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Original paper

Economic and environmental determinants of dermato-venereal diseases in the European community area. An econometric approach

CALCEDONIA ENACHE[1,2], MIRCEA TAMPA[3,4*], IONUȚ SILVIU BEIA[2], SIMONA ROXANA GEORGESCU[3,4]

[1]Academy of Economic Studies, Bucharest, Romania
[2]University of Agronomic Sciences and Veterinary Medicine, Bucharest, Romania
[3]"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
[4]"Victor Babes" Clinical Hospital for Infectious Diseases, Bucharest, Romania

Abstract Human skin acts as a barrier between the organism and the external milieu, being subjected and permanently responding to aggressions from various environment factors. Through alteration of cutaneous microbiome, production of reactive oxygen species, activation of aryl hydrocarbon receptor and induction of inflammation cascades within skin cells, pollutants trigger and/or aggravate a multitude of skin conditions, subsequently leading to a large number of consultations in dermatology services, and therefore, to greater health expenditures.

Our model proves that the number of hospital admissions in dermatology services throughout the European Union is positively correlated with air pollutants and current health care expenditure and negatively correlated with pollution abatement capital expenditures.

Keywords Skin diseases, air pollutants, healthcare.

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*Corresponding author: MIRCEA TAMPA·"Carol Davila" University of Medicine and Pharmacy, 37, Dionisie Lupu, 020021, Bucharest, Romania
E-mail: tampa_mircea@yahoo.com

Introduction

Skin diseases are ranked as the fourth most common cause of human illness, resulting in an enormous non-fatal burden. Despite this, many affected people do not consult a physician. Accordingly, the actual skin disease burden might be even higher since reported prevalence rates are typically based on secondary data that exclude individuals who do not seek medical care (TIZEK et al, 2019 [1]).

In the EU-27 countries, the average number of hospital discharges per 100,000 inhabitants with varicose veins of lower extremities decreased gradually from 86.6 in 2007 to 79.6 in 2009 and to about 60 in 2016. In fact, in 2016, in the case of this disease, most patients discharged per 100,000 inhabitants were in Lithuania (214.5), Austria (173.1), Czechia (136.4) and Romania (114.6), at the opposite pole, being Denmark (2.5), Sweden (2.3) and Netherlands (1.9). In addition, the average length of hospitalization was 4.1 days, Lithuania and Italy having the lowest levels of this indicator (1.6 days, respectively 1.9 days). Moreover, in the EU-27 countries, the average number of patients discharged with skin and subcutaneous tissue diseases per 100,000 inhabitants was 240.5 in 2007 and 243.1 in 2008, followed by an upward trend in 2010-2013 from 239.4 to about 242, oscillating over the next three years at around 240 (Eurostat [2]). It should be emphasized that only two of the Member States recorded average annual growth rates of the above-mentioned indicator over 5 percent between 2007 and 2016, namely Malta (9.4 percent, reaching 276) and Bulgaria (5.82 percent, reaching 698.9), while Poland got close to this threshold (3.57 percent, up to 280.1). On the other hand, Latvia and Italy recorded a strongly negative annual average dynamics (-6.4 percent and -5.72 percent, the starting bases being 411.4 and, respectively, 142.1). In 2016, in the segment of skin and subcutaneous tissue diseases, the average length of hospitalization fluctuated in the case of economies in Central and Eastern Europe (Bulgaria, Romania, Hungary, Poland, and Czechia) between 4.7 and 10.6 days, while in the Euro area, its level was 5 days in the Netherlands, between 5.9 and 6.4 days in Cyprus, France, Ireland, Sweden and Austria, 6.9 days in Italy and between 7.0 and 8.6 in Belgium, Germany, Spain, Finland and Malta. In the period 2007-2016, at the EU-27 level, with the exception of Estonia, on average, the number of hospital discharges with malignant neoplasms of skin per 100,000 inhabitants recorded minor oscillations, located on a range of values between 42.46 and 46. At the individual level, in 5 of the 26 countries (Cyprus, Netherlands, United Kingdom, Spain and Portugal) the number of hospital discharges per 100,000 inhabitants was less than 23 (Eurostat [2]). It should be noted that the average length of hospitalization for this category of disease fluctuated between 3.2 days in France and 8.2 days in Latvia, the modal value of 5.9 days being recorded by Romania, Germany and Cyprus. In the EU-27 countries, the highest level of the average number of patients hospitalized for inpatient day care with malignant neoplasms of skin in the last 10 years (around 70) was recorded in 2016, Ireland and United Kingdom being on the last two positions among the Member States. On the other hand, in the case of skin and subcutaneous tissue diseases and varicose veins of lower extremities, the number of patients hospitalized for inpatient day care generally trended downwards in most EU Member States between 2007 and 2016, with important increases in Malta and Bulgaria (less than 9 percent). In 2013, in the Euro area, 1.3 percent of people between the ages of 15 and 64 years reported work-related skin problems, compared with 2.1 percent in 2007. At EU-27 level, 4725.85 thousand persons were affected by long-standing skin diseases in 2011, most being recorded in France (1248.94 thousand persons), United Kingdom (542.93 thousand persons), Germany (528.71 thousand persons) and Spain (472.52 thousand persons). At the same time, the number of deaths due to skin and subcutaneous tissue diseases and malignant melanoma of skin increased from 23.931 persons in 2011 to 26.874 persons in 2016, the trend being given by Portugal, Greece, Slovakia, Poland and Ireland (Eurostat [2], WHO [3]).

