

The aim of this paper is to identify regions that can be considered homogeneous areas as regards mortality by age, sex and selected causes of death in Poland. A hypothesis stating that mortality is shaped by environmental factors related to the territory in which the population in question is living was verified.

Death is an event that must be experienced by every person, and thus any changes in mortality involve the distribution of risk of death by age. Because of the strong connection of mortality and the biological factor, every analysis is conducted taking into account a classification by age and sex. Introducing cause of death allows certain aspects of the determinants of the phenomenon in question to be explained. Medical conditions and disease processes, developmental abnormalities and injuries, which are treated as the direct causes of death in demographical statistics, should be handled as secondary in mortality analysis. The primary status belongs to milieu factors, which cause the medical condition, developmental abnormality, injury to appear. Modern demographical theories present causes of death in this way (Okólski 1988, Tabeau 1999).

An analysis of the spatial differentiation of mortality requires the application of appropriate methods and the introduction of new concepts. In such conditions, one of the significant factors is that the necessity of taking into account the increasingly complicated classifications (age, sex, cause of death, territorial unit) results in the appearance of populations of a small size. The events observed will also occur increasingly rarely. In this situation, the risk of death is strongly influenced by random fluctuations. In this situation the opportunities for applying Bayesian analysis are appearing, which is of interest both in the context of analysis and of interpretation. Such an approach has been adopted in this paper.

In order to identify areas which are similar with respect to risk of death by age, sex and certain causes of death in Poland, the hierarchical Bayesian introduced by Besag, York and Mollie (BYM) (1991) was taken into consideration. This model was used by Divino, Egidi and Salvatore (2009) to identify geographical mortality patterns in Italy.

### **BAYESIAN HIERARCHICAL MODELS**

The most common approaches to relative risk estimation involve hierarchical models with random effects (intercepts) for each region (see Lawson 2008).

Applying such constructions in the spatial analysis of differentiation of demographical phenomena is particularly interesting precisely because of their hierarchical structure. Due to this, it is possible to take into account in the model the spatial effects which can appear in the geographical distribution of the phenomenon in question (see Kopczewska 2007). These are:

1. clustering effect (*S*) (spatial dependence, structured heterogeneity), which results from the latent factors related to geographical structure. It is manifested as a spatial trend f.e. in the form of clusters.
2. heterogeneity effect (*H*) (spatial heterogeneity, unstructured heterogeneity), which is caused by random disturbances and the specific features (peculiarities) of each individual geographical region. It signifies the structural relations which change together with the location of the object.

The variability of these two components allows the assessment of, respectively:

- structural spatial variability, which expresses geographical patterns with visible homogeneous spatial conglomerations consisting of several neighbouring geographical regions (so-called clusters);
- variability without a geographical structure, which makes apparent areas in which the values observed differ significantly from those in other neighbouring regions.

The model proposed by Besag, York, Mollie (1990) is a hierarchical model which has been used for analysis of geographical mortality patterns in Italy (Divino, Egidi, Salvatore 2009). The model has been applied in a similar fashion in this paper; therefore, the interpretation of subsequent levels of the model has been adopted from the article by Divino, Egidi, Salvatore. The BYM model consists of four levels which are defined in relation to a set of territorial units:

- I. At the first level a conditional likelihood function for observations (deaths)  $Y = (Y_1, \dots, Y_n)$  is defined. Conditioning is performed on a random vector containing the relative risks of death  $\theta = (\theta_1, \dots, \theta_n)$ . This follows from the assumption that each of the observations  $Y_i, i=1, \dots, n$  is subject to (conditionally on  $\theta_i$ ) Poisson distribution with an expected value of  $\theta_i E_i$ , where  $E_i$  is the expected (hypothetical) number of deaths in a territorial unit  $A_i$ . Moreover, it is assumed that the random variables describing the occurrence of events are conditionally pairwise independent. This level can be expressed as follows:

$$Y_i | \theta_i \overset{iid}{\sim} \text{Poisson}(\theta_i E_i), \quad i = 1, \dots, n \quad (1)$$

The parameter of interest,  $\theta_i$ , is then modelled in a hierarchical fashion.

- II. At the second level, the relative risks of death  $\theta_i$  are defined. Their natural logarithms are explained through regression of two unobservable random effects, namely: the clustering effect (spatial dependence effect)  $S_i$ , the heterogeneity effect (spatial heterogeneity effect)  $H_i$ , and the intercept  $\alpha$ , representing the average level of relative risk for the whole area.

$$\log \theta_i = \alpha + H_i + S_i \quad (2)$$

In the model presented in the paper by Divino, Egidi, Salvatore (2009), the intercept is not present. However, a variable expressing the trend effect specified as:  $T_i = \beta \cdot \log SMR_{i,t-10}$  was introduced.

- III. The third level concerns the definition of the prior distribution for the free term in the regression equation and the distributions of the spatial dependence and spatial heterogeneity effects.

