

# COULD SOCIO-ECONOMIC TRANSFORMATION AND THE RESULTING PSYCHOLOGICAL STRESS INFLUENCE CANCER RISK IN OPOLE PROVINCE, POLAND?

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## SUMMARY

The paper presents the results of a risk assessment analysis of cancer morbidity in Opole province before and after a political transformation in Poland, i.e. in the 1985–1989 quinquennium and the following two equivalent periods of: 1990–1994 and 1995–1999. Measures of morbidity are given and its growth in males and females are compared with the ageing effect as well as with unemployment. In the paper a general conclusion has been drawn suggesting that the socio-economic transformation begun after 1989 and the resulting stress could have been the one of the possible background effects influencing the health status in the region. It must be accentuated, however, that the relation has not been a subject of statistical proving due to a methodological impossibility; a divagated question is offered for scientific concern and open discussion.

*Key words:* cancer morbidity, socio-economic transformation, ageing effect, unemployment, stress, risk assessment

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## INTRODUCTION

Among well-recognized risk factors for cancer are a person's age, gender, and family medical history. Others are linked to cancer-causing factors in the environment (still others are related to lifestyle choices such as tobacco and alcohol use, diet, and sun exposure). Cancer strikes people of all ages; however, it is more likely to affect the old (about 4/5 of all cancers are diagnosed in people aged 50 and older), and hence ageing is one of the most significant risk factors of the disease.

A striking link exists between advanced age and increased incidence of cancer. Several age-related molecular and physiological changes might act in concert to promote cancer, and in particular epithelial carcinogenesis. Experimental data indicate that an aged, cancer-prone phenotype might represent the combined pathogenic effects of mutation load, epigenetic regulation, telomere dysfunction and altered stromal milieu. Further verification of the role of these effects should in turn lead to the design of effective medication for the treatment and prevention of cancer in the aged (1). For example, concerning the incidence of colon tumours, if overall log rates for each age are plotted against log age, a straight line is seen to describe the data very well and there is no significant difference between the lines for males and females (2).

One area that is currently being studied is the effect of stress on people possibly increasing the risk for cancer development. Many factors come into play when determining the relationship between stress and cancer. At present, a link between psychological stress and cancer occurrence or progression has not been scientifically proven. However, stress reduction is of benefit for many other health reasons and some scientific results, although

preliminary, suggest that psychological stress may play a role in how the immune system responds to cancer.

Studies in animals – mostly rats – have slowly built the case for the link between stress, the immune system and the progression of cancerous tumors (3). For example, chronic and acute stressors, including forced swim, surgery and social disruptions, appear to promote tumor growth by a short decrease of activity of white blood natural killer (NK) cells in rats (of all the immune system cells, NK cells have shown the strongest links to fighting certain forms of the disease, specifically preventing metastasis and destroying small metastases). In addition, these types of stresses also cause a two-to five-fold increase in certain types of tumors, as well as promote tumor metastasis (4). Moreover, recently Quan et al. (5) found evidence that B lymphocytes (the type of white blood cell that produces antibodies) are involved in fighting tumor cells in the lungs of rats. This finding is exciting because B lymphocytes are the immune cells that are most influenced by stress. The earlier cited authors (4) believe it may be that the B cells are somehow associated with the decrease in NK cell activity, while another research (5) suggests that B cells can work on tumor cells in ways other than through their antibody system.

The link between stress and cancer is much stronger in animals than it is in humans. Indeed, there are no clear findings in human studies. Some retrospective studies find that people with cancer report more stressful life events before being diagnosed with cancer but others find no relationship. One theory says that this fact is likely related to the immune system.

The immune system is thought to guard against cancer by constantly scanning the body for mutated and potentially cancer-causing cells and destroying them before they can multiply to form a tumor. It is also well known that many types of stress

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activate the body's endocrine (hormone) system, which in turn can cause changes in the immune system, the body's defence against infection and disease (including cancer). However, the immune system is a highly specialized network whose activity is affected not only by stress but by a number of other factors. That is why it has not been shown that stress-induced changes in the immune system directly cause cancer.

Another big question is why the immune system mechanism should fail. Most experts believe that several things must happen before cancer starts: exposure to a carcinogen and tumor promoters, the activation of oncogenes and failure of tumor suppressor genes, for example, and that stress might affect one or more of those events (6).

