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# Obesity and the risk of type 2 diabetes mellitus and certain types of cancer

## Otyłość a ryzyko rozwoju cukrzycy typu 2 i niektórych nowotworów złośliwych

### ABSTRACT

**Obesity, type 2 diabetes mellitus and cancers are the most common chronic diseases. Data collected by world organizations for protection and promotion of health show a rapid increase in the prevalence of these illnesses over the last few decades. The rapid increase in prevalence of excess body weight globally is believed to be related to the growing proportion of people living in urban areas and the resulting changes in dietary and physical activity patterns.**

**The epidemic of overweight and obesity and the clear connection between raised BMI and many non-communicable diseases (such as cardiovascular diseases, type 2 diabetes, and cancers) make this issue a public health priority all over the world.**

**Estimates of future overweight and obesity prevalence assume that while keeping the current growth rate of prevalence, the numbers of people affected around the globe will rise to 2.16 billion for overweight and 1.12 billion for obesity in 2030. These numbers combined will constitute 58% of the world's population. Considering the above, we should expect a proportional increase in prevalence of the most serious health consequences of overweight and obesity — type 2 diabetes mellitus and some cancers, including breast cancer in postmenopausal women, endometrial, colonic and renal cancers.**

**In this paper we discussed the available data on prevalence of overweight and obesity and analysed a causal relationship between excess body weight, type 2 diabetes mellitus and selected types of malignancies. (Diabet. Klin. 2015; 4, 4: 163–171)**

**Key words: obesity, cancer, diabetes mellitus type 2, BMI**

### STRESZCZENIE

**Zarówno otyłość, jak i cukrzycę typu 2 oraz nowotwory złośliwe należy zaliczyć do najczęściej występujących obecnie schorzeń przewlekłych. Dane gromadzone przez światowe organizacje zajmujące się ochroną i promocją zdrowia wskazują na gwałtowny wzrost zapadalności na te choroby w ciągu ostatnich kilku dziesięcioleci.**

**Przyczyn wzrostu rozpowszechnienia nadmiernej masy ciała na świecie upatruje się w zwiększającym się odsetku osób zamieszkujących tereny miejskie oraz wiążącym się z tym trybem życia. Wzrastający odsetek nadwagi oraz otyłości w populacji światowej oraz jej związek z występowaniem wielu schorzeń czyni je istotnym wyzwaniem dla zdrowia publicznego i priorytetem światowej polityki zdrowotnej. Prognozy dotyczące występowania nadwagi i otyłości zakładają, że przy utrzymaniu aktualnego tempa wzrostu rozpowszechnienia częstość ich występowania na świecie wzrośnie do 2,16 mld osób w przypadku nadwagi oraz 1,12 mld osób w przypadku otyłości w 2030 roku, co łącznie będzie stanowić 58% populacji świata. Mając na względzie powyższe dane, należy spodziewać się**

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**równie nasilonego wzrostu występowania najpoważniejszych konsekwencji zdrowotnych otyłości, jakimi są m.in. cukrzyca typu 2 oraz wybrane nowotwory złośliwe, w tym nowotwory piersi u kobiet będących po menopauzie, nowotwory endometrium, jelita grubego oraz nerki.**

**W publikacji omówiono dostępne dane dotyczące epidemiologii oraz związku przyczynowo-skutkowego pomiędzy nadmierną masą ciała a ryzykiem rozwoju cukrzycy typu 2 oraz wybranych nowotworów złośliwych. (Diabet. Klin. 2015; 4, 4: 163–171)**

**Słowa kluczowe: otyłość, nowotwory, cukrzyca typu 2, BMI**

## Introduction

Overweight and obesity are the effects of disturbances in the body's energy processes. They occur when the amount of energy delivered to the body exceeds the expended energy for a long time. The resulting excess energy is then accumulated in the form of adipose tissue [1]. According to the World Health Organization (WHO), obesity is abnormal or excessive fat tissue accumulation leading to a significant deterioration of health. A measure commonly used to determine the degree of overweight and obesity in adults is body mass index (BMI), also known as Quetelet index, defined as the ratio of body weight in kilograms to height in metres squared. According to the WHO definition, overweight occurs when in adults this ratio has a value in the range of 25 to 29.5 kg/m$^2$. BMI value higher than 30 kg/m$^2$ indicates obesity [2].