As regards the clustering effect (spatial dependence effect), an intrinsic Gaussian conditional autoregressive distribution (intrinsic Gaussian CAR) was assumed. A consequence of this assumption and of the application of binary weights in the adjacency matrix is the following joint distribution of the component  $S = (S_1, \dots, S_n)$ :

$$p(S | \gamma_S) \propto \gamma_S^{N/2} \exp\left(-\frac{\gamma_S}{2} \sum_{i \sim j} (S_i - S_j)^2\right) \quad (3)$$

It is a pairwise Markov random field with a Gaussian specification (GMRF).

The parameter  $\gamma_S$  is a precision parameter (the inverse of variance) and, in accordance with the hierarchical and Bayesian approaches, is treated as a random variable. The sum in the exponent of the exponential function is calculated over all the adjacent pairs  $A_i$  and  $A_j$ .

The consequence of introducing the spatial dependence effect is that the changes in relative risks  $\theta_i$  may be spatially smooth. For this reason, the relative risks of death in neighbouring regions can show similar intensities.

It was assumed that the heterogeneity effect (spatial heterogeneity effect)  $H_i$  does not have a spatial structure. This effect represents the occurrence of certain heterogeneous areas due to differences in the sizes of the populations of different areas or to features specific to each location  $A_i$ .

The random effect  $H_i$  is subject to, conditionally on  $\gamma_H$ , normal distribution with an expected value of 0 and the precision parameter  $\gamma_H$ . The two random effects  $H_i$  and  $H_j$  are, conditionally on  $\gamma_H$ , independent for  $i \neq j$ . The joint density of the conditional distribution of the random vector  $H = (H_1, \dots, H_n)$  can thus be expressed as:

$$p(H | \gamma_H) \propto \gamma_H^{N/2} \exp\left\{-\frac{\gamma_H}{2} \sum_{i=1}^n H_i^2\right\}. \quad (4)$$

As it is not known which of the spatial effects appears in spatial distribution of mortality by cause, they have both been taken into account in the model.

For the free term representing the average level of the logarithms of relative risks for all areas, an improper distribution defined on the whole real axis was assumed:

$$p(\alpha) \propto 1$$

The assumption of an improper distribution for the parameter  $\alpha$  is necessary in order to ensure the identifiability of the model in question (see Lawson 2003). It should be noted that the improper distribution of GMRF, taken into account in the differences of logarithms of relative risks, and not in levels, does not lead to an improper posterior distribution (see Congdon 2003:208).

IV. At the fourth level, the hyperparameters governing the distributions of spatial effects defined at the third level are defined. It was assumed that the hyperparameters  $\gamma_H$  and  $\gamma_S$  are independent and are subject to a gamma distribution with parameters specific to each of the effects (which is reflected in their indexing, which uses the names of the individual random effects):

$$p(\gamma_h; \nu_h; \alpha_h) \propto \exp\left\{(\nu_h - 1) \log \gamma_h - \alpha_h \gamma_h\right\}, h \in \{S, H\} \quad (5)$$

At the last level, we assume values of the parameters for the distributions of hyperparameters from the previous levels, taking for each  $h$ :  $\nu_h = 0,001$  and  $\alpha_h = 0,001$ .

This procedure closes the hierarchical modelling.

Model BYM:

I.  $O_i | \theta_i \sim \text{Poisson}(\theta_i E_i)$

II.  $\log(\theta_i) = \alpha + H_i + S_i$

III.  $H_i | \gamma_H \sim \text{Normal}(0, \gamma_H^{-1})$

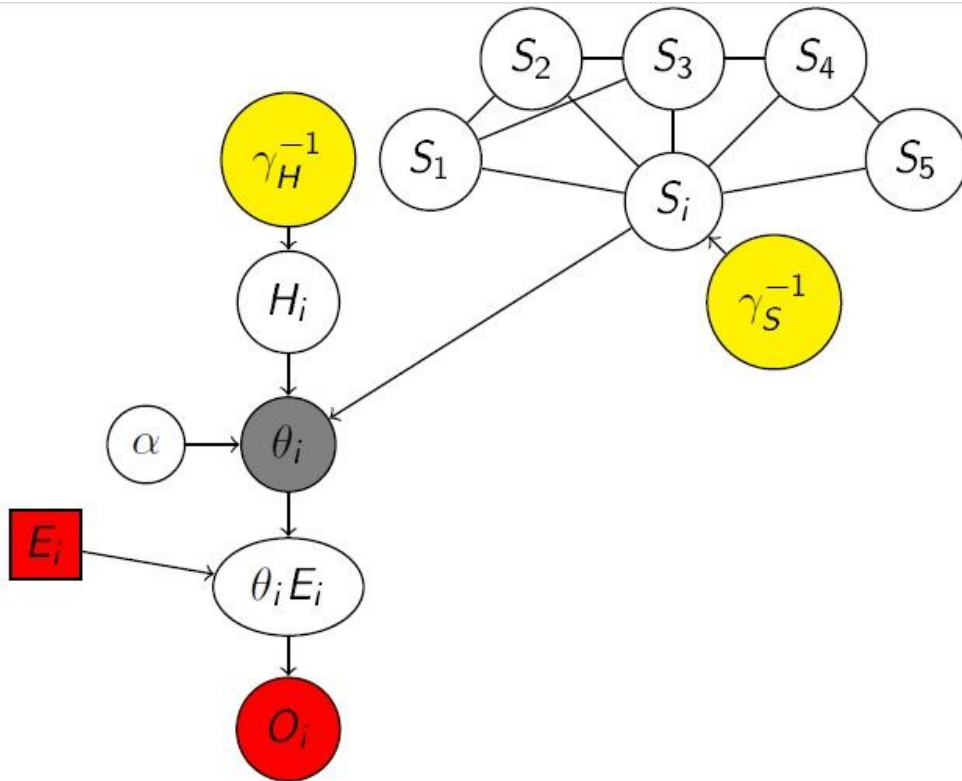
$$S_i | S_{-i}, \gamma_S \sim \text{Normal}\left(\sum_{j \neq i} S_j / n_i, \gamma_S^{-1} n_i\right)$$

