

# Comparison of the incidence of new malignancies in diabetic patients in urban and rural populations in Poland in the years 2008–2014 based on the database of the National Health Fund

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## Abstract

**Introduction:** Many epidemiological studies show a correlation between the risk of cancer and type 2 diabetes mellitus in various populations.

**Material and methods:** The material was obtained from the database of the National Health Fund. This publication presents a comparison of the incidence of new malignancies in rural and urban populations of diabetic patients in Poland based on the database of the National Health Fund for the period between 1.05.2008 and 30.09.2014.

**Results:** Comparison of the mean incidence of selected malignancies in diabetic patients in the population analysed indicated significant differences between the incidence rate in the urban and rural populations ( $p < 0.001$ ). The mean incidence of gastric cancer, colorectal cancer, kidney cancer, brain tumours and leukaemia in both sexes was significantly higher in rural areas compared to urban. The mean incidence of oesophageal cancer and pancreatic cancer in females was significantly higher among in the urban population compared to the rural areas ( $p < 0.001$ ). No differences in the incidence rate of these neoplasms were observed in men ( $p > 0.05$ ).

**Conclusions:** The incidence of gastric cancer, colorectal cancer, laryngeal cancer, lung cancer, testicular cancer, kidney cancer, lung cancer, lymphocytic leukaemia and myeloid leukaemia is higher in diabetic males in rural areas than the incidence in the urban population. The incidence of the malignancies liver cancer, malignant skin melanoma, malignant skin, prostate cancer, urinary bladder cancer and multiple myeloma in male diabetic patients living in urban areas is higher than the incidence in rural areas.

**Key words:** diabetes mellitus, incidence, urban areas, rural areas, malignancies.

## Introduction

Many epidemiological studies show a correlation between the risk of cancer and type 2 diabetes mellitus in various populations. Both type 2 diabetes mellitus and obesity are independent factors that affect the in-

cidence of some malignancies, have a detrimental effect on the prognosis and result in a higher mortality rate [1].

A correlation between malignancies and diabetes was observed as early as in the 19<sup>th</sup> century. When insulin and oral antidiabetic agents were introduced into treatment the life of diabetic patients was prolonged but at the same time the incidence of neoplastic complications and diseases increased in this population compared to non-diabetic patients [2]. Artur Czyżyk was one of the first authors in Poland to present correlations between diabetes and malignancies [3].

Approximately 70% of malignancies are associated with a lifestyle, diet or result from detrimental environmental factors. Cancer predictors include the following: smoking in 30%, unhealthy diet in 30%, infections in 5%, alcohol in 3% and environmental pollution in 2%. Age is also a predictive factor [4, 5].

In 2001 in the USA cardiovascular diseases, cancer and diabetes mellitus accounted for 1.5 million deaths, namely two thirds of all deaths. In 38.5% of cases it was due to cardiovascular disorders, in 22.9% due to cancer and in 3% due to diabetes mellitus [6, 7].

Shikata *et al.* performed an extensive meta-analysis and found that the risk of liver cancer, pancreatic cancer and uterine body cancer in diabetic patients is twice as high as that in the general population, the risk of colon cancer, breast cancer in women, and urinary bladder cancer is 1.2–1.5 times higher, no correlation for lung cancer was found, and a reduced risk of prostate cancer was observed [8].

Czeleko *et al.* found that the presence of diabetes could have an effect on the occurrence of malignancies and overall mortality [9].

The effect of the pharmacological treatment of diabetes on the occurrence of some malignancies and general mortality was evaluated in 2 studies performed on the basis of NHF data in Poland in the years 2008–2014 [10, 11].

This publication is a unique study that presents differences in the incidence of malignancies in diabetic patients in Poland depending on where they live (cities or rural areas).

This publication presents a comparison of the incidence of new malignancies in rural and urban populations of diabetic patients in Poland based on the database of the National Health Fund (NHF) for the period between 01.05.2008 and 30.09.2014.