Obesity is an increasingly growing population problem in the world [3]. Numerous epidemiological studies have shown a constantly increasing share of obese and overweight people in the general population [4]. The reasons for this significant increase in the prevalence of overweight and obesity are seen in the development of civilisation entailing lifestyle changes, significant from the health point of view, which involve a substantial reduction of physical activity while introducing high-energy diet (excessive consumption of highly processed and high-calorie foods) [5]. Other factors affecting the prevalence of overweight and obesity in populations are genetic and environmental factors [1].

It is well known that excessive body weight can lead to significant health consequences, including type 2 diabetes, cardiovascular disease, lipid disorders, gout, respiratory disorders and disorders of the musculoskeletal system [6–8]. As shown in numerous studies, obesity is also associated with a higher risk of developing malignancies, including breast cancer in postmenopausal women, endometrial cancer, colorectal carcinoma and kidney cancer [9].

Below we discuss the available data on epidemiology and causal relationship between abnormal body weight and the risk of developing type 2 diabetes and selected cancers.

## Obesity is a growing epidemiological problem in the 21st century

Due to the significant prevalence in populations, obesity has been classified as a disease of civilisation. Prior to 1980, excess body weight was not a significant epidemiological problem and its prevalence in the world was well below 10%. Since then, the prevalence of overweight and obesity doubled or even tripled in selected countries [10, 11].

According to World Health Organization data, the prevalence of obesity has more than doubled over the years 1980–2014. In 2014, more than 1.9 billion of the world's adult population were people with excess body weight (BMI > 25 kg/m$^2$), including approximately 600 million with obesity. This means that in 2014 thirteen (13) % of the global population aged 18 years or older, including 11% of men and 15% of women, were obese, and 39% (38% of men and 40% women) were overweight. This problem is increasingly more common also among children [2].

An analysis prepared by the Organisation for Economic Co-operation and Development (OECD) revealed that in 2010 more than half of all adult citizens of the European Union (52%) were overweight. The prevalence of overweight and obesity exceeded 50% in 18 of the 27 member states of the European Union. Data collected by the OECD also demonstrate significant differences between Member States in the prevalence of obesity — from approximately 8% in Romania and Switzerland to 25% in Hungary and the UK. The average incidence of obesity in the 27 EU member states in 2010 was 17%. The collected data also indicate a more than twofold increase in the prevalence of obesity in selected countries over the last 20 years [12].

According to the results of National Health and Nutrition Examination Survey (NHANES) cross-sectional study, conducted in the years 2011–2012, in the USA obesity was diagnosed in about 35% adults and 17% children between 2 and 19 years of age. In the adult population the highest incidence of obesity was found in the age group 40–59 years (39.5% vs. 30.3% for the age group 20–39 years and 35.4% for the age group ≥ 60 years). Analysis of the data from years 2003–2004 and 2011–2012 demonstrated the greatest increase of obesity rate (percentage of obese people

in the studied population) for the group of women aged > 60 years (31.5% in the years 2003–2004 vs. 38% in the years 2011–2012). No significant differences were found for obesity rates in children (17.1% in the years 2003–2004 vs. 16.9% in the years 2011–2012). Analysis performed in age subgroups revealed a significant decrease of the percentage of obese children in the age group from 2 to 5 years (14% in the years 200–2004 vs. 8% in the years 2011–2012) [13]. The prevalence of obesity in the Polish population was analysed, among others, in the national population-based studies, NATPOL PLUS and WOBASZ. The percentages of people with overweight and obesity presented in the NATPOL PLUS study for 2002 were 29% and 19% for women and 39% and 19% for men, respectively, which gives the combined percentage of people with a BMI > 25 kg/m$^2$ of 52.7% [14, 15]. In the WOBASZ study, presenting data from the years 2003–2005, overweight and obesity were present in 27.9% and 20.2% of women and 40.4% and 20.6% of men, respectively, which gives the percentages of individuals with a BMI > 25 kg/m$^2$ equal to 50.3% for women, and 61.6% for men [14, 15]. The most recent, cross-sectional epidemiological study NATPOL 2011, which was an extension of the NATPOL PLUS study, showed that in 2011, the problem of obesity affected as many as approximately 25% of men in Poland, which means an increase by 5% over the last 10 years [16, 17].