In addition, oncologists are still debating the importance of the immune system in fighting cancer – the primary mechanism investigated in the animal literature. And while researchers are looking at the immune system as a mechanism, they are also examining other options. One of these is given in a study by Keicolt-Glaser (7) saying that stress impedes cells' ability to repair DNA damage, whilst failure to repair DNA damage is one of the first stages of cancer development. Another one is concentrated on the role of aerobic exercise affecting the metabolism of fat, lowering blood viscosity, and vastly improving oxygen transport in the body (oxygen available to tissue cells is decreased because of elevated blood fats and increased blood viscosity which follow stress). It likewise decreases oxygen available to the lymphocytes, the protective white cells of the body's immune system, thus debilitating them. It has been shown that physical fitness provides enormous protection against physical and emotional stress; in fact, every single body function becomes more efficient, including the function of the immune system – a most crucial factor in cancer (8). An example of a stressful event (by the traditional definition of psychologists) that demonstrates the linking of the stress mechanism with perceived dangers and inappropriate responses to threatening situations is overcrowding of humans in urban areas [in Poland, cancer incidence is 20–30 % higher in these areas than in rural ones (9)].

Following the latest animal experiment reports, stress may increase women's risk of breast and endometrial cancer more than drinking alcohol. Researchers found stressed-out female monkeys who were subservient to other monkeys had a higher risk of endometrial cancer than the more dominant monkeys (10). This study shows that in monkeys, social status was more important than chronic moderate alcohol consumption in endometrial and breast biology of surgically postmenopausal females and social subordination stress was associated with initial cellular changes that may increase endometrial cancer risk (11).

Some results of common experiments using two groups of mice caged under identical conditions but with one group provided with an exercise wheel, confirmed that the group with no wheel had a significantly higher cancer incidence than the group with the exercise wheel only. It was assumed that the exercise wheel provided a psychological advantage to the mice in that group, but it is more likely that the benefit was a physical one (8).

It turns out that learned helplessness has far-reaching effects. Visintainer et al. (12) performed an experiment demonstrating how mastery and helplessness affect health. The authors put three groups of rats through the same shock and the day before the experiment they implanted a few cancer cells on each rat's flank. Under normal conditions, 50 % of the rats would reject the cancer cells and live. As expected, 50 % of the rats who were

not shocked had died, and the other half had rejected the tumor. Of the rats who were allowed to escape the shock by pressing a bar, the rate who had learned mastery, 70 % rejected the tumor. But only 27 % of the helpless rats, the rats who had experienced uncontrollable shock, rejected the cancer cells. In short Visintainer et al. (12) became the first to demonstrate that the psychological state of helplessness produces a more rapid growth of cancer. They also showed, of course, that the psychological state of mastery enhances the ability to reject the tumor and went on to demonstrate that the rats who had experienced mastery when young were better protected against tumors as adults.

In fact, animal studies show a very wide range of tumor response to stress, depending on the type of stressor used, the ability of the animal to modify or escape the stressor, the species being tested, the gender, the animal's previous experience with this stress, whether the tumor was chemically induced or transplanted, whether the tumor is primary or a metastasis, and so on (13). Human studies to date have been somewhat less aimed at measuring stress and tumor response. Obviously, animal studies on this topic are difficult to perform because it is not possible to know with certainty what animals are feeling, so most studies are done on humans. This implicates that the research itself is fraught with methodological problems. Most human studies so far have relied on retrospective self-reports of stress levels prior to the cancer diagnosis and this method of collecting information is often criticized as of dubious reliability (the best study design would follow cancer-free people for years, recording stressful events and subsequent cancer diagnoses). This is because of differing perception and reactions of individuals to stressful events.

Applying a wide psychological stress definition, the political changes that occurred in Poland (and the rest of Eastern Europe) in 1989 and subsequent economic and social transformation should without doubt, have become long-term stressful events in peoples' lives. The same must be said for the awareness of the need for further adaptations in such heretofore unseen changes. A free market victory over a planned economy is seen as a psychological hypothesis, and is based on the ability of humans to mobilize motivations and use their creativity. A free market ideology assumes that everyone has a chance to reach success, but people have different aptitudes and often the distribution of this chance is not uniform across various social groups (in the majority of societies there are categories of needless people). The greater the effectiveness of this mechanism, the larger the number of people in this category. The competitive nature of this economic system touches not only those who are defeated. The people getting on better also feel it. Most of them live in a state of anxiety, under the constant threat of unforeseen market changes. Stress, induced by the situation, may mobilize a man but overloads his psyche. Effects of this psychological status manifest themselves in giving rise to conflicts, aggression, mental disturbances, neurosis, depression, and somatic diseases (14).