In this context, this study aims to evaluate the effects exerted by the determining factors on the occurrence of dermatological diseases in the European community area, between 2007 and 2016, when the Member States initiated a series of programmes aimed at supporting sustainable economic growth and of competitiveness, the reform of the public administration, the protection of the environment.

Material and Method

This study utilizes the linear panel regression model, similar to the one presented by Baltagi, 2005 [4] and Greene, 2008 [5].

The variables included in the analysis are the following:

- Hospital discharges with dermato-venereal diseases, in-patients, per 100 000 inhabitants (HDSD);
- Air pollutants (nitrogen oxides, sulphur oxides, particulates < 2.5 µm, particulates < 10 µm), total sectors of emissions for the national territory, tonne (AP);
- General government expenditures for pollution abattement, euro per inhabitant (PA);
- Current health care expenditures, euro per inhabitant (CHE).

The series of data have been collected from the websites of the World Health Organisation and of the Statistical Office of the European Union (Eurostat [2], WHO [3]).

Initially, the EU-27 group of countries was selected. The estimation of the model and the graphical representation of the average level of each country for the interval 2007-2016 suggested the fact that the results are sensitive to inserting Lithuania and Latvia into the analysis, as the two countries have an atypical trend for some of the variables. Consequently, these two countries were excluded from the analysis, as were Bulgaria, Estonia and Malta, whose data were incompletely obtained.

PA and CHE have been deflated with the consumption price index (for the base year 2015). Moreover, all series have been logarithmated.

Furthermore, the relations between countries were assessed using the average values for each country, utilizing Pearson correlation coefficient. This led to a first picture of the relations between each variable and the number of hospital discharges with dermato-venereal diseases per 100,000 inhabitants.

Figure 1 reveals the existence of a direct relation between HDSD and AP, and between HDSD and CHE, respectively, as well as an inverse relation between HDSD and PA. These relations, confirmed at theoretical level, are based on non-conditional correlations and on the variation between countries. Next, the estimation of the panel model should establish a relation between HDSD and the determining factors, based on rigorous econometric arguments.