Also, epidemiological analyses carried out by the Central Statistical Office of Poland (CSO) for the years 2004 and 2009 demonstrated a continuous increase in the average body weight of Poles [18, 19]. According to the CSO, in 2009, 15.2% of women and 16.6% of men were obese, and 29.4% of women and 44.8% of men were overweight, giving a total of approximately 53% of Poland's adult population with excessive body weight [19]. The results of CSO research have also shown an increase in the percentage of obese and overweight people relative to figures of 1996 by 19 per cent points among women and by 32 per cent points in men [20]. In a report published by the CSO, "Health and health care in 2011", it was estimated that approximately 54% of adult Poles (64% of men and 46% of women) had excessive body weight [21].

Data collected by the OECD indicate that the epidemic of obesity shows no signs of stopping; however, its increase seems to be slower than in the previous 5 years [22]. Over the period of the last 10 years the percentages of people with overweight and obesity in the populations have stabilised in Italy, England, the United States, and only slightly increased in Canada, Korea and Spain. The country with the largest increase in severity of obesity is France, where the proportion of obese people reached a value higher than predicted over 10 years. However, it should be emphasised that, despite the almost doubling of obesity rates in France, the percentage is still lower than in the United Kingdom, which is among the countries with the highest percentage of people with a BMI > 25 kg/m$^2$ [22].

While so far obesity has been considered the problem of rich countries with a high degree of urbanisation, today we can see that it is also a growing problem in countries with medium and low national income (according to the World Bank classification) [2]. One example here is Mexico, where, according to the OECD data, the prevalence of overweight in the general population increased from 62.1% to 69.9% and obesity from 23.7% to 30.4% in the period 2000–2006 [10].

Correlation analyses between the occurrence rates of overweight and obesity and socioeconomic factors suggest a higher incidence of obesity in groups with lower economic status. This trend is particularly evident in the case of women [23, 24]. There was also a correlation between the level of education and obesity — the lowest percentages of obese people were in the group of the best educated [25]. A systematic literature review conducted by Dinsa et al., analysing the relationship between socioeconomic status and obesity in low-income countries proved that in these countries, obesity is more common in the population of better educated people and those with higher incomes. For middle-income countries, this relationship is not equally evident [23, 26].

On the basis of the presented data it is clear that obesity, which is an increasingly common health disorder, becomes a significant problem from the public health point of view. Forecasts regarding the prevalence of overweight and obesity assume that, at the current growth rate, its prevalence in the world will rise to 2.16 billion people for overweight and 1.12 billion people for obesity in 2030, corresponding jointly to 58% of the world's adult population [27]. In view of the above, we should expect an equivalent increase in the incidence of the most serious health consequences of obesity, including type 2 diabetes and selected cancers.

## Obesity and type 2 diabetes

For many years, studies have shown that increased prevalence of overweight and obesity in the world is accompanied by increased prevalence of metabolic syndrome and type 2 diabetes mellitus (T2DM) [8]. The latter (T2DM) is a chronic disease that is considered to be highly correlated with excess body weight. It also represents the second-to-obesity disease of civilisation, which is a growing epidemiological and social, as well as economic problem in recent decades. Similar

to obesity, the reasons for the increasing proportion of patients with diabetes are believed to be related to lifestyle changes, including urbanisation, change in eating habits and reduced physical activity, as well as ageing of the population [28].

In countries with a high income type 2 diabetes represents between 85% to 95% of all diabetes cases [29, 30], and over the last few years many reports have been prepared and published on the epidemiology of diabetes, as well as forecasts of its expected prevalence in the future. Currently, the most recent estimates of the incidence, prevalence and projected morbidity of diabetes in the world were published by the International Diabetes Federation (IDF) in the sixth edition of the Diabetes Atlas [30].

The data available to the IDF indicate that in 2014 diabetes affected 387 million people, or 8.3% of the world's population (type 1 and 2 combined), and by 2035 this figure will increase to 592 million [30]. In 2014, diabetes was the cause of 4.9 million deaths worldwide [30]. According to IDF, in 1980 the number of patients with diabetes globally was 153 million, which means an increase of 234 million cases over 34 years [31]. More than half of the adult population diagnosed with diabetes are individuals between 40 and 59 years of age, 80% of them living in countries with low and middle income. The forecasts assume that by 2035, 86% of people in this age group will live in countries with low and middle income [30].

In Europe, in 2014 diabetes was diagnosed in 52 million people aged 20 to 79 years, representing 7.9% of the adult population. The number of people with undiagnosed diabetes in Europe in 2014 was 17.2 million, giving a total diabetic population of 69.2 million. In 2035, the projected prevalence of diabetes in Europe is 68.9 million, which means a 22% increase as compared with the figure of 2013 for this region [30].