$f(\alpha) \propto 1$

IV.  $\gamma_H \sim \text{Gamma}(0.001, 0.001)$

$\gamma_S \sim \text{Gamma}(0.001, 0.001)$

Figure 1. The scheme of BYM model



The full Bayesian model:

$$p(S, H, \alpha, \gamma_H, \gamma_S | Y) \propto \exp \left\{ -\frac{\gamma_S}{2} \sum_{i \sim j} (S_i - S_j)^2 - \frac{\gamma_H}{2} \sum_{i=1}^n H_i^2 + \sum_{i=1}^n [Y_i \log(\theta_i E_i) - (\theta_i E_i)] + \left( \nu_S + \frac{n}{2} - 1 \right) \log \gamma_S - \alpha_S \gamma_S + \left( \nu_H + \frac{n}{2} - 1 \right) \log \gamma_H - \alpha_H \gamma_H \right\}.$$

After considering the full conditional distributions for all unknown parameters included in the model, further statistical inference was conducted using the Monte Carlo Gibbs Sampler method, supplemented by the Metropolis-Hastings method in the case of conditional distributions whose form made direct sampling impossible.

The above model was implemented in the R statistical environment. 700 000 iterations were run with 200 000 burn-in iterations.

For the model under consideration, the point estimate of the Bayesian estimator of relative risk of death was assumed to be the expected value of the posterior distribution for the parameter  $\theta$ .

$$\hat{\theta}_i = \hat{E}_\theta(\theta | Y) = \sum_{s=1}^N \exp(\hat{\alpha}_{i,s} + \hat{S}_{i,s} + \hat{H}_{i,s})$$

where N is number of iterations after the burn-in.

### **STATISTICAL DATA AND RISK MEASURES**

The territorial unit considered in this paper is the voivodeship (NUTS 2).

Specific mortality rates by age, sex and cause of death were calculated for each voivodeship.

Three age groups of age were distinguished:

- 1-29,
- 30-54
- 55-69

The following criteria were assumed for the selection:

- the age group 1-29 encompasses a period of life with a relatively low number of deaths,
- 30-54 and 55-69 are ages in which the risk of death rises.

The latter two populations were handled separately, which takes into account the fact that mortality at ages 30-54 contributes to a reduction in the labour force, which, in the case of an aging population and a reduction of the population entering the labour market, is of significant importance to the economy. The 55-69 population, meanwhile, is treated as immobile.

Infant mortality was omitted, as it was recognized that due to the specific nature of mortality, also by cause of death, it should be a separate research problem. This period of life was omitted also due to methodological reasons. In this case (as in that of age 70 and above), a direct standardization was not possible.

The following three groups of causes of death, using the ICD X classification updated in 1989, were taken into account:

- circulatory system diseases,
- neoplasms,
- certain infectious and parasitic diseases.

In selecting the age groups and causes of death, the differentiation of the risk of death by age and cause of death were the factors taken into consideration. The 1-29 population has a

relatively low risk, by all the causes taken into account. Infectious and parasitic diseases rarely occur as a cause of death in any age group. Risk of death due to diseases of the circulatory system and neoplasms is high.

Data come from Polish Central Statistical Office (Główny Urząd Statystyczny)

Two types of risks are considered, that is:

- absolute risk, understood as the probability of death within a calendar year, of a person at risk, in the population of the territorial unit in question. The estimator of this probability is the number of deaths, related to the population at risk;
- relative risk, which was obtained by relating the absolute risk of a given territorial unit to the risk which has been assumed as reference.

We consider relative risk, which expresses the degree to which the risk of death in a given voivodeship is higher or lower than the country average, taken as equal to one.

Basing on the assumption that the occurrences of death are subject to Poisson distribution or binomial distribution and are independent, the classical estimator of the relative risk is the standardized mortality ratio (SMR). For a given territorial unit, this is the ratio of the observed number of deaths to those expected.

$$SMR_{iad} = \frac{O_{iad}}{E_{iad}}$$

where:

voivodeship:  $i = 1, 2, \dots, 16$ ; age groups:  $a = 1, 2, 3$ ; causes of death:  $d = 1, 2, 3$ .