## Material and methods

Health services in Poland are financed by the National Health Fund (NHF) based on the act [12]

and regulations of the Minister of Health that result from this act [13, 14].

Services with the diagnosis of group C malignancies and non-malignant neoplasms from D00 to D50 and Z51.1 and Z51.2 are performed as part of hospital treatment, namely in hospitals. The regulations of the NHF president determine organisation, financing and settlement of such services [15, 16].

In 2008 homogeneous patient groups were introduced into the settlement system and since that time therapies have been funded in the system of such special groups.

The PESEL (personal ID no.) number was considered to be a unique patient ID number [17].

A correlation between the PESEL number of diabetic patients and services provided after the diagnosis of cancer was made and evaluated in various stages, as follows:

In the period between 1 May 2008 and 30 April 2009 reports for services associated with diabetes with the main diagnosis of “diabetes mellitus” were found in NHF resources with the following determinants: E10.X – insulin-dependent diabetes mellitus, E11.X – non-insulin-dependent diabetes mellitus, E12.X – malnutrition-related diabetes mellitus, E13.X – other unspecified forms of diabetes mellitus, E14.X – unspecified diabetes mellitus, or the patient had filled a prescription for any medicinal product belonging to the following groups: A10A.X (insulins), A10B.X (oral antidiabetic agents), specialist diagnostic tests. In total, there were (PESEL no.) 2,146,728 cases.

In the period between 01.01.2004 and 30.04.2008 there were reports presenting services provided for group C malignancies and non-malignant neoplasms from groups D00 to D50, Z51.1 or Z51.2 – in total, 305,411 cases based on the PESEL number. Patients with a diagnosis of neoplasm before 30.04.2008 were not analysed in this study. For the remaining 1,840,973 patients a report for services with the diagnosis of a group C malignancy in the period between 1.05.2008 and 30.09.2014 was analysed. The date for the first report of services with the diagnosis of a malignancy was considered to be the year when cancer developed in a given person with the PESEL number.

## Statistical analysis

Numerical values for studies were taken from resources of the NHF database using the structured query language ([https://pl.wikipedia.org/wiki/J%C4%99zyk\\_angielski](https://pl.wikipedia.org/wiki/J%C4%99zyk_angielski) *Structured Query Language* – SQL) and analysed with statistical tools such as SAS and Statistica (Student’s *t*-test for independent samples). Differences were considered to be significant at the significance level of 95% ( $p < 0.05$ ).

## Results

In the period between 1 May 2008 and 30 September 2014 in the analysed cohort of diabetic patients including 1,840,979 patients 173,929 patients with new group C malignancies were identified based on the database of the National Health Fund and their place of residence was determined to be urban or rural areas. In the case of 411 patients their place of residence was not determined, and therefore they were not included in the analysis presented below.

In the analysed period in diabetic patients living in urban areas there were 129,165 new malignancies, and 44,764 cases in those living in rural areas.

In the group of 173,929 patients with malignancies there were 85,175 men and 88,754 women. In the group of male patients 63,778 were living in urban areas, and 21,397 in rural areas. In the group of female patients 65,387 were living in urban areas and 23,367 in rural areas.

Table I presents a list of new malignancies among 1,840,973 diabetic patients in the period between 1.05.2008 and 30.09.2014 in Poland, taking into account their place of residence (rural and urban areas), and the Regional Division of the Health Fund.

Table II presents a list of new malignancies in the subpopulation of 1,840,973 diabetic patients, taking into account their sex, place of residence (rural and urban areas), and the Regional Division of the Health Fund.

The later section of the paper analyses the incidence of selected malignancies in the period between 1.05.2008 and 30.09.2014 in individual regional divisions of the NHF, taking into account sex and place of residence. The incidence of each selected group C malignancy in every regional division of the NHF in a given period was determined. Then, the results were presented as the mean incidence for the whole of Poland, taking into account standard deviations.