The aim of this research was a risk assessment of cancer incidence in Opole province before and after the political transformation in Poland, i.e. in the 1985–1989 quinquennium and the following two equivalent periods of 1990–1994 and 1995–1999. Measures of morbidity are given and its growth in males and females are correlated with ageing effects as well as compared to unemployment. From the work some divagations can be drawn about the possible effects of underlying socio-economic changes

and resulting stress on the health status in the region. It must be accentuated, however, that the relation has not been a subject of statistical proving due to a methodological impossibility and a divagated question is offered for scientific concern and open discussion. It was only assumed that the unemployment is not an instant process in a regional scale and it should have origin in preceding socio-economic background. In this meaning, the unemployment in the region discussed in the final part of the epidemiologic study was only a consequence of some situation that existed much earlier before the economic crisis occurred.

To realize the aim of the paper, first, information on census and epidemiologic data are provided. Then chosen statistical methods based on spatial Bayesian modeling and disease clustering are briefly described. The results are presented graphically in thematic maps and scatter plots in the following section of the paper. A discussion of findings and some general conclusions are located in the final parts of the paper.

## MATERIALS

Information on population by age groups and unemployment in the province of Opole was obtained from the Census Bureau in Opole. For the midpoints of the analyzed quinquenniums, i.e. 1987, 1992 and 1997, the total population in the region was estimated at 1,014,673, 1,009,836, and 1,005,066, respectively (decreasing by approximately five thousand from period to period).

Epidemiologic data on cancer were taken from the Provincial Cancer Registry in Opole – the International Agency for Research on Cancer collaborator (15), which has been providing a highly reliable service following Finnish Cancer Registry instructions since 1<sup>st</sup> January 1985: data collection relied on an active programme of cancer registration, with follow-back/follow-up verifications and a set of eight other medical criteria to confirm the disease. In the examined 1985–1989, 1990–1994, and 1995–1999 periods the following numbers of cases were registered in the region: 12,240, 12,983 and 14,720, respectively.

Demographic as well as epidemiologic information covered a total of 944 census municipalities within 92 administrative units of the province of Opole (for the formerly standing administration division) and was analyzed using computer-based geographical information system maps.

## METHODS

Maps of regional morbidity to determine spatial patterns of the disease were created based on a hierarchical spatio-temporal modelling following Waller et al. (16). The computation of standardized morbidity ratios (SMRs) was performed in WinBUGS 1.4 software (17).

To evaluate space-time disease clusters and to check their statistical significance, SaTScan 3.0.5 software (18) was used in the study. The clusters' investigation was based on a Poisson model where the number of events in an area is Poisson distributed according to a known underlying population at risk (the general statistical theory behind the spatial and space-time scan statistic for the Poisson models is described in detail by Kulldorff (19).

To express the ageing effect, a simple measure was adopted

$$\sum_x w_x \times \frac{(P_x^{1999} - P_x^{1985})}{P^{1985}}$$

where  $w_x$  is the weight of the particular age group  $x$  (= midpoint of the age group/maximal age of the population – 100 years), and are the referring population numbers in age group  $x$  in the years 1985 and 1999, respectively, while  $P^{1985}$  is the total 1985 population. In its simplest definition, the measure expresses a growth of years of the population in 1999 in reference to the 1985 population.

The growth rates were calculated according to Bernardinelli and Montemoli (20), and Congdon (21). Based on the model, the relative cancer risk within administrative units in the region in each period and the average level were estimated. The computation was performed in WinBUGS 1.4 software (17).

The maps of estimates were created in MapInfo 6.5 software (22). Comparisons between cancer growth rates, ageing effect, as well as unemployment rates were exposed in scatter plots in STATISTICA 5.0 program (23). Associations between these variables were estimated based on the linear correlation (Pearson's  $r$  product).

## RESULTS

Maps of the modeled SMRs of cancer in males and females in the analyzed periods are presented in Fig. 1 and 2.