$O_{iad}$  - number of deaths in age group  $a$ , from cause  $d$ , which would occur if the population structure of the voivodeship in question ( $i$ ) were the same as the structure used as the standard (standard population is the population of Poland in 2008),

$E_{iad}$  - expected number of deaths obtained by multiplying the population of each of voivodeship by age specific mortality rate for Poland in age group  $a$  from cause  $d$ .

### **INTERPRETATION OF THE RESULTS**

Table 1 contains standardized death rates by gender, age, and cause of death in Poland.

Table 1. Standardized death rates by gender, age, and cause of death (per 10 000)

Total	<i>Certain infectious and parasitic diseases</i>	<i>Neoplasms</i>	<i>Diseases of the circulatory system</i>	<i>Other causes</i>
<b>Males</b>				
<b>1-29</b>				
7,25	0,09	0,58	0,45	6,13
<b>30-54</b>				
54,88	0,83	10,12	14,14	29,80
<b>55 - 59</b>				
214,37	1,78	73,39	77,31	61,89

Females				
1-29				
2,36	0,08	0,37	0,19	1,72
30-54				
18,67	0,28	8,24	3,62	6,54
55 - 69				
85,42	0,74	38,93	25,65	20,10

Source: own calculations

For the more detailed presentation we chose models estimated for:

- I. cardiovascular disease: males aged 30-54 and 55-69 because of high mortality level and significant progress during social – economic transition;
- II. neoplasms: females aged 30 – 54 and 55 – 69 as the mortality level is still high;
- III. infectious and parasitic diseases: males and females aged 1-29 – for methodological point of view because of relatively low number of death.

Spatial distributions of mortality for groups not mentioned in the text are included in Appendix.

Estimates of relative risk of death achieved on the basis of the model are juxtaposed with the classic SMR measure and presented in the following figures (2-7) in the form of maps. In the case of BYM model of the maps demonstrate the estimations of expected values of  $\theta$  parameter of *a posteriori* distributions. Uniform colour means a similar intensity of a phenomenon and is a certain arbitrary criterion for classification.

Figure 2. Estimate of the relative risk of death from circulatory system diseases: SMR, BYM for female aged 30-54

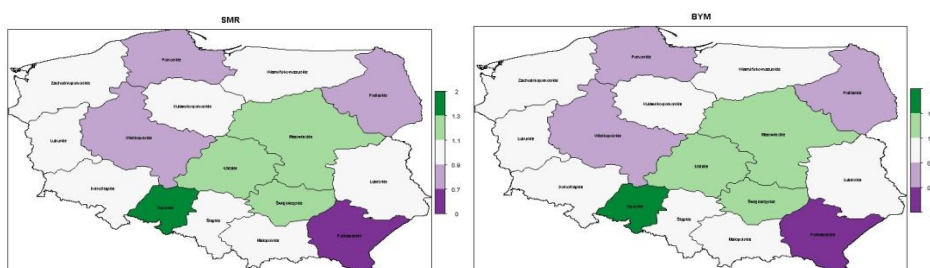


Figure 3. Estimate of the relative risk of death from circulatory system diseases: SMR, BYM for female aged 55-69

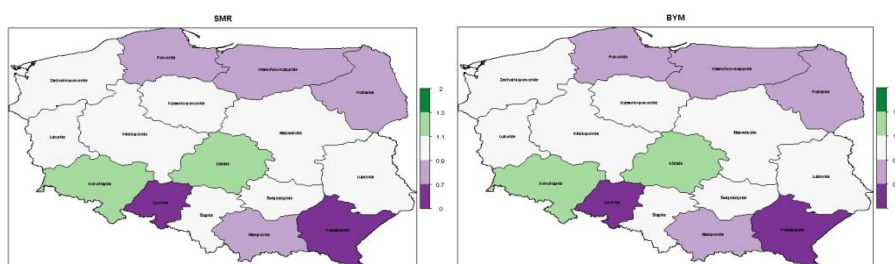


Figure 4. Estimate of the relative risk of death caused by neoplasms: SMR, BYM for females aged 30-54

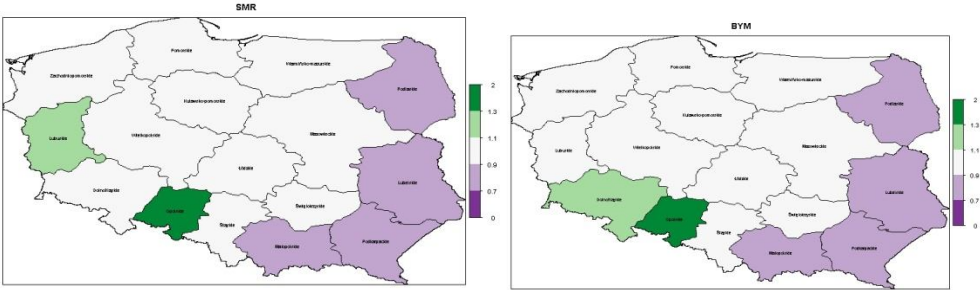


Figure 5. Estimate of the relative risk of death caused by neoplasms: SMR, BYM for females aged 55-69