Similar estimates for Poland indicate that in 2014 diabetes was diagnosed in approximately 2.05 million people. It is estimated that undiagnosed diabetes was present in this period in approximately 0.70 million of Poles, giving a total diabetic population of 2.75 million [30]. It is worth emphasising that, according to the IDF, Poland is among 10 countries with the highest percentage of people with impaired glucose tolerance (4th place, 16.5%), and according to forecasts, in 2035 Poland will reach the top of the ranking in terms of this parameter (19.3%) [30]. According to the database records of the National Health Fund, in Poland in 2013 there were 2,312,919 patients registered, who utilized diabetes-related medical services or purchased anti-diabetic medications and/or test strips, while in 2014 this number was 2,431,611 patients.

The forecasts regarding prevalence of diabetes among US residents indicate that, assuming low increase in incidence and high mortality associated with diabetes, in 2050 diabetes (diagnosed or undiagnosed) will affect 21% of the adult US population [32]. Assuming no change in the incidence rate for diabetes, its prevalence in the adult population of the United States can reach as much as 33% [32].

United Kingdom is a country with one of the highest percentages of obese people in the world [12]. The performed analyses indicate an alarmingly high prevalence of both obesity and type 2 diabetes in the populations of England, Scotland, Wales and Northern Ireland [33, 34]. In 2013, in England, people with obesity or overweight accounted for 62% of the adult population, whereas 6% of the adult population were diagnosed with diabetes. Given the high percentage of undiagnosed diabetes, it should be assumed that approximately 7.4% of the adult population in England has diabetes [33, 34]. The National Diabetes Audit also indicated that in the years 2009–2010, approximately 90% of English people aged 16–54 diagnosed with type 2 diabetes were obese or overweight, and 12.4% of obese English population above 18 years of age were diagnosed with diabetes. This gives a 5-fold higher incidence of type 2 diabetes in obese people than in those with normal body weight (the prevalence of diabetes in adults with normal body weight was estimated at 2.4%) [33–35].

The causal link between excess body weight and type 2 diabetes mellitus has been confirmed in many studies. The analyses performed focused not only on the relationship between the presence of overweight and obesity and the risk of type 2 diabetes, but also the risk of type 2 diabetes depending on the time of occurrence of excess body weight, the degree of overweight and obesity, and their duration.

In 1990, the Nurses' Health Study analysed the risk of type 2 diabetes in women depending on BMI, over the years 1976 to 1984. The results suggest that even with BMI between 23 and 23,9 kg/m$^2$ the risk of developing type 2 diabetes is 3.6 times higher compared to BMI < 22 kg/m$^2$. This risk increases with increasing BMI values. The results obtained in the cohort of women have been confirmed over a longer observation period (years 1976–1990) [36, 37]. The study by Vinciguerra et al. 2013 demonstrated that grade II obesity (BMI > 40 kg/m$^2$) was associated with a higher risk of developing diabetes than grade I obesity (BMI 30–39.9 kg/m$^2$) [38]. Another study, which examined the relationship between body weight measured with BMI and the risk of developing type 2 diabetes, was that by Chan et al., 1994. The results of a 5-year

follow-up in a group of 51,529 healthy men showed a strong correlation between excess body weight and type 2 diabetes — the risk increased with increasing BMI values, and the relationship was statistically significant for each of the BMI categories > 24 kg/m$^2$. In men with BMI > 35 kg/m$^2$, compared to men with BMI < 23 kg/m$^2$, with adjustment for such confounding factors as age, smoking and family history, the relative risk (RR) for developing type 2 diabetes was RR = 42.1 (95% CI: 22.0; 80.6). This study indicated that also BMI at the age of 21 years, total weight gain after the age of 21 years and abdominal obesity measured by the waist to hip ratio (WHR) coefficient are independent risk factors for developing type 2 diabetes [39].