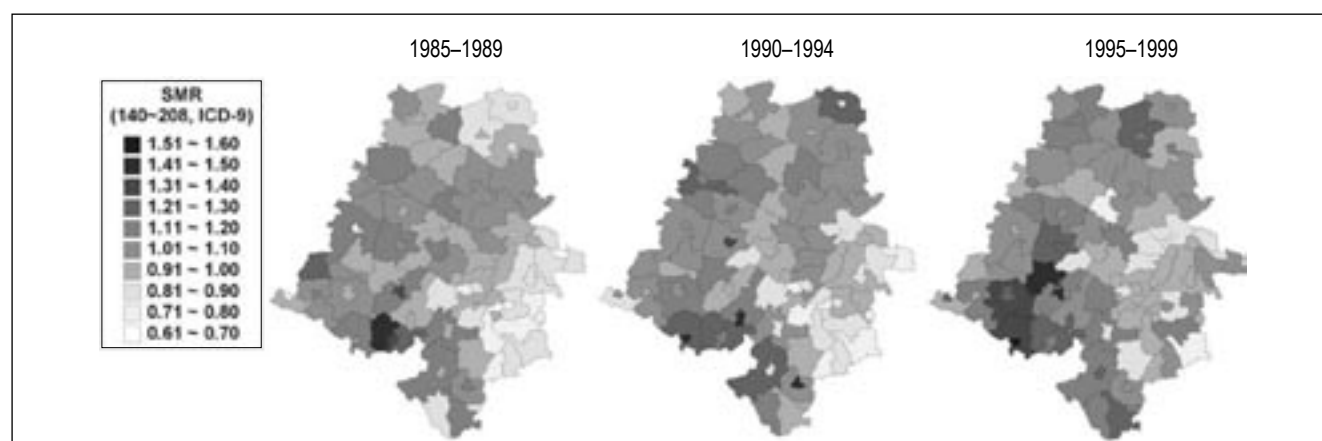


Fig. 1. SMRs of cancer (all sites combined) in males in Opole province.

Figures 1 and 2 provide evidence of an increase of mosaic tendency of the SMR models in the region in subsequent quinquenniums (especially in females). However, some characteristic patterns of administrative units with similarly elevated or lowered risk can be distinguished throughout the region (especially in males). Moreover, in males an increasing number of units with

elevated SMRs in the succeeding periods is observed, while in females the tendency is reversed.

Following a cluster analysis (at the municipality level), the candidates of extreme cancer risk territories with a given relative risk (RR) are presented in Fig. 3 and 4.

In Fig. 3 and 4, an increasing tendency of cancer risk within

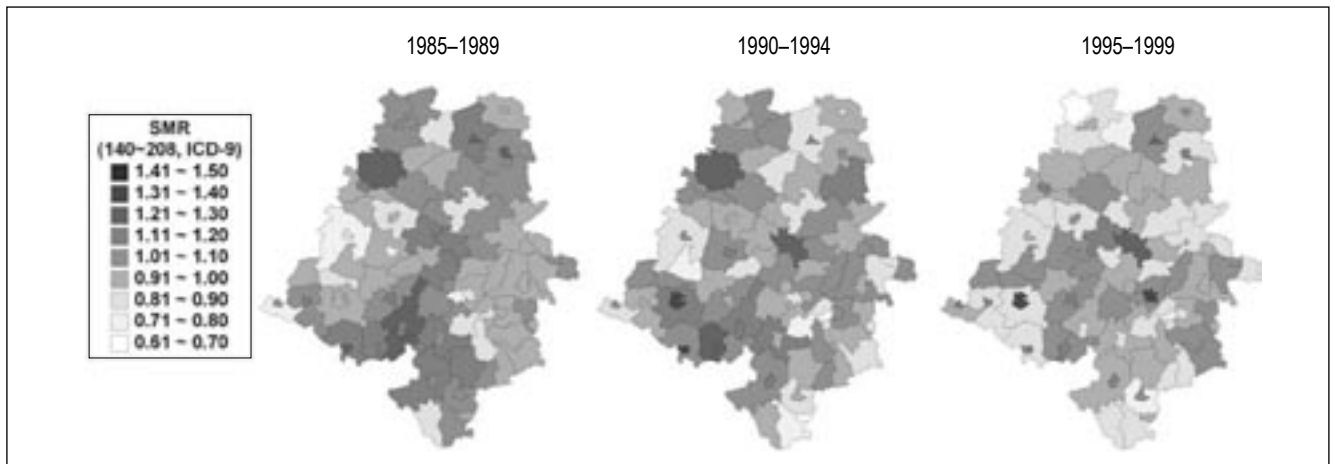


Fig. 2. SMRs of cancer (all sites combined) in females in Opole province.