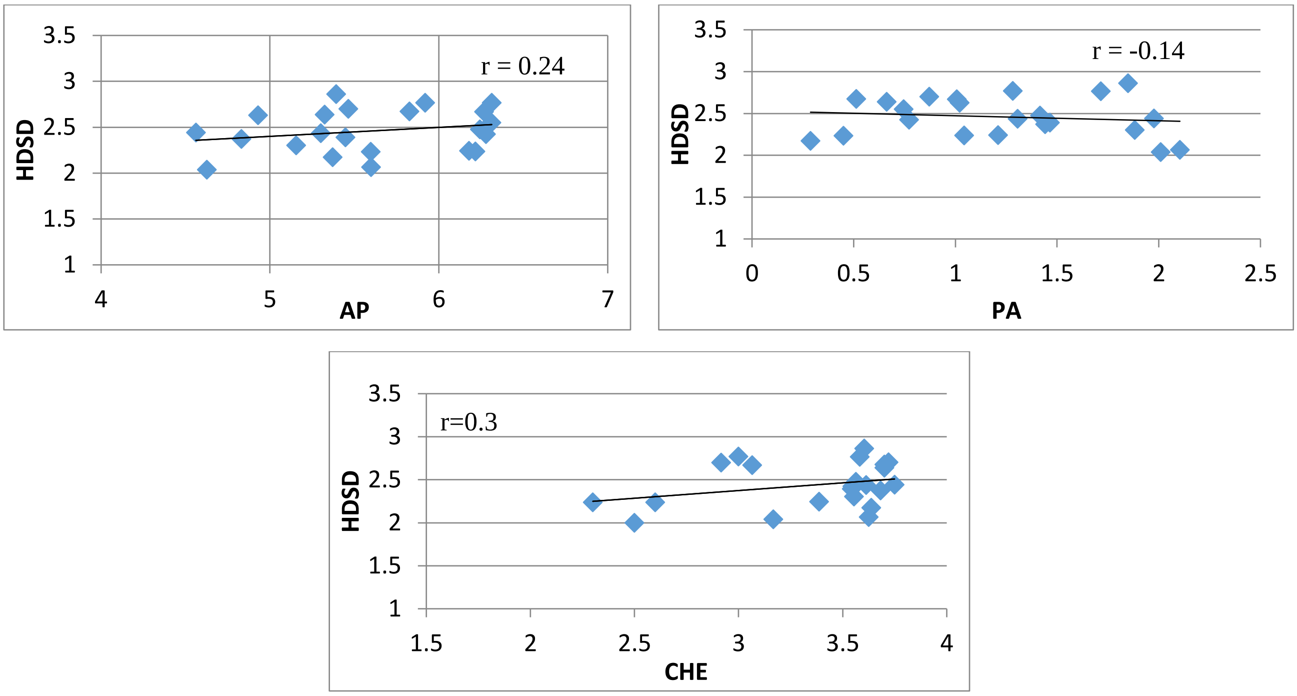

Figure 1. Cross country relationship – averages 2007-2016

Model estimation and Results

In order to estimate the model (ONETE, DINA and VLAD, 2013 [6]), the variables have been tested to identify the unit roots (ENACHE, 2016 [7]), using the tests Levin, Lin and Chu (LLC) (LEVIN et al, 2002 [8]), Im, Pesaran and Shin W-stat (IPS) (IM et al, 2003 [9]), ADF – Fischer chi-square (ADF) (DICKEY and FULLER, 1979 [10]) and PP – Fischer chi-square (PP) (PHILLIPS and PERRON, 1988 [11]).

The results of the stationarity tests, displayed in Table 1, suggest the fact that AP, PA and CHE are zero-order integrates, whereas HDSD will be stationary after first-order differencing.

Table1. Results of panel unit root test

Unit Root Test		LLC	IPS	ADF	PP
		H_0: Unit root (common unit root process)	H_0: Unit root (individual unit root process)		
Level	HDSD	-6.64771*	0.36595	44.3214	43.2734
	AP	-8.20746*	-0.88009	61.6389**	107.601*
	PA	-7.75674*	-2.42150**	73.0182**	66.2128**
	CHE	-6.27198*	-1.40524***	46.2857**	37.5343***
First difference	HDSD	-7.81506*	-2.50810**	66.6867**	95.9837*
	AP	-17.4374*	-8.06206*	147.286*	210.526*
	PA	-31.8712*	-5.77150*	83.2817*	101.211*
	CHE	-6.89555*	-2.63938**	48.9975*	58.2836*

The *, **, *** indicate the rejection of the null hypothesis at a significance level of 1%, 5%, 10% respectively.

