6119	-0.5668
Peptic ulcer	-0.4465	0.5199	-0.4825	-0.5211
CVD	-0.6141	0.4422	-0.6402	-0.6435
Digestive diseases	-0.5904	0.6667	-0.6015	-0.6691
Alzheimer	0.5796	-0.4306	0.5726	0.4362
Cancers				
Stomach	-0.6216	0.5790	-0.6142	-0.6006
Colorectal	0.0309	-0.3927	0.1287	0.3916
Liver	-0.3210	0.5050	-0.4081	-0.5081
Cervix	-0.4800	0.3746	-0.5279	-0.3746
Ovarian	0.1835	-0.3745	0.1308	0.3848
Lymphoma	0.3897	-0.6576	0.4876	0.6606

The ASDRs of most of the illnesses (18/21) were found to be negatively correlated with cars and internet connections, while Alzheimer’s disease, pancreas cancer, and lymphoma showed specular positive correlations.

Pancreatic cancer and chlamydia were the only illnesses showing a positive correlation with cellular phones.

DISCUSSION

In a previous study, a more sophisticated analysis (stochastic and non-stochastic) was done in the 191 countries (the complete list according to WHO) without considering the ASDRs [13]. In terms of LEEDLEs, similar correlations were found for GDPs, PM, and for those variables characteristic of developed countries (cars, mobile phones, internet connections), while the classical ecological variables were in consistent in terms of LE.

Table 10. Correlation between diseases/cancers Vs life style variables: significant correlations only (*r* <0.01) were reported in *Italics* characters.

Diseases	<i>r</i> Vs Cars10 ³	<i>r</i> Vs Cells10 ³	<i>r</i> Vs Internet10 ³
2DM M/F	-0.4609	0.0270	-0.4206
2DM F	-0.4412	-0.0570	-0.4557
IDA F	-0.4063	0.0517	-0.4333

TBC	-0.5121	-0.0631	-0.5087
STD	-0.4945	-0.2569	-0.4358
Chlamydia Females	-0.2590	0.3772	-0.1796
Diarrheal diseases	-0.4093	-0.1697	-0.4626
Isch stroke	-0.5100	0.0047	-0.4416
Hem stroke	-0.6261	-0.1470	-0.5809
Hepatitis	-0.3788	-0.0338	-0.4047
Peptic ulcer	-0.3811	-0.0429	-0.3850
Respiratory infections	-0.4574	-0.2445	-0.3870
CVD	-0.5721	-0.075	-0.5428
Digestive diseases	-0.5886	-0.0756	-0.6295
Chronic Kidney diseases	-0.4319	-0.1933	-0.3795
Alzheimer	0.4710	-0.0319	0.5607
Cancers			
Stomach	-0.5875	0.0696	-0.4892
Liver	-0.4260	-0.1137	-0.3772
Pancreas	0.4545	0.3995	0.4868
TBL	-0.3394	0.0070	0.3849
Cervix	-0.5414	-0.1512	-0.4603
Lymphoma	0.5246	0.0659	0.5198

The results of the present investigation have the limitations due to the differences between the 49 SC and the rest of the 142 countries in terms of LEEDLEs (see **Table 2**).

This means that the results cannot be taken as a worldwide picture, and have to be considered within the limit of the 49 SC which represent about 20 % of the total population.

The choice of ASDRs as main variable can be a further limitation, because each disease could be concomitant with other illnesses which may precipitate the death. Furthermore, for chlamydia it was not possible to differentiate between *Chlamydia trachomatis* or *Chlamydia pneumoniae* since no

data were available.

Despite these limitations, some interesting observations can be drawn from the analysis. Between 2000 and 2016 in the 49 SC the ASDRs of almost all the diseases were significantly reduced a part of liver, kidney, brain cancer, which were not significantly modified, while pancreatic cancer was increasing by about 7 %. The overall improvement of the diseases can be to the therapies prolonging the survival, and also some positive modifications of the environment cannot be excluded.