A meta-analysis of the results of 15 cohort studies showed a stronger relationship between type 2 diabetes and early weight gain than between type 2 diabetes and late weight gain, although the difference between groups was not statistically significant. The early weight gain was defined as occurring in relation to body weight in the age of 18–24 years, whereas late weight gain was defined as the gain relative to baseline body weight measured at the age of 25 years or later. All studies included in the analyses indicated a statistically significant association between excess body weight and the development of diabetes. The relative risk for developing diabetes in case of early incremental weight gain by 5 kg m$^{-2}$ in the early adulthood was RR = 3.07 (95% CI: 2.49; 3.97; p < 0.0001), and for late weight gain it was RR = 2.12 (95% CI: 1.74; 2.58; p < 0.0001) [40].

Of importance from the public health point of view is also the question of factors resulting from abnormal body weight, which increase the risk of developing type 2 diabetes in obese people. It was found that these risk factors include the location of body fat and the duration of disease.

In terms of fat distribution, there are two types of obesity — central obesity and peripheral obesity. Research suggests that, in addition to BMI, waist circumference is also an indicator showing correlation between excess body weight and type 2 diabetes [41]. According to reports, waist circumference in excess of 102 cm for men and 88 cm for women is strongly correlated with the risk of medical complications such as type 2 diabetes, cardiovascular complications and arterial hypertension [42].

While the relationship between excess body weight and the risk of type 2 diabetes has been widely recognised and confirmed, results of the studies examining the correlation between the duration of obesity and type 2 diabetes are not fully consistent. Most reports, however, indicate that such a relationship does exist [43–45]. A cohort study conducted on a population of 1,256 people to verify the above relationship with a follow-up of 48 years demonstrated a relationship between the duration of obesity and the risk of diabetes. The hazard ratio (HR), unadjusted for confounders, for developing diabetes in men is HR = 1.13 (95% CI: 1.09; 1.17) and in women HR = 1.12 (95% CI: 1.08; 1.16) for additional 2 years of obesity. Adjustment for confounding factors does not introduce significant changes in the obtained results [46].

While analysing the risk of type 2 diabetes in people with BMI > 25 kg/m$^2$, we should also have in mind that not all obese people have the other elements of metabolic syndrome. According to literature, approximately 30% of obese people do not present these other features, and they are referred to as "metabolically healthy" [47, 48]. A meta-analysis comparing the risk of type 2 diabetes in "metabolically healthy" obese patients and "metabolically healthy" persons with normal body weight showed a 4-fold higher risk of type 2 diabetes in the obese group (RR = 4.03; 95% CI: 2.66; 6.09). Similarly, in a group of obese patients with comorbid additional factors of metabolic syndrome, compared to those of normal body weight, the relative risk of type 2 diabetes was RR = 8.93 (95% CI: 6.86; 11.62) [49].

Obesity is also an important factor increasing the overall risk of death and death from any cause, as well as death from coexisting type 2 diabetes. Available scientific reports indicate the significant role of obesity in increasing the risk of death due to type 2 diabetes relative to a normal body weight (HR = 0.79; 95% CI: 0.77; 0.82 in the group with BMI = 15–25 kg/m$^2$ vs. HR = 1.29; 95% CI: 1.27; 1.32 in the group with BMI > 25 kg/m$^2$) [50].

## Obesity and cancer

While type 2 diabetes is a very well documented health consequence of abnormal body weight, the relationship between obesity and carcinogenesis became the subject of epidemiological studies only in the late twentieth century. As significant interest in these issues has emerged over the recent years, there has been an increasing amount of scientific evidence for a link between obesity and the risk of certain malignancies and death due to cancer [11, 51]. This interest is further exacerbated by the increasing rate of the epidemic incidence of both obesity and cancer.

Initial reports analysing the relationship between abnormal body weight and risk of cancer were published already in the 70s of the twentieth century. The study by Lew et al., conducted on a population of 750,000 adults in the years 1959 to 1972, suggested

a relationship between overweight and obesity and increased risk of death from cancer [52].

In 2001, the International Agency for Research on Cancer (IARC) announced that excessive body weight is associated with an increased risk of developing several types of cancer. This report indicated that obesity may be associated with 11% of cases of colon cancers, 9% of breast cancers in postmenopausal women, 39% of endometrial cancers, 25% of renal cancers, and 37% of cases of oesophageal adenocarcinoma [53]. This was the first official statement emphasising the role of excess body weight as a modifiable risk factor associated with the development of cancer. It started the era of research on the mechanisms of carcinogenesis in the context of the pathophysiology of obesity. In 2007, in its publication "Food, Nutrition, Physical Activity and the Prevention of Cancer" based on a literature review, the World Cancer Research Fund indicated a relationship between high BMI values and the risk of cancer of the oesophagus, pancreas, colon, breast cancer in postmenopausal women, cancer of the endometrium, kidney and the likely relationship with the risk of cancer of the gallbladder. An inverse relationship was then described between BMI and the risk of breast cancer in premenopausal women, and lung cancer (higher BMI value seems to be a protective factor) [54].