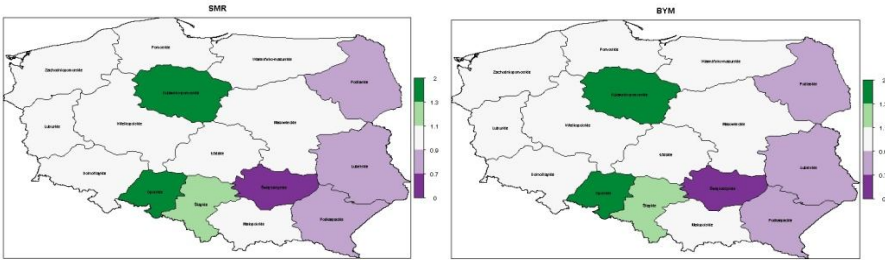


Figure 6. Estimate of the relative risk of death from certain infectious and parasitic diseases: SMR, BYM for males aged 1-29

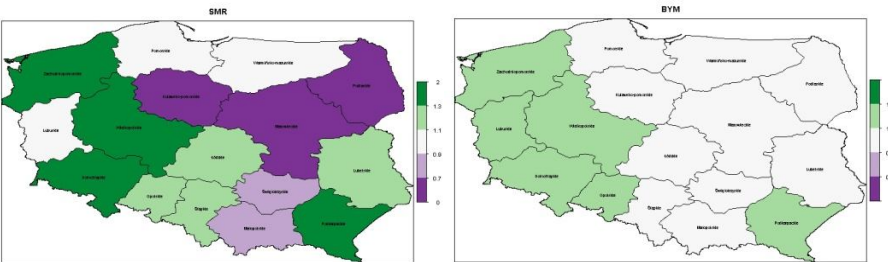
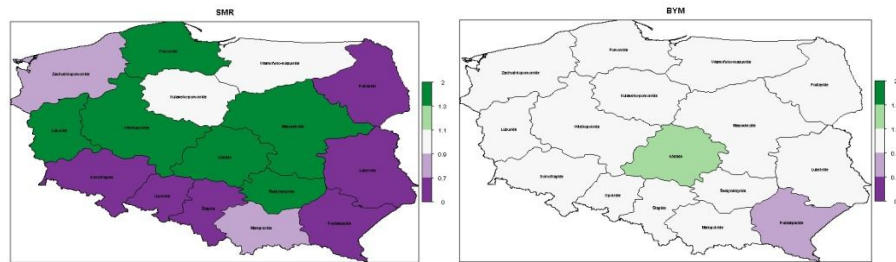




Figure 7. Estimate of the relative risk of death from certain infectious and parasitic diseases: SMR, BYM for females aged 1-29



### **ANALYSIS OF SPATIAL COMPONENTS OF MORTALITY DISTRIBUTIONS**

We start with the analysis of the strength of the spatial effects taken into account in the model. The results are contained in Table 2, as a juxtaposition of point estimates of the posterior variance of spatial effects  $S$  and  $H$ .

Table 2. Posterior estimates of clustering effect  $S \hat{v}(S|Y)$  and heterogeneity effect  $H \hat{v}(H|Y)$

Circulatory system diseases				
Age	Males		Females	
	$\hat{v}(H Y)$	$\hat{v}(S Y)$	$\hat{v}(H Y)$	$\hat{v}(S Y)$
1-29	0,0586	0,0435	0,0283	0,0204
30-54	0,1018	<u>0,1257</u>	0,0108	<u>0,0170</u>
55-69	0,1064	0,0656	0,0356	0,0221
Neoplasms				
Age	Males		Females	
	$\hat{v}(H Y)$	$\hat{v}(S Y)$	$\hat{v}(H Y)$	$\hat{v}(S Y)$
1-29	0,0960	<u>0,1351</u>	0,0321	0,0222
30-54	1,1025	0,7501	0,0070	<u>0,0103</u>
55-69	3,3618	2,2622	0,0266	0,0206
Certain infectious and parasitic diseases				
Age	Males		Females	
	$\hat{v}(H Y)$	$\hat{v}(S Y)$	$\hat{v}(H Y)$	$\hat{v}(S Y)$
1-29	0,0271	0,0196	0,0409	0,0257
30-54	0,1746	0,0698	0,0488	<u>0,1118</u>
55-69	0,4530	0,3117	0,1202	<u>0,1875</u>

Source: own calculations

colour red underlined indicates populations with clustering effect

Clustering effect ( $\hat{v}(S|Y) > \hat{v}(H|Y)$ ) is observed for mortality caused by:

- circulatory system diseases: males and females aged 30-54,
- neoplasms: males aged 1-29 and females aged 30-54,

- certain infectious and parasitic diseases: females aged 30-54 and 55-69.