Table 2. Results of Hausman test

Variable	Fixed	Random	Var(Diff.)	Prob.
AP	0.435960	0.377422	0.000270	0.0004
PA	-0.006903	-0.009185	0.000001	0.0122
CHE	0.098137	0.028937	0.001059	0.0335

$Chi^2(3)=17.202$; $Prob>chi^2=0.0006$

Further on, the Hausman test was performed (HAUSMAN, 1978 [12]) in order to find out which of the models is more suitable: the random effects or the fixed effects one. As the probability resulted was less than 0.01, the conclusion was that the second model is more suitable. Next, in order to obtain the panel data model, pooled ordinary least squares were used, whose results are displayed in Table 3.

Table 3. Panel fixed effects model

Variable	Coefficient	Std. Error	t-Statistic	P-value
AP	0.441139	0.029852	14.77755	0.0000
PA	-0.010079	0.003492	-2.886459	0.0046
CHE	0.134722	0.055756	2.416304	0.0171
Constant	-1.105763	0.695600	-1.589655	0.1144
R-squared	0.994775			
F-statistic	1015.436			
Prob(F-statistic)	0.000000			

Discussion

Skin is the largest organ of the human body; its chief function is to provide a barrier between internal milieu and external ambient, therefore being in permanent contact with environmental aggression factors, such as chemicals, physical factors (ultraviolet radiation – UV, temperature changes, mechanical stressors), and infections of various types. Far from being a static shield separating the body from the environment, the skin is continuously adapting to the surroundings, through various mechanisms, alterations of which lead to pathological changes that may exceed the level of skin.

Ambient air pollution is an already known public health hazard that negatively impacts not only the skin, but also non-cutaneous organs and systems; exposure to air pollutants has been proven to lead to various health-related problems, such as cardiovascular diseases, respiratory diseases, increased risk for microbial and viral infections and even psychiatric comorbidities (HAMANAKA and MUTLU, 2018 [13], SZYSZKOWICZ et al, 2016 [14], ROBERTS et al, 2019 [15]); while it stands true that pollutants reach the human body through various non-cutaneous gateways (respiratory, digestive, conjunctival membranes, etc.), it has been proven that pollutants can also create breaches in the skin barrier and penetrate in depth, generating systemic toxicity (REMBIESA et al, 2018 [16]).

In respect to deleterious effects on skin, the pollution is involved in either (or both) onset and aggravation of various skin conditions, such as atopic dermatitis (KANTOR and SILVERBERG, 2017 [17], KIM et al, 2015 [18]), psoriasis (TAMPA et al, 2018 [19]), acne (KRUTMANN et al, 2017 [20]), cellulitis (SZYSZKOWICZ et al, 2016 [14]), urticaria (KOUSHA and VALACCHI, 2015 [21]) and even skin cancer. Exposure to air pollution also accelerates extrinsic skin ageing – manifesting as pigmentation spots and coarse wrinkles, independent from other environmental factors such as cigarette smoke and UV radiation (VIERKÖTTER et al, 2010 [22], PARK et al, 2018 [23]).

Up to date, four mechanisms through which air pollutants provoke nocent effects on cutaneous health stand out: (a) alterations in skin microbiome (b) generation of free reactive oxygen species (ROS), (c) induction of the aryl hydrocarbon receptor (AhR) signaling pathways, and (d) activation of inflammatory cascades, with subsequent deterioration of the skin barrier (MANCEBO and WANG, 2015 [24]).

Air pollution leads to changes in skin microbiome, in favor of the pathogenic flora; while air pollutants decrease residual skin flora, cutaneous surface is colonised with *Staphyloccocus* and *Streptococcus spp*., leading to infections such as caruncles and cellulitis, and it also alters the sebium production and blocks the skin pores, creating an anaerobic microenvironment that favors the growth of *Propionibacterium spp*, a comensal bacterium involved in acne; all these alterations of cutaneous microbiome conduct to skin inflammation and wreckage of the skin barrier (REMBIESA et al, 2018 [16]).