The results of one of the largest population-based studies, whose main objective was to analyse the causal relationship between obesity and the risk of development of cancer, was published in 2003. It was then demonstrated that obesity with a BMI of > 40 kg/m$^2$ in a period of 25 years is associated with a relative risk of death of 1.52 (95% CI: 1.13; 2.05) in men and 1.62 (95% CI: 1.40; 1.87) in women [55]. This study also highlighted the link between obesity and the risk of other neoplasms than those indicated by the IARC — pancreatic cancer, liver cancer, non-Hodgkin lymphoma and leukaemia. Compared to women with BMI values of < 25 kg/m$^2$, women with overweight or obesity had a risk of developing cancer higher by 8% (for BMI = 25–29.9 kg/m$^2$), by 18% (for BMI = 30––34,9 kg/m$^2$), by 32% (for BMI = 35–39.9 kg/m$^2$) and by 62% (for BMI > 40 kg/m$^2$). For men, only BMI values of > 30 kg/m$^2$ were correlated with a higher risk of developing cancer; the respective percentages were: 9% for BMI = 30–34.9 kg/m$^2$, 20% for BMI = 35––39.9 kg/m$^2$, and 52% for BMI > 40 kg/m$^2$ [55].

The relationship between obesity and deaths from selected types of cancer was confirmed later by an analysis carried out on the basis of published studies on the populations of Europe and North America. This analysis included 900,000 adults. The results confirmed that for both sexes the risk of death is lowest in the groups, in which BMI values corresponded to normal body weight (22.5–25 kg/m$^2$). It was also proved that any increase in BMI by 5 kg/m$^2$ was accompanied by a 5% increase in the risk of death from cancer, and a 30% increase in risk of death from any cause [50].

In 2008, Renehan et al. conducted a systematic literature review to analyse the relationship between obesity and the risk of malignancy. The results of the review showed that in men an increase in BMI by 5 kg/m$^2$ was strongly correlated with increased risk of developing adenocarcinoma of the oesophagus (RR = 1.52, $p < 0.0001$), thyroid (RR = 1.33; $p = 0.02$), large intestine (RR = 1.24; $p < 0.0001$) and kidney (RR = 1.24; $p < 0.0001$). In women, there was a strong correlation between BMI increase by 5 kg/m$^2$ and increased risk of endometrial cancer (RR = 1.59, $p \leq 0.0001$), gallbladder cancer (RR = 1.59, $p = 0.04$), oesophageal adenocarcinoma (RR = 1.51; $p < 0.0001$) and kidney cancer (RR = 1.34; $p < 0.0001$). There was poor correlation (RR < 1.20) between increased BMI and the risk of rectal cancer and malignant melanoma in men, and postmenopausal breast cancer, pancreatic, thyroid and colon cancer in women, and leukaemia, non-Hodgkin lymphoma and multiple myeloma in both sexes [51].

One of the well documented relationships is the effect of obesity on the risk of developing colon cancer. This relationship has been the subject of numerous cohort studies [56–58]. It has been observed that it is stronger for men than for women. Due to the high variability of the effect magnitude reported in the studies, this relationship was also analysed in the context of systematic reviews and metaanalyses, aimed to provide information on the cumulative amount of risk. A systematic review by Ma et al. Performed in 2013 [59] included the results of 41 prospective cohort studies that investigated the relationship to BMI, and 13 studies in which the evaluated parameter was waist circumference. Excessive values of both BMI and waist circumference, which is the indicator of abdominal obesity, were correlated with a higher risk of developing colorectal cancer compared to the population with normal values of these parameters. The relative risk of developing colorectal cancer for obesity relative to a normal body weight, measured with BMI parameter, was RR = 1.33 (95% CI: 1.25; 1.42). For the calculations using waist circumference, this relative risk was RR = 1.45 (95% CI: 1.33; 1.60). Stratification by cancer site demonstrated the effect of obesity regardless of tumour location, for both colon cancer and rectal cancer [59]. In the case of stratification by sex, there was a higher risk of cancer in both groups, both in case of calculations performed using waist circumference and BMI, although the risk was higher in men (RR = 1.47,

95% CI: 1.36; 1.58 for men vs. RR = 1.15 (95% CI: 1.08; 1.23 for women) [59]. Similar results were obtained in the review by Ning et al., which also included the results of retrospective studies. The review also demonstrated that each increase in BMI by 5 kg/m$^2$ was associated with an increase in the risk of developing cancer by 18% [60].