Applying as a pattern the proposition of F. Divino V. Egidi M. Antonio Salvatore (2009) five classes of mortality are defined:

- (1) below the national average: low 0,0 – 0,7;
- (2) below the national average: moderate; 0,7 – 0,9;
- (3) around the national average 0,9 – 1,1;
- (4) above the national average: 1,1 – 1,3;
- (5) above national average - high: more than 1,3.

The macro-regions NUTS-1 (Central, South, East, North-West, South-West, North) are added in order to approach the geographical position of each of voivodeships,

On the figure 8 BYM, clustering (*S*) and heterogeneity (*H*) effects for circulatory system diseases for males aged 30-54 are put together.

Figure 8. Circulatory system diseases, males 30-54: BYM, clustering effect, heterogeneity effect



It is presented on the figure 9.

There are following clusters with similar intensity of mortality:

Figure 9. Clusters of mortality caused by cardiovascular diseases for males aged 30 – 54  
Cardiovascular diseases – males 30 – 54



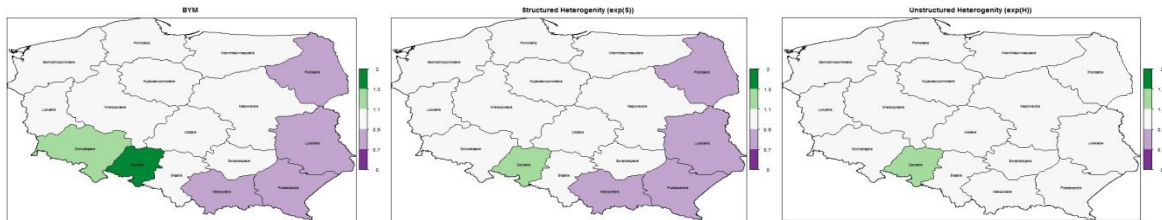
- (1) **below the national average:**  
**moderate (0,7 – 0,9):**  
pomorskie (*North*), wielkopolskie (*North-West*),
- (2) **around the national average (0,9 – 1,1):**  
a) dolnośląskie (*South-West*), lubuskie (*Nord-West*), zachodniopomorskie (*Nord-West*), kujawsko-pomorskie (*Nord-West*), warmińsko-mazurskie (*Nord*),  
b) małopolskie (*South*), śląskie (*South*);
- (3) **above the national average: 1,1-1,3**  
łódzkie (*Central*), świętokrzyskie (*East*), mazowieckie (*Central*);

There are three separated units:

- below the national average: podkarpackie (*East*) (0,0 – 0,7); podlaskie (*East-north*); **national average** lubelskie (*East*), above national average - **high: >1,3** opolskie *south – west*.

The figure 10 demonstrates BYM, clustering ( $S$ ) and heterogeneity ( $H$ ) effects for neoplasms diseases for females aged 30-54.

Figure 10. Neoplasms females 30-54: BYM, clustering effect, heterogeneity effect



The spatial distribution of mortality caused by neoplasms for females aged 30-54 is presented on the figure 11. There are following clusters with similar intensity of mortality:

### Neoplasms – Females 30 – 54



(1) below national average (0,7-0,9) małopolskie (*South*), podkarpackie (*East*), lubelskie (*East*), podlaskie (*East*),

(2) Ten voivodeships constitute the region with the level of the relative risk of death classified as **around the national average**.

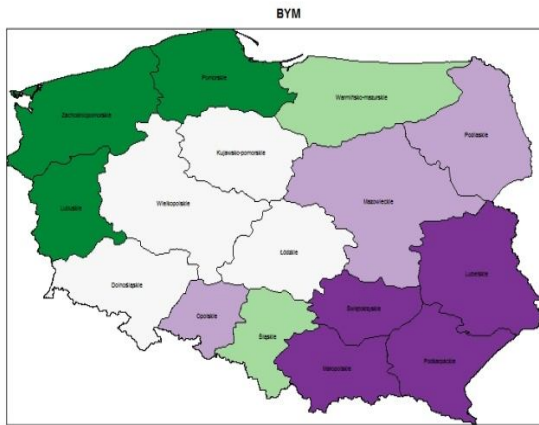
Dolnośląskie *south-west* and opolskie *south – west* are separated units above average.

The figure 12 demonstrates BYM, clustering ( $S$ ) and heterogeneity ( $H$ ) effects for certain infectious and parasitic diseases for females aged 30-54:

Figure 12. Certain infectious and parasitic diseases females 30-54: BYM, clustering effect, heterogeneity effect



There are following clusters with similar intensity of mortality:  
 Certain infectious and parasitic diseases –  
 Females 30 – 54



- (1) below national average (0-0,7) małopolskie (*South*), podkarpackie (*East*), lubelskie (*East*), świętokrzyskie (*South-East*),
- (2) below national average (0,7-0,9) mazowieckie (*North-East*), podlaskie (*North-East*)
- (3) national average (0,9-1,1) dolnośląskie (*West*), wielkopolskie (*West*), kujawsko-pomorskie (*West*), łódzkie (*Center*)
- (4) **above the national average: >1,3** zachodniopomorskie (*North-West*), pomorskie (*North-West*), lubuskie (*North-West*)

There are three separated units:  
 below the national average: śląskie (*South*)  
**(0,0 – 0,7):**  
 above national average - **high: >1,3** opolskie (*South – West*), warmińsko-mazurskie (*North*).