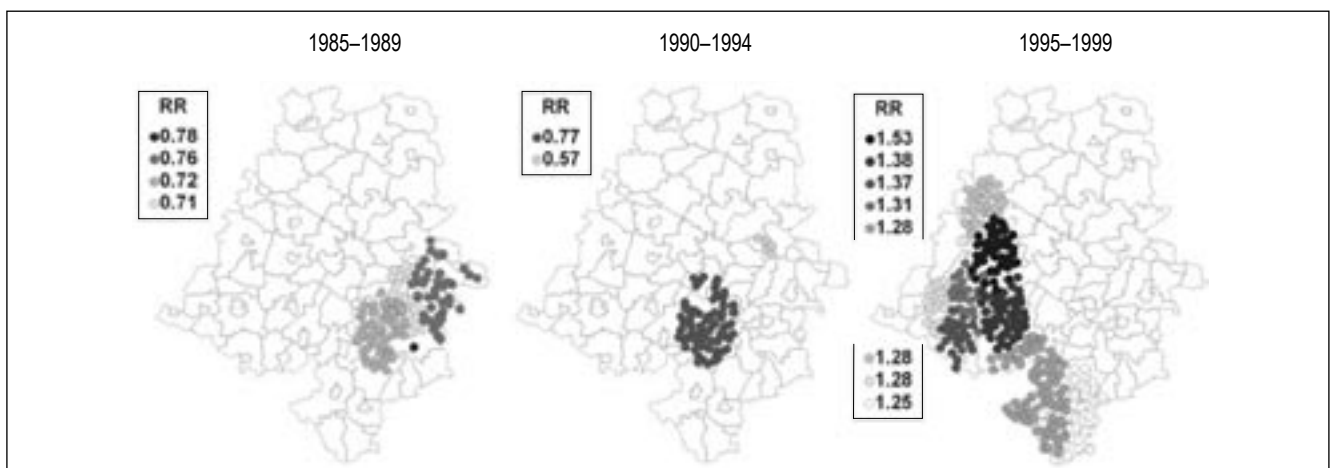


Fig. 3. Extreme risk cancer clusters in males in Opole province.

