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The increasing risk of mortality in breast cancer: A socioeconomic analysis between countries

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Abstract. The risk of mortality in breast cancer among women is a critical health issue worldwide. Scholars argue that breast cancer mortality rates have decreased in many advanced countries overall. However, about 50% of world population in 2017 was in poor and developing countries (more than 3,652 million with 50.24% female) and breast cancer mortality rates differ among nations also because of socioeconomic factors. This study investigates, at global level, breast cancer mortality in association with breast cancer incidence and some factors of socioeconomic ecosystem between poor and rich countries, to explain trends that can be used to gain insights into country-level "best practices" for health improvement. Global data regarding breast cancer incidence and mortality as the age standardized rate per 100,000 population in 78low-to-middle income countries (LMICs), 50 upper-to-middle-income countries (UMICs) and 63 high income countries (HCIs) were obtained from IARC/WHO for 2012 and 2018. Data regarding GDP per capita, population and mammography (MMG) were obtained from World Bank, United Nations and WHO. Data, transformed in log scale to have normal distribution, were analyzed with descriptive statistics, partial correlation, regression analyses and paired-Samples *T* Test procedure to assess the statistical significance of increase or decrease of mortality and incidence in breast cancer from 2012 to 2018.Results reveal that a 1% higher level of breast cancer incidence, increases the expected mortality by 0.79% (*p-value* < .001) in LMICs, by 0.50% (*p-value* <.001) in UMICs and by 0.31% (*p-value* < .008) in HICs. These results, confirmed by other analyses here, seem to suggest that breast cancer mortality is increasing over time worldwide in rich and in particular developing countries. The global analysis here reveals that though an improvement of wealth and wellbeing worldwide, the risk of incidence and mortality in breast cancer is increasing. This result suggests that situational factors in the ecosystem of countries support the growing increase and mortality of breast cancer that improvement in healthcare and medicine of the last 40 years are not been sufficient to slowdown. These conclusions need for much more detailed research to investigate into the interaction between factors of socioeconomic systems, health improvement, and breast cancer causes.
Keywords. Breast cancer, Wealth of nations, Epidemiology.
JEL. I14, I15, I18, I39, O10, O3, O55, Q50.

1. Introduction

About 40 years ago, Myron Moskowitz argued "How Can We Decrease Breast Cancer Mortality?", suggesting: "The data reviewed indicate that early detection is vital in decreasing breast cancer mortality. Early biopsy of minimally suspicious findings is important. Mortality can be reduced by perhaps 50 percent through

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physical examination and mammography." (Moskowitz, 1980, pp.276-277). However, although efforts in this direction of healthcare system in many counties, the risk of breast cancer mortality and incidence is still high in both rich and poor countries (Canto *et al.,* 2001)[1]. Hence, Moskowitz's question in 1980 is still a current problem in2019.

The purpose of this study is to analyze the risk of mortality in breast cancer, both in rich and poor countries, though a global analysis of this disease per nations to clarify comprehensive trends between countries and support appropriate health policies.

2. Theoretical backround

In medicine, cancer is an organism which lives off a host organ, growing by bio-genetic-molecular mechanism. In the world, 9.6 million people died of cancer in 2018 – more than from HIV, malaria and tuberculosis combined. The incidence of cancer is estimated to double by 2030s, with most of these cases expected to occur in low-to-middle income countries: in particular, 60% of cancer cases and 75% of cancer deaths occur in poor countries (cf., Prager *et al.,* 2018). Table 1 shows that lung and breast cancer have the highest mortality rate worldwide (cf. also, Bray *et al.,* 2018; Parkin *et al.,* 2005).

Table 1. *Incidence and mortality of big 8 cancers in 2018 (worldwide data for both sexes, all ages)*

Cancer	Incidence ASR (W)*	Mortality ASR (W)*
Lung	22.5	18.6
Breast	46.3	13.0
Colorectum	19.7	8.9
Prostate	29.3	7.6
Stomach	11.1	8.2
Pancreas	4.8	4.4
Ovary	7.8	3.9
Liver	9.3	8.5

Note: *Age-Standardized Rate-ASR (W): A rate is the number of new cases or deaths per 100,000 persons per year. An age-standardized rate is the rate that a population would have if it had a standard age structure.
Source. World Health Organization, International Agency for Research on Cancer (2019).