Table III presents the mean incidence of selected malignancies in urban and rural areas, with regard to age, in the period 2008–2014.

In the urban population in male patients with diabetes mellitus the following malignancies were observed: 1) prostate cancer; 2) lung cancer; 3) colorectal cancer; 4) skin cancer; 5) urinary bladder cancer. In the rural population in male patients the following malignancies were observed: 1) lung cancer; 2) prostate cancer; 3) colorectal cancer; 4) skin cancer; 5) urinary bladder cancer.

**Table I.** List of new malignancies among 1,840,973 diabetic patients in the period between 1.05.2008 and 30.09.2014 in Poland, taking into account their place of residence (rural and urban areas), and the Regional Division of the Health Fund, based on the database of the National Health Fund (NHF)

Division of NHF Province	All together	Urban	Rural
1 Lower Silesia	14 024	11 172	2 852
2 Kujawy-Pomerania	9 602	7 092	2 510
3 Lublin	7 776	4 805	2 971
4 Lubuskie	4 190	3 136	1 054
5 Łódź	12 682	9 784	2 898
6 Małopolska	14 348	9 483	4 865
7 Mazovia	24 496	19 249	5 247
8 Opole	4 628	2 766	1 862
9 Podkarpacie	6 542	3 501	3 041
10 Podlasie	3 907	2 909	998
11 Pomerania	11 020	8 700	2 320
12 Silesia	26 266	21 940	4 326
13 Świętokrzyskie	6 333	4 102	2 231
14 Warmia-Masuria	5 091	3 570	1 521
15 Wielkopolska	14 677	10 318	4 359
16 West Pomerania	8 347	6 638	1 709
Total	173 929	129 165	44 764

**Table II.** List of new malignancies among 1,840,973 diabetic patients in the period between 1.05.2008 and 30.09.2014 in Poland, taking into account the place of residence (rural and urban areas), sex and the Regional Division of the Health Fund, based on the database of the National Health Fund (NHF)

Division of NHF Province	Urban		Rural	
	Men	Women	Men	Women
1 Lower Silesia	5 438	5 734	1 320	1 532
2 Kujawy-Pomerania	3 398	3 694	1 187	1 323
3 Lublin	2 348	2 457	1 403	1 568
4 Lubuskie	1 545	1 591	503	551
5 Łódź	4 703	5 081	1 429	1 469
6 Małopolska	4 582	4 901	2 276	2 589
7 Mazovia	9 666	9 583	2 469	2 778
8 Opole	1 316	1 450	860	1 002
9 Podkarpacie	1 736	1 765	1 506	1 535
10 Podlasie	1 503	1 406	470	528
11 Pomerania	4 528	4 172	1 124	1 196
12 Silesia	10 525	11 415	1 975	2 351
13 Świętokrzyskie	1 924	2 178	1 176	1 055
14 Warmia-Masuria	1 806	1 764	688	833
15 Wielkopolska	5 310	5 008	2 187	2 172
16 West Pomerania	3 450	3 188	824	885
Total	63 778	65 387	21 397	23 367

In the urban population in female patients with diabetes mellitus the following malignancies were observed the most often: 1) breast cancer; 2) skin cancer; 3) colorectal cancer; 4) lung cancer; 5) uterine body cancer. In the rural population in female patients the following malignancies were observed the most often: 1) breast cancer; 2) skin cancer; 3) colorectal cancer; 4) uterine body cancer; 5) lung cancer.

A comparison of the mean incidence of selected malignancies in diabetic patients in the population analysed indicated significant differences between the incidence rate in the urban and rural populations.

The mean incidence of gastric cancer, colorectal cancer, kidney cancer, brain tumours, myeloid leukaemia and lymphatic leukaemia in both sexes was significantly higher in rural areas compared to urban areas. The mean incidence of liver cancer, urinary bladder cancer and myeloma in both sexes was significantly higher compared to the mean incidence in rural areas. The mean incidence of oesophageal cancer and pancreatic cancer in females was significantly higher among in the urban population compared to the mean incidence in rural areas. No differences in the incidence rate of these neoplasms were observed in men.