Air pollutants enhance the production of reactive oxygen species (ROS). The term ROS refers to a wide range of oxygen free radicals, e.g. superoxide anion radical (O_2), hydroxyl radical (OH), as well as non-radical oxidants, e.g. hydrogen peroxide (H_2O_2) and singlet oxygen (O_2) (ZOROV, 2014 [25]).

These are chemical compounds that can alter cellular and subcellular structures, and, eventually, kill normal cells, while also being capable of creating nuclear acids mutations that lead to cancer (REMBIESA et al, 2018 [16], IONESCU TOPA et al [26]) Endogenous antioxidants like superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GP), vitamin C and E, carotenoids and thiol antioxidants normally either eliminate or attenuate the noxious effects of ROS on skin, acting as ROS natural scavangers. When the antioxidant capacity is overwhelmed, the resulting cellular oxidative stress causes oxidative damage of membrane lipids and proteins, and also to nuclear DNA; while this sequence of events is encountered in cutaneous exposure to various chemicals and UV radiation, it is also of a paramount importance in explaining the effects of pollutants on skin (REMBIESA et al, 2018 [16], DINU et al, 2014 [26], NICOLAE et al, 2014 [27]).

Some pollutants also penetrate the surface of the skin into deeper layers, where they stimulate the Aryl hydrocarbon receptor (AhR) pathway, a versatile cascade of biochemical events that is involved in cellular growth, differentiation and proliferation. As a consequence, all measurable skin parameters are altered: skin lipid ratio is modified, epidermal cholesterol and fatty acids content increases, sebum secretion escalates, lipids and proteins are oxidated, skin pH increases, while the barrier function of the skin is disturbed (REMBIESA et al, 2018 [16], NICOLAE et al, 2013 [28]).

Alterations of microflora, activation of oxidative stress and AhR pathway activation lead, altogether, to the induction of inflammatory cascades in the skin. The production of pro-inflammatory cytokines, such as IL1B, IL6, IL8 and TNFa is intertwined with the accumulation of inflammatory cells in skin. Overproduction and building up of cytokines have been related to inflammatory skin diseases, skin ageing and skin cancer (REMBIESA, 2018 [16]).

Our model proves that an increase of 1% in air pollutants leads to a subsequent increase of 0.44% in hospital admissions in dermatology services throughout the selected UE countries; this could easily be explained by previously described mechanisms accounting for the deleterious effects of pollution on the skin barrier and functionality; as previously shown, current scientific evidence shows that air pollutants lead to an enhanced incidence of a wide variety of skin diseases, from atopic dermatitis to acne, from skin ageing to skin cancer, therefore, environmental pollutants conduct to an augmented burden of skin diseases.

We have also found that increasing PA by 1% have led to a marginal though significant decrease in dermatology hospital discharges; fighting pollution leads to less people at risk of developing skin conditions.

The depth of the decrease is, however, smaller than that of the effect of AP on admissions in skin services; we assume that this might be due to the fact that a part of air pollutants effect on skin is irreversible and indelible – such as skin ageing, skin cancer and chronic diseases as atopic dermatitis and psoriasis, all of which could be controlled by medical services, to a certain extent, but not entirely cured, continuing to manifest, from an economic perspective, as hospital periodic admissions throughout patients' life, disregarding of subsequent efforts aimed to diminishing air pollution.

We have also observed that augmented current healthcare expenditure leads to increased number of hospital admissions, as a better financed healthcare system provides a higher rate of adequate prevention and access to an earlier diagnostic; moreover, a better financed system comes with a higher addressability of patients to secondary and tertiary medical treatment units.

Conclusions

Environmental pollutants have been shown to encompass a wide range of pernicious effects in human skin; however, up to date, our knowledge regarding the extent of the effects of pollution on skin health continues to be limited.

To the best of our knowledge, this is the first study aimed to assess the effect of pollutants on the burden of skin diseases directly through linking hospital admissions in dermatology services to air pollutants, pollution abatement capital expenditures and current healthcare expenditure.

Healthcare professionals and economists must speak out to support policies aimed to cleaner air, augmented energy efficiency and transition from fossil fuel combustion to sustainable renewable clean energy production.

Conflicts of Interest

The authors declare no conflict of interest.

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