The R&D in oncology is supporting the convergence of different research fields, such as genetics [2], genomics [3], nanotechnology, nanomedicine, computer sciences, etc., that are generating new

[1]*Abbreviations in the text*: LMICs, low-to-middle income countries; UMICs, upper-to-middle income countries; HICs, high income countries; MPI, mortality-per-incident breast cancer ratio; MMG, mammography; GDP, Gross Domestic Product per capita.

2 Genetics studies the molecular structure and function of genes in the context of a cell or organism.

3 Genomics is a discipline in genetics that studies the genomes of organisms. In particular, it determines the entire DNA sequence of organisms and fine-scale genetic mapping efforts.

technological pathways for diagnostics and therapeutics (Coccia, 2014, 2016; 2017, 2018, 2019, 2019a, 2019b; Coccia & Wang, 2015)[4].

Breast cancer is the most frequent cancer worldwide among women (see tab. 1; cf., Chagpar & Coccia, 2019). Studies based on advanced countries show that the incidence of breast cancer is increasing. Breast cancer incidence tends to be higher in more developed countries due to delayed childbearing, a higher use of hormone replacement therapy and oral contraceptives, a higher rate of screening, and improved tumor registries (Coccia, 2013). Some studies have also argued that higher income countries may generate a higher fat diets and an increased rate of obesity, both correlated with higher breast cancer incidence rates. In general, scholars note that many Western populations have a higher incidence rate of breast cancer than poor regions in Africa and Asia (Coccia, 2013; cf., Chagpar & Coccia, 2019; Engmann *et al.*, 2017).

3. Methods

Sample

Global data of this study are divided according to the classification by The World Bank (2018) to create homogenous groups for analysis, given by N_1=78 low-to-middle income countries (LMICs), N_2=50 upper-to-middle-income countries (UMICs) and N_3=63 high income countries (HCIs). These three groups are analyzed over a period from 2012 to 2018.

Measures and sources of data

Breast cancer incidence and mortality are measured in age standardized rate per 100,000 population and data were obtained from IARC/WHO (Globocan, 2018). Socioeconomic factors of nations under study here are Gross Domestic Product (GDP) per capita in 2015 year and Total Population 2017 using data obtained from The World Bank (2018). Screening for detection of breast cancer is measured with density of mammographs (per million females aged between 50 and 69 years old) using data of 2014 year from World Health Organization (2018).

Data Analysis Procedure

Data, in the presence of not normal distribution, are transformed in log scale. Our samples N_1, $N_2$and N_3were analyzed with descriptive statistics, partial correlation (using as control variables density of mammographs 2014 and GDP per capita 2015) and regression analyses. Some variables of the study here have a time lag to logically assess the effects on incidence and mortality in breast cancer. Linear regression is used to analyze the predicted value of the dependent variable of breast cancer mortality in 2018

4 For other studies about drivers and effects of science and technology in society, see Cavallo *et al.*, 2014; Coccia 2005, 2005a, 2005b, 2006, 2007, 2008, 2009, 2010, 2010a, 2011, 2012, 2012a, 2012b, 2012c, 2013, 2014, 2014a, 2014b, 2014c, 2014d, 2014e, 2015, 2015a, 2015b, 2015c, 2016, 2016a, 2016b, 2017, 2017a, 2017b, 2017c, 2017d, 2018, 2018a, 2018b, 2018c, 2018d, 2018e, 2018f, 2018g, 2018h, 2018i, 2018l, 2018m, 2019, 2019a, 2019b, 2019c, 2019d; Coccia and Rolfo, 2002, 2009, 2013, Coccia & Wang, 2015, 2016.

on breast cancer incidence in 2012 (independent variable). The study also calculates from this model a new variable given by predicted values of breast cancer mortality in 2018 on breast cancer incidence in 2012 (the first stage). Then, in the second stage, using a linear regression model, it is estimated a new dependent variable on GDP per capita in 2015 to assess future trend in breast cancer. The analysis also calculates the burden of population with an increasing risk and decreasing risk of breast cancer considering the population in 2017. Finally, a paired-Samples *t*-Test compares two means of variables under study in 2012 and 2018 within the same group of nations LMICs, UMICs and HICs. The purpose of the test is to determine whether breast cancer incidence and mortality aresignificantly increased or decreased from 2012 to 2018.