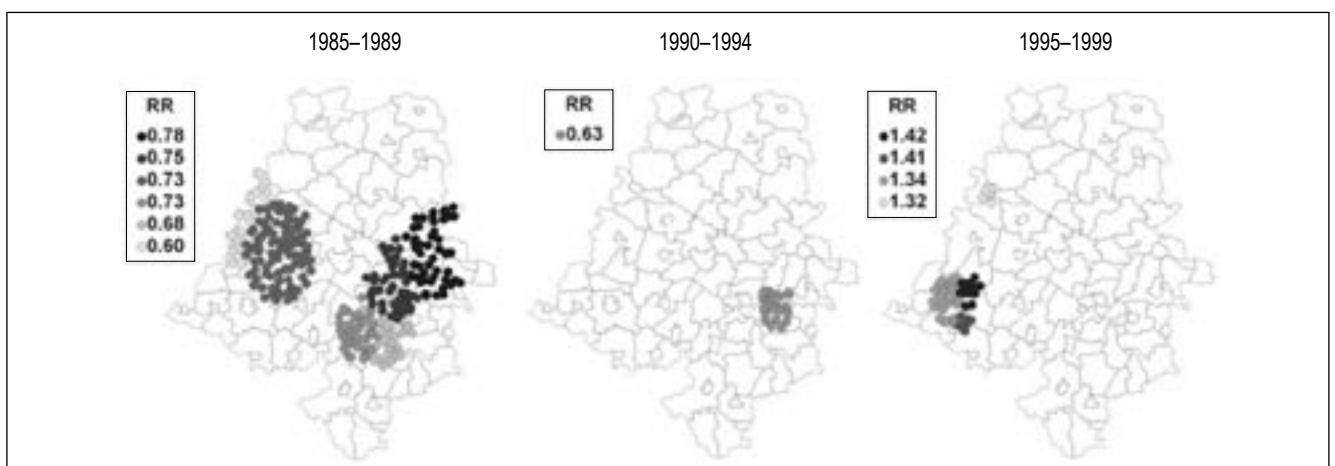
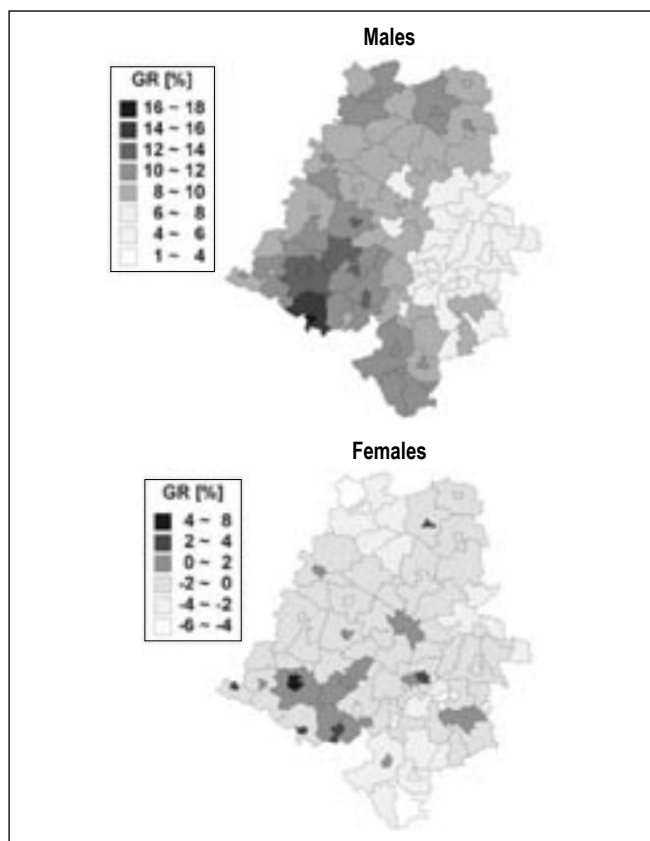
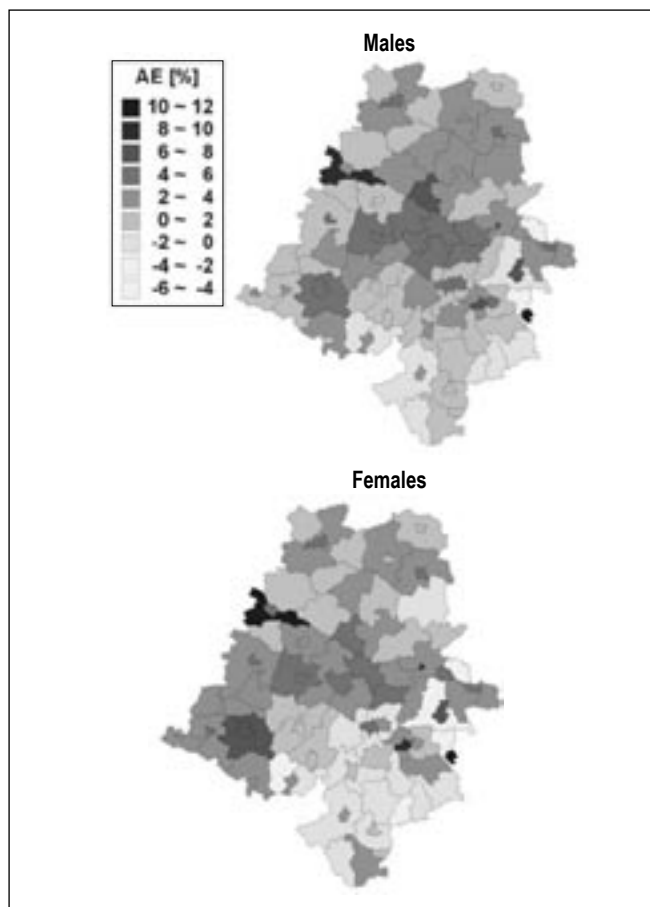


Fig. 4. Extreme risk cancer clusters in females in Opole province.