The mean incidence of laryngeal cancer and lung cancer in males was significantly higher in the rural population compared to the urban population. On the other hand, the mean incidence of laryngeal cancer and lung cancer in women was significantly higher in the urban population compared to the mean incidence in the rural population.

The mean incidence of gall bladder cancer in women was significantly higher in the rural population compared to the urban population. No differences were observed in the incidence rate of this neoplasm in males. The mean incidence of skin cancer and malignant skin melanoma was significantly higher in males in the urban population compared to the incidence in the rural population. The mean incidence of malignant skin melanoma in women was significantly higher in the rural population compared to the mean incidence in the urban population.

No differences were observed with regard to the incidence rate of skin cancer between urban and rural populations. The mean incidence of breast cancer was significantly higher in women in the urban population compared to the rural population. The mean incidence of uterine body cancer was significantly higher in women in the

**Table III.** Mean incidence of 23 malignancies in Poland with standard deviations, among diabetic patients in the years 2008-2014, taking into account sex and place of residence according to the NHF database (mean  $\pm$  standard deviation; Student's *t*-test for independent samples)

Malignancies ICD-10*	Men			Women		
	Urban	Rural	P-value	Urban	Rural	P-value
Oesophagus C15	0.904 $\pm$ 0.373	0.875 $\pm$ 0.275	0.245	0.384 $\pm$ 0.201	0.314 $\pm$ 0.230	< 0.05
Stomach C16	3.64 $\pm$ 0.613	4.671 $\pm$ 2.377	< 0.001	2.705 $\pm$ 0.510	3.215 $\pm$ 0.703	< 0.001
Colorectal C18–C21	12.083 $\pm$ 1.136	12.35 $\pm$ 1.574	< 0.001	10.745 $\pm$ 1.215	11.24 $\pm$ 1.692	< 0.001
Liver C22	2.164 $\pm$ 0.558	1.811 $\pm$ 0.408	< 0.001	1.610 $\pm$ 0.329	1.506 $\pm$ 0.295	< 0.001
Gallbladder C23	0.417 $\pm$ 0.127	0.437 $\pm$ 0.146	0.269	1.266 $\pm$ 0.242	1.607 $\pm$ 0.336	< 0.001
Pancreas C25	3.193 $\pm$ 0.599	3.204 $\pm$ 0.476	0.626	3.452 $\pm$ 0.393	3.396 $\pm$ 0.696	< 0.05
Larynx C32	1.460 $\pm$ 0.339	1.825 $\pm$ 0.406	< 0.001	0.390 $\pm$ 0.130	0.355 $\pm$ 0.170	0.437
Lungs C34	12.99 $\pm$ 1.996	14.98 $\pm$ 1.907	< 0.001	7.552 $\pm$ 2.688	6.083 $\pm$ 1.352	< 0.001
Malignant melanoma C43	1.313 $\pm$ 0.300	1.095 $\pm$ 0.362	< 0.001	1.243 $\pm$ 0.240	1.339 $\pm$ 0.415	< 0.001
Skin C44	11.013 $\pm$ 0.122	9.156 $\pm$ 0.766	< 0.001	12.378 $\pm$ 1.871	12.365 $\pm$ 1.542	0.713
Breast C50				13.848 $\pm$ 2.355	13.41 $\pm$ 1.209	< 0.001
Cervix C53				2.867 $\pm$ 0.835	2.813 $\pm$ 0.507	0.064
Endometrial C54				7.230 $\pm$ 1.469	7.974 $\pm$ 0.493	< 0.001
Ovaries C56				3.285 $\pm$ 1.899	3.244 $\pm$ 0.640	< 0.05
Prostate C61	14.275 $\pm$ 2.668	13.333 $\pm$ 1.775	< 0.001			
Testis C62	0.367 $\pm$ 0.186	0.469 $\pm$ 0.177	< 0.001			
Kidneys C64	4.893 $\pm$ 0.968	5.049 $\pm$ 1.559	< 0.001	4.032 $\pm$ 1.768	4.295 $\pm$ 0.884	< 0.001
Urinary bladder C67	7.697 $\pm$ 1.481	7.105 $\pm$ 1.925	< 0.001	3.336 $\pm$ 0.584	2.111 $\pm$ 0.491	< 0.001
Brain C71	2.038 $\pm$ 0.776	2.119 $\pm$ 0.326	< 0.001	2.299 $\pm$ 0.788	2.652 $\pm$ 0.646	< 0.001
Thyroid C73	0.784 $\pm$ 1.019	0.617 $\pm$ 0.649	0.087	1.328 $\pm$ 0.558	1.278 $\pm$ 0.694	0.287
Multiple myeloma C90	0.956 $\pm$ 0.257	0.852 $\pm$ 0.343	< 0.001	1.240 $\pm$ 0.207	1.16 $\pm$ 0.212	< 0.001
Lymphatic leukaemia C91	1.444 $\pm$ 0.366	1.590 $\pm$ 0.290	< 0.01	1.510 $\pm$ 0.589	1.769 $\pm$ 0.432	< 0.001
Myeloid leukaemia C92	0.649 $\pm$ 0.177	0.737 $\pm$ 0.166	< 0.001	0.547 $\pm$ 0.179	0.727 $\pm$ 0.208	< 0.001