4. Results

Table 1 shows that breast cancer incidence is higher in HICs than LMICs and UMICs both in 2012 and 2018. The average burden of mortality in 2012 and 2018 also shows a higher level in rich countries than poor countries. However, temporal comparison of the groups of countries under study shows that from 2012 to 2018, breast cancer mortality is increased in LMICs and UMICs, whereas in HICs it has a moderate decline. Temporal variation of breast cancer incidence over 2012-2018 shows a general increase worldwide in each group of country under study.

Table 1. *Descriptive statistics*

Category			Breast Cancer Incidence 2012	Breast Cancer Incidence 2018	Breast Cancer Mortality 2012	Breast Cancer Mortality 2018
LMICs	N	Valid	73	71	73	71
		Missing	5	7	5	7
	Mean (M)		27.84	30.58	13.53	14.70
	Std. Deviation (SD)		10.67	11.84	5.16	5.81
MUICs	N	Valid	44	45	44	45
		Missing	6	5	6	5
	Mean		42.00	46.08	14.30	15.35
	Std. Deviation		16.49	15.26	5.58	5.85
HICs	N	Valid	54	53	54	53
		Missing	9	10	9	10
	Mean		68.36	71.87	15.18	14.89
	Std. Deviation		21.78	19.96	3.84	4.69

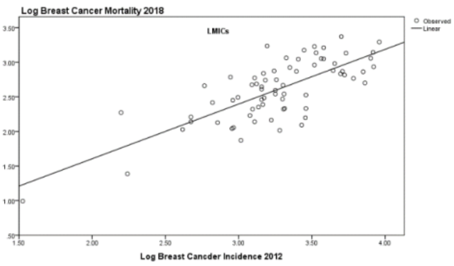
The partial correlation of variables between breast cancer mortality 2018 and breast cancer incidence 2012, controlling density of mammograms (2014) and GDP per capita (2015) shows a significant high association: LMICs (r=.75, p-value<.001), UMICs (r=.53, p-value<.004) and HICs (LMICs (r=.62, p-value<.001).

Table 2. *Estimated relationships*

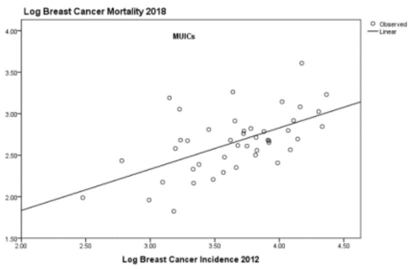
		Unstandardized Coefficients		Stand. Coefficients					
		B	Std. Error	Beta	t	Sig.	F	Sig.	R^2 adj
LMICs	Log Breast Cancer Incidence 2012	.790	.084	.753	9.450	.001	89.298	.001	.561
	(Constant)	.025	.275		.089	.929			
MUICs	Log Breast Cancer Incidence 2012	.497	.109	.577	4.577	.001	20.945	.001	.317
	(Constant)	.841	.400		2.104	.041			
HICs	Log Breast Cancer Incidence 2012	.313	.113	.362	2.770	.008	7.672	.008	.288
	(Constant)	1.348	.474		2.847	.006			

Notes: The dependent variable is Log Breast Cancer Mortality 2018; Explanatory variable is Log Breast Cancer incidence 2012.

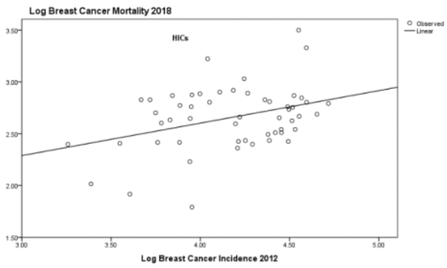
Table 2 shows estimated relationships of breast cancer mortality in 2018 on breast cancer incidence in 2012. In LMICs, results indicate that a 1% higher level of breast cancer incidence, increases the expected mortality by 0.79% (*p-value* < .001, *F*=89.30, *sig*.=0.001, Adjusted R^2=0.56). In UMICs, results indicate that a 1% higher level of breast cancer incidence, it increases the expected mortality by 0.50% (*p-value* <.001, *F*=20.95, *sig*. =0.001, Adjusted R^2=0.32). Finally, in rich countries (HICs), results indicate that a 1% higher level of breast cancer incidence, increases the expected mortality by 0.31% (*p-value* < .008, *F*=7.67, *sig*. =0.008, Adjusted R^2=0.29). In general, statistical evidence here shows that the breast cancer mortality has an expected increase worldwide, though with different magnitude that is lower for rich countries, whereas it is higher for poor countries (cf., trends of regression lines are in Fig. 1).