In the situation which appears in the most cases, i.e. when the ratio of  $\hat{v}(H|Y)$  and  $\hat{v}(S|Y)$  is larger than 1, estimates on the basis of the BYM model are influenced by the heterogeneity effect and any assessment of the geographical structure of the distribution of mortality is impossible without decomposition of these two effects. In this case we find some difficulties with interpretation of our results.

The figures 12-13 presents maps demonstrated BYM, clustering (S) and heterogeneity (H) effects respectively for mortality caused by circulatory system diseases for males aged 55-69 (fig. 11) and for mortality caused by neoplasms for females aged 55-69

Figure 12. Diseases of circulatory system man 55-69: BYM, clustering effect, heterogeneity effect



Figure 13. Neoplasm – Females 55 – 69: BYM, clustering effect, heterogeneity effect



The classifications presented above imply that the domination of heterogeneity effect should be treated as perturbation. It is difficult to connect the clusters presented on the map BYM as resulting from this effect. The special patterns of mortality are deformed.

## **CONCLUSIONS**

1. There are not unique homogenous mortality patterns by age, sex and cause of death in Poland.
2. Bayesian hierarchical model has enabled to demonstrate clustering effects observed for mortality caused by:
  - circulatory system diseases for males and females aged 30-54,
  - neoplasms for males aged 1-29 and females aged 30-54,
  - certain infectious and parasitic diseases for females aged 30-54 and 55-69.

For this populations clusters are relatively clearly defined. It imply that environmental factor connected with geographical structure significantly shape spatial mortality distributions. On the basis of this results the regions with high and low risk of death are determined.

3. We meet serious interpretive troubles when heterogeneity effect dominate. One of the reason of this situation could be a space of voivodeship.
4. In the light of this result the future directions of research are postulated, namely:
  - a) analysis of the mortality by age, sex, and cause of death by smaller administrative units (NUTS4),
  - b) analysis of sensitivity of the results in the context of *a priori* distributions,
  - c) analysis of *a posteriori* distribution of variance ratio of spatial effects.

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## APPENDIX

The appendix includes spatial distributions of mortality for groups not mentioned in the text. Colour blue underlined shows which effect dominates spatial distribution.

### *Diseases of circulatory system*

Figure 14. Diseases of circulatory system – Males 1 – 29: BYM, clustering effect, heterogeneity effect

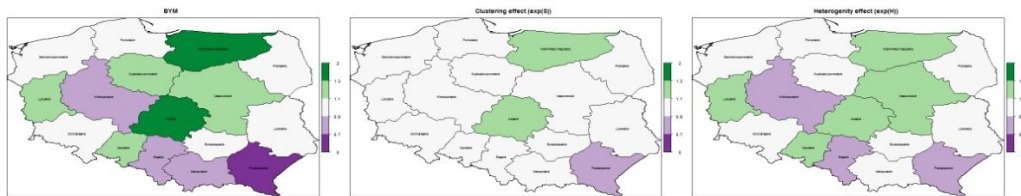


Figure 15. Diseases of circulatory system – Females 1 – 29: BYM, clustering effect, heterogeneity effect



Figure 16. Diseases of circulatory system – Females 30 – 54: BYM, clustering effect, heterogeneity effect

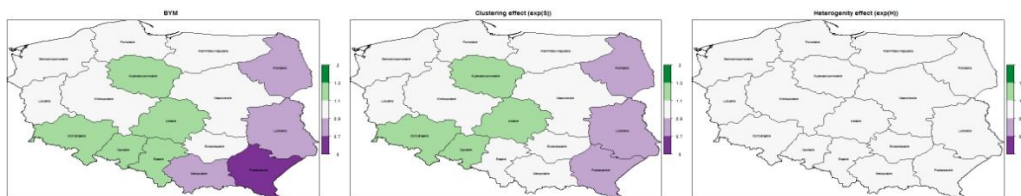


Figure 17. Diseases of circulatory system – Females 30 – 54: BYM, clustering effect, heterogeneity effect





## Neoplasm

Figure 18. Neoplasm– Males 1 – 29: BYM, [clustering effect](#), heterogeneity effect

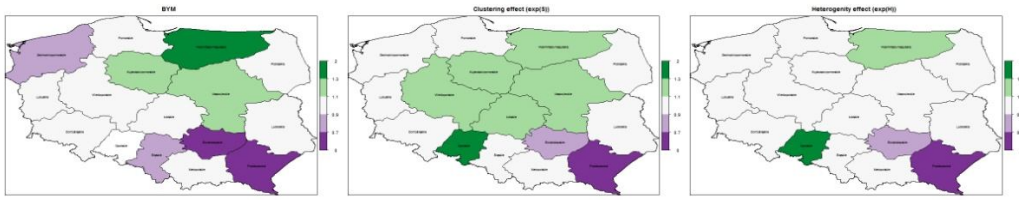


Figure 19. Neoplasm – Males 30 – 54: BYM, clustering effect, [heterogeneity effect](#)