\*International Statistical Classification of Diseases and Related Health Problems 10<sup>th</sup> Revision.

rural population compared to the urban population. The mean incidence of prostate cancer was significantly higher in men in the urban population compared to the mean incidence in the rural population. The mean incidence of testicular cancer was significantly higher in men in the rural population compared to the mean incidence in the urban population.

No differences were observed in the mean incidence of thyroid cancer in both men and women, and no differences were observed for ovarian and cervical cancer between women in the urban and rural populations.

## Discussion

This is the first global epidemiological study comparing of the incidence rate of cancer among diabetic patients in rural and urban populations.

In this study 74.3% of diabetic patients with a malignancy lived in urban areas, and 25.7% in rural areas. With regard to available information on the effects of rural and urban environments and resulting differences, including, among others, environmental pollution affecting the morbidity and mortality rates, it was demonstrated that they may contribute to higher incidence of lung diseases and lung cancer in urban areas [18, 19].

The mortality rate due to all malignancies in the general population of patients in the cities of Northern Ireland was 21% higher ( $p < 0.001$ ) than the mortality rate due to all malignancies in the rural population. The mortality rate due to lung cancer in the urban population was 43% higher ( $p < 0.001$ ) than the mortality rate in the rural population [20].

The authors emphasise that urban and rural populations differ significantly with regard to sociodemographic parameters and health protection. However, it is difficult to determine whether living in urban or rural areas and the resulting pollution affect the morbidity and mortality rates [19].

Other authors emphasise that sometimes it is difficult to determine whether a given person lives in a rural or urban area [20].

The general mortality rate in the years 2002–2004 due to all malignancies in the general population was 12% higher ( $p < 0.05$ ) in males and 9% ( $p < 0.05$ ) in women in the urban population in England than the mortality rate in the rural population [21].

In the general population the mortality rate due to lung cancer was significantly higher by 7% ( $p < 0.05$ ) in males living in urban areas than the mortality rate in males with lung cancer living in rural areas. However, a similar correlation in females in the study population was not observed in the UK [21].

On the other hand, in Wales the mortality rate due to all malignancies was 9% higher ( $p < 0.05$ ) in males in the urban population than the mortality rate in the rural population. The mortality rate due to lung cancer was 15% higher ( $p < 0.05$ ) in the urban population than the mortality rate due to lung cancer in men in the rural population [19].