LMICs



UMICs



HICs

Figure 1. *Increasing trends of the risk of mortality in breast cancer across homogenous group of countries.*

Moreover, paired samples test shows, from 2012 to 2018, the significant increase in LMICs of breast cancer mortality (t_{69}=2.26,*p*-value<0.03) and breast cancer incidence (t_{69}=2.64,*p*-value<0.01); in the same period, MUICs have an increase of mortality not significant, whereas the increase of breast cancer incidence is significant (t_{43}=2.69,*p*-value<0.01). Finally, this test shows that in rich countries (HICs), breast cancer mortality from 2012 to 2018 has a not significant decrease, whereas breast cancer incidence has a significant increase (t_{52}=2.87,*p*-value<0.006).

Empirical data also shows that countries reducing breast cancer mortality over 2012-2018 have 42.30% of worldwide population in 2017, whereas the countries increasing breast cancer mortality over 2012-2018 represent 57.70% of worldwide population in 2017. Breast cancer incidence shows a higher difference over 2018-2012 between countries that are reducing incidence (about 40% of worldwide population) and countries that are increasing incidence (roughly 60% of worldwide population).

Finally, the estimated relationship of predicted breast cancer mortality 2018 with breast cancer incidence 2012 (from curve fit of model linear in log scale) on GDP per capita 2015 is significant only in rich countries. In particular, HICs show that a 1% higher level of GDP per capita, increases the expected breast cancer mortality (based on breast cancer incidence 2012) by 0.1% (*p*-value <.001, *F*=17.80, sig.=0.001, Adjusted R^2=0.25). These results seem to confirm that breast cancer mortality in rich countries can continue to increase also in the future (Figure2).

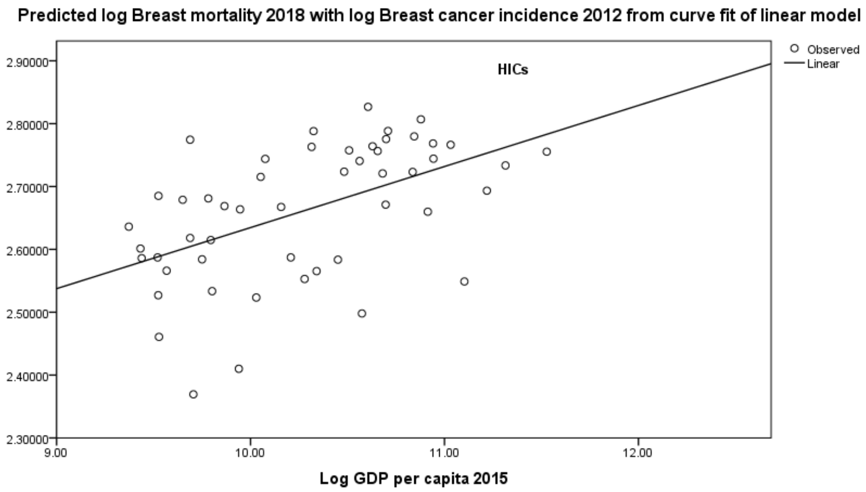


Figure 2. *Estimated relationship of expected increase of the risk of mortality in breast cancer on GDP per capita*

Figure 3 shows the spatial analysis of the variation of incidence across countries. Results reveal a general increase of breast cancer incidence from 2012 to 2018, except in USA, Ecuador, Guyana, Libya, some countries in Central Africa, Saudi Arabia, India, Pakistan, Iraq, Uzbekistan and some other.

Figure 4 shows that the increase of breast cancer mortality is mainly in Mexico, some countries of Central America, Venezuela, Colombia, Bolivia, Paraguay, sub-Saharan Africa, India and China.