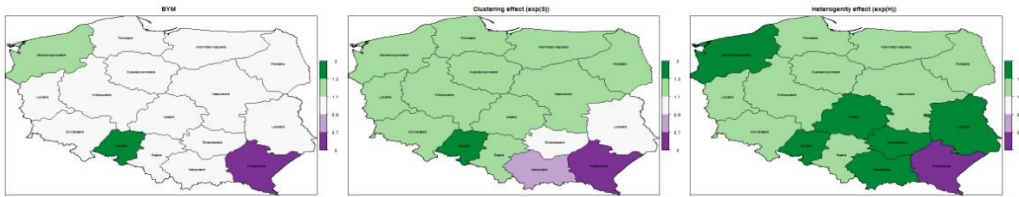


Figure 20. Neoplasm – Males 55 – 69: BYM, clustering effect, [heterogeneity effect](#)

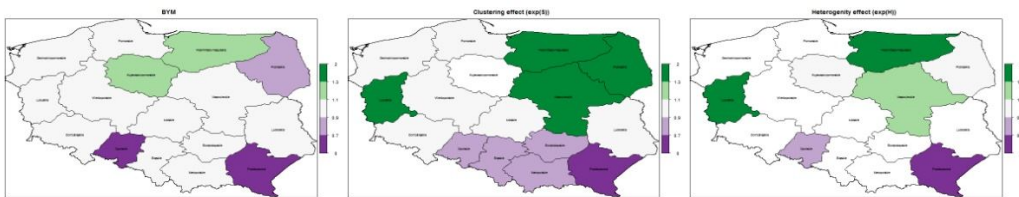
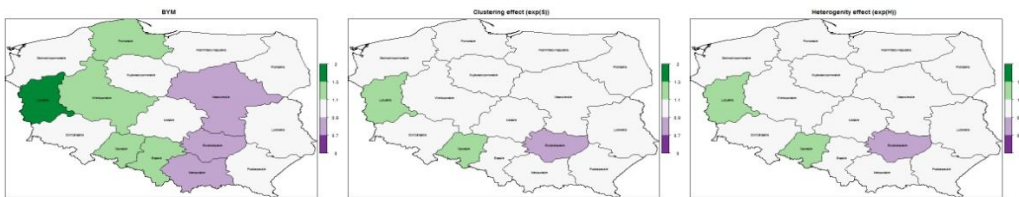


Figure 21. Neoplasm – Females 1 – 29: BYM, clustering effect, [heterogeneity effect](#)



## Certain infectious and parasitic diseases

Figure 22. Certain infectious and parasitic diseases – Males 1 – 29: BYM, clustering effect, [heterogeneity effect](#)



Figure 23. Certain infectious and parasitic diseases – Males 30 – 54: BYM, clustering effect, [heterogeneity effect](#)

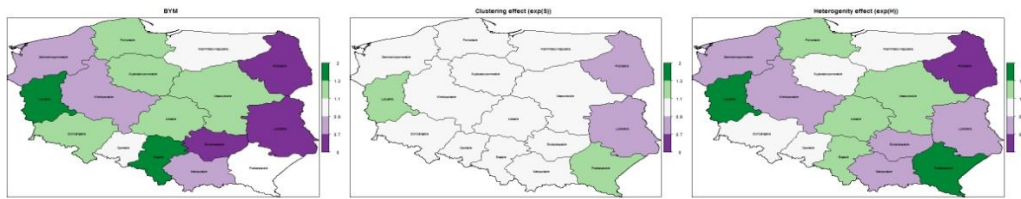


Figure 24. Certain infectious and parasitic diseases – Males 55 – 69: BYM, clustering effect, [heterogeneity effect](#)

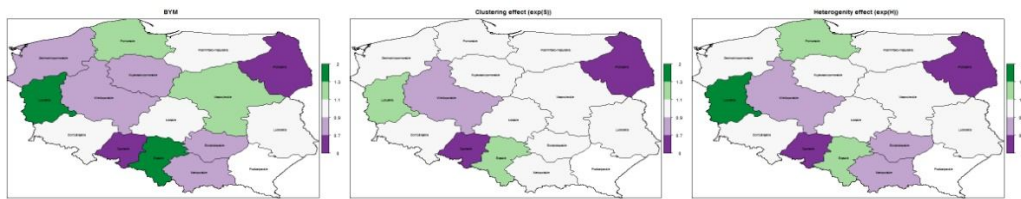


Figure 25. Certain infectious and parasitic diseases – Females 1 – 29: BYM, clustering effect, [heterogeneity effect](#)



Figure 26. Certain infectious and parasitic diseases – Females 55 – 69: BYM, [clustering effect](#), heterogeneity effect