**Fig. 5.** Cancer growth rates in Opole province in each period 1985–1989, 1990–1994, and 1995–1999.



**Fig. 6.** Ageing effect in Opole province's population (1985–1999).

**Table 1.** Means of cancer growth rates in Opole province in each period 1985–1989, 1990–1994, and 1995–1999.

	Mean	Standard deviation	95% confidence interval
Males	0.0896	0.0081	(0.0739, 0.1056)
Females	–0.0111	0.0102	(–0.0313, 0.0075)

clusters can be observed in males and females, respectively (extreme low risk clusters appeared in the years 1985–1989, while clusters of the ‘highest risk’ came out in the region in 1995–1999; the middle period was characterized by the lowest cluster number with the minimal risk as well).

Bayesian cancer growth rates (GRs) in the region in each period are presented in maps in Fig. 5.

In Fig. 5 an increasing tendency in cancer morbidity is observed in males within the entire region, but especially in the south-western part of the province. Elevated cancer growth rates for females in this subregion are also present (particularly in the urban areas), but in the remaining parts of the region females’ rates trend negatively. The average estimates of the GRs in the region in males and females are detailed in Table 1.

It can be established that the average growth rate of cancer morbidity in males oscillates around 9 % every 5 years (Table 1), whereas in females, this mean is not significant.

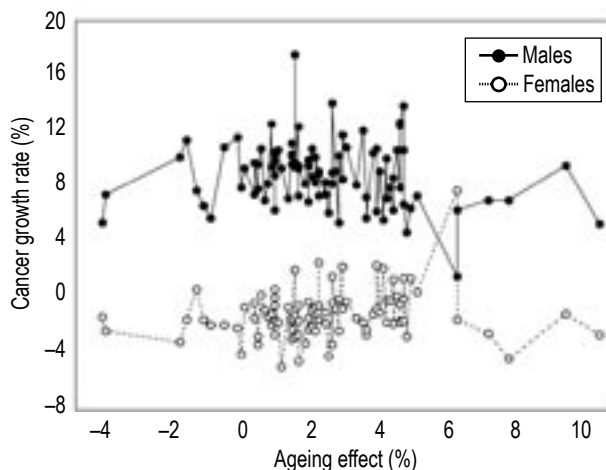
The first question raised by an increase of cancer risk is whether it is related to the ageing effect (AE) of the population with such a growth. The maps of AEs from 1985 to 1999 in males and females in the region of Opole are presented in Fig. 6.

Maps in Fig. 6 indicate quite similar patterns of AEs across the region (negative ageing was prevalent in the southern part of the region, while a positive effect was more concentrated in the center and northern territories). Graphical relations between GR and AE in particular administrative units in Opole province for males and females are given in a scatter plot in Fig. 7.

The estimated Pearson’s linear correlation coefficients for males ( $r = 0.161$ ,  $p = 0.125$ ) and females ( $r = 0.172$ ,  $p = 0.102$ ) indicate no relationship between the ageing effect of the population and the cancer growth rates in the analyzed periods.

A spatial socio-economic pattern of unemployment (U) in the region in recent time is given in Fig. 8.

It is apparent in Fig. 8 that the succeeding socio-economic si-



**Fig. 7.** Cancer growth rates vs. ageing effect in Opole province.

tuation roughly overlaps the preceding health tendency presented in Fig. 5, especially in males. Certainly, the subsequent economic condition could not influence foregoing health conditions. However, it allows speculation whether the origins and effects of unemployment or economic underdevelopment – and the resultant stress – could have underlied past cancer morbidity rates, considering joblessness was not a sudden event in the region. A comparative linear analysis of GR in reference to U (with linear trends) in administrative units of Opole province is showed in Fig. 9.

Both linear trends showed in Fig. 9 as well as Pearson's  $r$  products of 0.662 ( $p < 0.001$ ) for males and of 0.313 ( $p = 0.002$ ) for females provide evidence of increasing risk for cancer in territories presently experiencing an elevated unemployment level. Moreover, the relation is approximately twice as strong in males than in females.