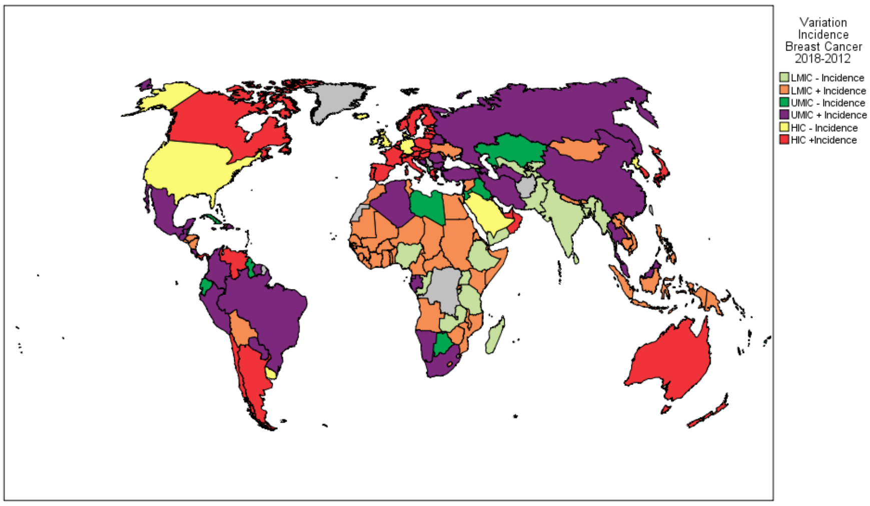


Figure 3. *Global map of the variation of breast cancer incidence over 2012-2018 in countries*

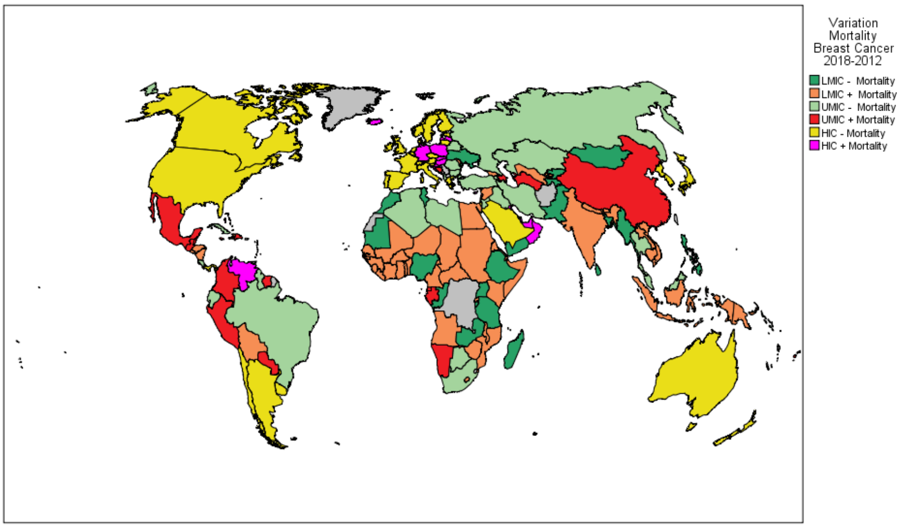


Figure 4. *Global map of the variation of breast cancer mortality over 2012-2018 in countries*

5. Discussion and Conclusion

DeSantis *et al.*, (2017) and Mettlin (1999) argued that breast cancer mortality is declining in the United States and Canada, as well as in other advanced nations because of increasing screening (cf., Brentnall *et al.*, 2018) and new therapies (cf., Bray *et al.*, 2018). The global analysis here reveals that though an improvement of world-wide wellbeing, the risk of incidence and mortality in breast cancerseems to be increased. Countries with a problematic socioeconomic system (LMICs and UMICs) are at high risk also because of demographic growth that in 2017 showed a world-wide population more than 49% in LMICs (more than 3,652 million with 50.24% female) with an average rate of growth of 1.93% annually and roughly 16% of population in HICs with a mere rate of growth of about 0.86%. Overall, then this study shows that though higher wealth and wellbeing within and between countries, it seems that the risk of mortality and incidence in breast cancer is continuing to growth likely associated to the dynamics of socioeconomic evolution of nations.

Future efforts in this research field should provide more statistical evidence to substantiate the results here. Hence, to reiterate, the study here is exploratory in nature and there is need for much more detailed research to shed further theoretical and empirical light on patterns of incidence and mortality of breast cancer within and between countries.

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