The aspect of environmental modifications opens the door to many hypotheses. All the ecological variables, with exception of PM (see later), seemed not important. LE increase together with the decrease of almost all the illnesses witness that the present environment does not seem so negative. One may speculate about the quality of life which was not considered in the present study. However, the human needs are primarily to stay alive and to improve the welfare of immediate and future generations. The second need is food, and the choice to substitute forests with crops is consequential on that. If it is true that pollution has been the consequence of this, it is also true that starvation has been strongly reduced in the last 20 years, and the aim of FAO Sustainable goals WHO was to allow all humans by 2030 to have access to sufficient food for surviving (Zero Hunger Challenge) [14].

The challenge will be to reach this goal reducing the pollution, accomplishing this task with the contribution of every generation.

Among the environmental variables, those related to welfare (GDP 2+3, cars, internet, cells) were increasing LE. The inconsistency of investment in education and the hospital beds in terms of LE, can be considered in the light of the profit: once resources are sufficient, it is much easy to take advantage of the available institutions (school, hospitals) despite some limitation.

From the analysis it seems evident that LE was reduced either by non-cancer illnesses (TBC, strokes, peptic ulcer, digestive diseases, CVD, diabetes type 2, HIV, STD) and also by some cancers (stomach, cervix, and prostate), but for all the other illnesses no correlation was found. Some of the illnesses (16/34) were shown to be reduced by the improvement of life style (see **Table 10**), Alzheimer's disease and lymphomas being the only two exceptions since they came out with specular correlations, probably a natural consequence of living longer. Some illnesses (10/34) were more typical for poor living conditions (high % GP1) such as TBC, STD, strokes, peptic ulcer, CVD, and digestive diseases, among non-cancer diseases, and stomach, liver, and cervix among cancers (see **Table 9**).

Other diseases (6/34) did not belong to any of the LEEDELS (see **Table 5**: variable = 0) all were cancers (breast, bladder, brain, thyroid and leukemia) a part of glomerulonephritis. A couple of issues should be mentioned concerning cell phones and PM.

The cell phones

The cell phones have been addressed as a cause of cancer by a consistent number of authors.

Based on research reports done before 2014, the electromagnetic field (EMF) produced by mobile phones was classified by the international Agency for Research on Cancer (IARC) as possibly carcinogenic to humans [15]. More recently, the European EMF guidelines were established [16], addressing all the possible sources of pollution (e.g. cell, tablets, TV broadcast antennas), concluding that certain diseases such as Alzheimer and male infertility may be the consequences of this event.

The American Cancer Society (ASC) in 2018 stated that the reports of the US National Toxicology Program (NTP) “were still inconclusive, and that, so far, a higher cancer risk in people has not been seen, but that people who concerned should wear an earpiece when using the cell phone” [8].

In the present research, the only significant correlations were shown for pancreatic cancer and chlamydia infection in females. No other diseases were emerging, and brain cancer seemed to be unaffected.

However, the activity of EMF was documented to reduce insulin secretion from in vitro insulinoma [17] and in rats the exposure to EMF impacts insulin secretion by influencing the size of pancreatic islets [18].

On the basis of experimental studies, suggestions were made to enhance intracellular insulin concentration in insulin-secreting cells in that they could be useful for cell transplantation in diabetes mellitus [19].

More recently the High-Frequency EMF was found to modify both insulin secretion and blood glucose levels in rats [20].

In humans, for the moment it is not documented whether EMF increases or decreases the insulin secretion in diabetes type 2 (2DM). In a research done using the same ASDRs as in the present study [35], 2DM was shown to reduce the risk of pancreatic cancer, which may mean that blood glucose increases and hyper insulinemia are not culprits of the cancer development. More attention should be paid to the reduction of pancreas cells apoptosis driving them toward the malignancy. In other terms, under EMF stimulation, no matter whether the influence is positive or negative, it seems evident the Langerhans islets can be affected.

There is no clear explanation about the relationship between cell phones and pancreatic cancer in humans. However, when cell phones are not used but still operating, usually

they are kept in the pockets or in the bags: the relative EMF can impact easily the anatomic position of pancreas which is very close.

Chlamydia also was positively correlated with cell phones, and despite no specific data are available in the literature, this infection could be affected by EMF. The sensitivity of bacteria to EMF has been documented with conflicting results. Some authors described for both Gram-positive and Gram-negative bacteria a reduction of growth together with a morphology modification [21], while more recently other authors showed a growth increase of some *E. coli* strains using irradiation frequencies between 60 and 40 Hz [22]. The differences between results could be determined by the experimental conditions, particularly by the frequencies which were used, or even by the anatomical parts where bacteria were isolated [23]. One aspect should be analyzed in that angiogenesis seems to be stimulated by EMF [24,25]. Although all these investigations should be confirmed, the hypothesis seems consistent that the angiogenesis stimulation may allow chlamydia to spread locally, and also far from the common anatomical part where it usually resides.