## DISCUSSION

The epidemiologic situation in the region of Opole has drastically changed in the analyzed 15-year period encompassing extraordinary political transformations. Especially in males, an increase of cancer risk over time can be seen in the patterns of standardized morbidity ratios. In the period preceding this historic moment and the subsequent quinquennium, the disease clustering analysis displays clusters of low risk for cancer, whereas in more recent time clusters of high risk occur for both genders. A time and (slight) space concordance between the genders is observed. This increasing time trend in morbidity is also confirmed in the Bayesian analysis of the disease growth showing the global regional raise of cancer rates from period to period in males, whilst in females, this upward trend is observed in roughly half of the examined territory; in the remaining area a slow decay of risk is present. Again, a similarity in growth rate distributions between the genders is worthy of note and it is interesting whether these patterns could be related to any underlying processes. The first analysis regards one of the main risk factors for cancer, i.e. the aging effect. Since an easy graphical comparison as well as the estimated statistical correlation shows no relationship between these variables, the factor of getting old can be removed from further consideration.

The comparison of cancer growth in relation to unemployment provides speculation over the possible effect of a poor socio-economic status and a consequent stressful condition on cancer incidence. The presented problem has been already highlighted in the scientific literature (24, 25), and the achieved results only verify an observed epidemiological fact. In the case of this study, however, it makes sense only with the assumption of a similar pattern of economic activity across the region conditioning the preceding unemployment situation. Then, the possibility of socio-economic conditions acting as an underlying influence on psychological stress, and consequently the disease process cannot be logically rejected. In the author's opinion these results are worthy of public and academic concern.

## CONCLUSIONS

From the presented study, the following conclusions can be drawn:

1. Cancer incidence has increased after the socio-economic transformation in the region of Opole, especially in males and partly in females. These changes in risk have been statistically proven using three independent methods, i.e. spatio-temporal modeling of standardized morbidity ratios, disease clustering and growth rate estimation.
2. The growth of cancer is likely not related to the effect of ageing in the analyzed population.
3. The results of a comparison between growth rates (in males and females) and unemployment rate support speculation over the possible socio-economic effect and resultant stress (as a result of unemployment-related frustration) on the cancer risk (higher risk for cancer is observed in the territories with presently elevated joblessness rate and vice versa; the correlation is twice stronger in males than in females).
4. The study signals the problem only, and to verify such a thesis more extensive research in the field of socio-economic and psychological epidemiology of cancer is required.

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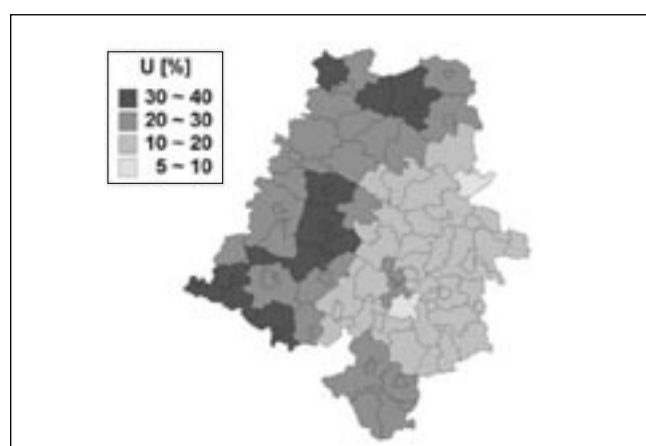


Fig. 8. Unemployment in Opole province (2001).

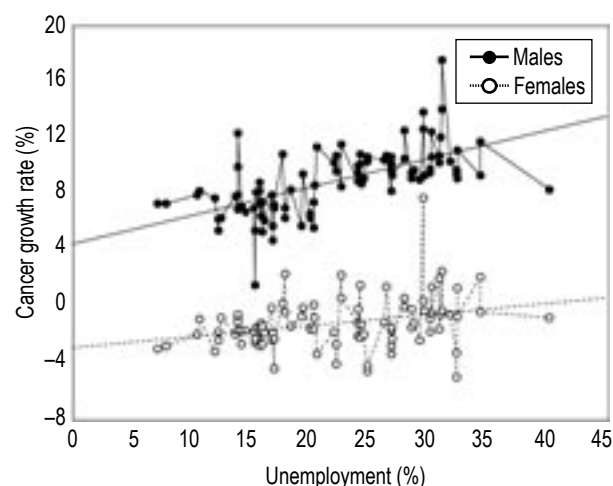


Fig. 9. Cancer growth vs. unemployment in Opole province – with linear trends (comparative analysis).

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