In females in Wales the mortality rate due to all malignancies was 6% higher than the mortality rate due to all malignancies in females in the rural population. However, this difference was not statistically significant. In females in Wales the mortality rate due to lung cancer in the urban population was 12% higher ( $p < 0.05$ ) than the mortality rate due to lung cancer in rural areas [19].

Our study regarding the incidence rate of malignancies among diabetic patients living in rural areas in both sexes showed a higher incidence of the malignancies gastric cancer, colorectal cancer, kidney cancer, brain tumours, myeloid leukaemia and lymphoid leukaemia compared to those living in urban areas.

Higher incidence of gall bladder cancer, malignant skin melanoma, skin cancer and uterine body cancer was observed in women living in rural areas compared to those living in urban areas. Higher incidence of laryngeal cancer and lung

cancer was observed in men living in rural areas compared to those living in urban areas.

In the population of diabetic patients living in urban areas in both sexes the incidence rate of the neoplasms liver cancer, urinary bladder cancer and multiple myeloma was higher compared to those living in rural areas.

Higher incidence of skin cancer in males, oesophageal cancer, pancreatic cancer, laryngeal cancer and lung cancer in females was observed in those living in urban areas compared to the incidence rate in these populations in rural areas.

In diabetic women living in urban areas the incidence of breast cancer is higher compared to those living in rural areas.

The incidence rate of prostate cancer was higher in the urban population compared to the rural population. On the other hand, the incidence of testicular cancer was significantly higher in the rural population.

Causal relationships for neoplastic diseases are mainly hypothetical. Many of them require further studies and specific evidence from experimental and clinical studies. Type 2 diabetes mellitus, but not type 1 diabetes mellitus, and malignancies are linked by numerous pathogenic factors associated with carbohydrate metabolism, obesity, chronic inflammation, metabolic balance, immunogenicity and presence of oxidative stress. Providing nutrition according to the rules of dietetics, regular physical effort, moderate consumption of alcohol, discontinuation of tobacco smoking, limitation of detrimental effects of the environment – all these are necessary elements of informed prophylaxis.

Each physician treating a patient with cancer and diabetes should know numerous mechanisms linking these two disorders, from epidemiology to cellular pathophysiology.

In some patients there were limitations that made it difficult to perform some assessments: for example, it was not possible to determine the type of diabetes, its duration, method of treatment, metabolic compensation of diabetes, or whether a person was overweight or obese.

The diagnosis of diabetes was based on reports of services and filling prescription for antidiabetic agents and glucose meter test strips. Patients outside the National Health Fund system were not covered, and it might have affected the results. In the case of 411 patients with diabetes and a new neoplasm it was not possible to determine their place of residence. This is a preliminary report, and the results of this study indicate that there are differences in the incidence rate of some malignancies that are more commonly observed in diabetic patients living in rural areas.

In conclusion, the place of residence (urban or rural) of a diabetic patient increases or decreases

the risk of malignant neoplasia. The incidence of gastric cancer, colorectal cancer, laryngeal cancer, lung cancer, testicular cancer, kidney cancer, lymphocytic leukaemia and myeloid leukaemia is higher in diabetic males in rural areas compared to the incidence rate in the urban population. The incidence of the malignancies liver cancer, malignant skin melanoma, malignant skin, prostate cancer, urinary bladder cancer and multiple myeloma in male diabetic patients living in urban areas is higher than the incidence in rural areas. The incidence of gastric cancer, colorectal cancer, gall bladder cancer, malignant skin melanoma, uterine body cancer, kidney cancer, brain tumours, lymphatic leukaemia and myeloid leukaemia in diabetic women was significantly higher in the rural population than the incidence in the urban population. The incidence of the malignancies liver cancer, pancreatic cancer, laryngeal cancer, lung cancer, urinary bladder cancer and multiple myeloma in female diabetic patients living in urban areas is higher than the incidence in rural areas.

#### Conflict of interest

The authors declare no conflict of interest.

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