PM value

This variable has some peculiar aspects that need to be clarified. The first is that PM values were relative to cities with >100,000 inhabitants which represent only a part of the total population. Furthermore, PM is a complex mixture of chemical components, to be considered together with many gases such as methane (CH₄), ozone (O₃), carbon monoxide (CO), sulfate (SO₃), nitrogen dioxide (NO₂) aerosols, and all the possible widespread air pollutants present wherever people live. These particles are able to penetrate deeply into the respiratory tract, and therefore constitute a risk for health. The WHO estimated in 2000 that the exposure to PM caused 800,000 deaths and 6.4 million years lived with disability (YLDs) in the developing countries accounting for two thirds of this burden [26].

In general, WHO stated that there is no evidence of a safe level of exposure to PM or a threshold below which no adverse health effects occur. In the recent study, >30 % of the population was found to live in areas exceeding the WHO level target of 35 mcg/m³. This safe limit was reached only in some of 49 SC countries, and the levels were found to be even worse in the remaining countries (see Table 2).

Furthermore, the data recorded in this study represent an average of the cities where the monitoring stations were available. In order to present air quality largely representative for human exposure, measurements of residential areas, commercial and mixed areas were used.

Stations characterized as particular “hot spots” or exclusively industrial areas were not included, and in some of the country’s particles < PM₁₀ was largely based on estimates [27].

There are several studies conducted in different parts of the world showing the negative effect of the PM on health [26-30], but still there is need for further research to define the long term toxicity [31] and whether some components and sources of PM may be more toxic than others [32]. The indoor air pollution is also something that should be considered since it is causing apparently 3.7 million deaths [33].

In the WHO Update report of 2016 [34] a comparison was done to determine the trend of PM in the world between 2008 and 2013, ending up with an estimation of 5% increase, despite some fluctuation within the macro-regions that were analyzed. In the same period the LE was also increased in practically every of the 191 countries considered in this study, no matter whether the PM was increasing or not. This indicates that more precise measures should be taken for PM, because in the present scenario it seems that they have some positive effect on LE. The present findings of a negative correlation with Alzheimer's disease (a decrease of Alzheimer corresponding to an increase of PM) and positive correlation with ischemic stroke (an increase of ischemic stroke corresponding to an increase of PM) have no clear explanation, unless some hypotheses about microvascular thrombosis, and brain inflammation is made.

CONCLUSION

The most interesting issues emerging from the present study were the non-interference of the classical ecological variables on LE, a part of PM showing positive and negative interference respectively for Alzheimer's disease and ischemic stroke. In relation to the illnesses in general, it seemed evident they have different patterns, most of the time showing that welfare variables (GDP, cars, internet connections) have a positive effect in reducing the burden of ASDRs.

Despite being limited to the 49 SC, the world tendency is to live longer and keep the diseases under control through the improvement of life style and financial resources. For some diseases this is not sufficient since, at the opposite, they may appear late in the age such as Alzheimer's disease and lymphoma.

An interesting finding concerns the connection between pancreatic cancer and EMF pollution, witnessing that the increase of cell phones use may be relevant to the increase of this cancer which was the only disease growing significantly (+7%) in the period from 2000 and 2016.

It is time that ecologists, climatologists and clinicians started a crosstalk.... it's never too late, provided they are minded the solutions reside in the evolution and never in the revolution.

ACKNOWLEDGEMENT

We are thankful to the WHO that allowed the public availability of the data base: the use of these data can be extremely helpful for authors who need details on the epidemiology of different diseases.

AUTHOR CONTRIBUTIONS

Cornelli U conceived the trial, retrieved some of the WHO data and wrote the article; Belcaro G retrieved part of the WHO data; Martino Recchia was responsible for the statistical analysis.

All the authors read and approved the final manuscript.

FUNDING

No funding was requested or received by the authors.

CONFLICT OF INTEREST

No conflict of interest.

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