A systematic review with metaanalysis of the results, which sought to examine whether obese people are screened more often for colorectal cancer compared to those of normal weight (BMI: 18.5–24.9 kg/m$^2$), showed no such relationship. Moreover, in the population of white obese women, the frequency of screening was lower than in the population of white women of normal body weight (OR = 0.87, 95% CI: 0.82; 0.93 for grade I obesity, BMI: 30–34.9 kg/m$^2$, OR = 0.80, 95% CI: 0.65; 0.99 for grade II obesity, BMI: 35–39.9 kg/m$^2$, OR = 0.73, 95% CI: 0.58; 0.94 for grade III obesity, BMI > 40 kg/m$^2$). In the population of white men, similar results were obtained only for grade II obesity [61].

The researchers are also interested in breast cancer due to its very high incidence and the fact that it is the main cause of cancer death in women. Weight gain is considered to be associated with the risk of breast cancer; however, studies have shown a higher incidence of proliferative lesions in overweight postmenopausal women. A metaanalysis of prospective studies showed that postmenopausal women with a BMI of 25, 30 and 35 kg/m$^2$ have a relative risk of breast cancer of RR = 1.02 (95% CI: 0.98; 1.06), RR = 1.12 (95% CI: 1.01; 1.24), and RR = 1.26 (95% CI: 1.07; 1.50), respectively, compared with women of normal body weight [62]. There is, however, no similar relationship for premenopausal women. Moreover, the published results of studies even suggest a protective effect of obesity in these women in the context of the risk of developing breast cancer [63]. The results of metaanalyses also indicate a worse prognosis in obese patients with breast cancer relative to breast cancer patients with normal body weight [64]. Higher BMI values in this population are associated with lower overall survival and survival due to breast cancer. The relative risk of death from any cause is RR = 1.41 (95% CI: 1.29; 1.53) for obese people, RR = 1.07 (95% CI: 1.02; 1.12) for overweight people, and RR = 1.10 (95% CI: 0.92; 1.31) for underweight people compared to people of normal body weight. The relative risk of death from breast cancer in obese premenopausal women is RR=1.75 (95% CI: 1.26; 2.41), and for postmenopausal women RR = 1.34 (95% CI: 1.18; 1.53) compared to people of normal body weight [64].

Also the risk of the fourth most common cancer in women, i.e. endometrial cancer, appears to be correlated with obesity. Epidemiological studies indicate different magnitudes of relationships between BMI values and the risk of endometrial cancer. However, the available quantitative analyses suggest a clear link between BMI and the relative risk of developing this cancer — RR = 1.62, (95% CI: 1.39;1.89) for BMI > 25 kg/m$^2$ and RR = 2.54 (95% CI: 2.11; 3.06) for obesity, and RR = 1.32 (95% CI: 1.16; 1.50) for overweight [65].

For renal cancer, obesity is also considered a risk factor increasing the probability of developing the disease. Metaanalyses showed a significant association between obesity and kidney cancer. Based on the available reports, Bergström et al. estimated the overall risk of renal cancer in obese people at RR = 1.07 (95% CI: 1.05; 1.09) per BMI increase of 1 unit (corresponding to body weight gain of 3 kg for a person with a constant height) [66]. Epidemiological studies also point to the greater strength of this relationship for women than for men. A metaanalysis of cohort studies demonstrated that, compared with normal body weight, in overweight people the relative risk of developing kidney cancer was RR = 1.28 (95% CI: 1.24; 1.33), and for obese people this risk was RR = 1.77 (95% CI: 1.68; 1.87). The authors of the metaanalysis emphasise that, in accordance with the performed quantitative and qualitative analysis of the results of epidemiological studies, the increased risk seems to apply equally to both women and men [67].

The investigators also point out the important role of reduction of body weight in the prevention of cancer [68]. In 2012 Birks et al. published a systematic review aimed to identify scientific reports on the relationship between body weight loss and the risk of neoplastic changes, as well as the risk of death from cancer. The review included 34 studies. The results suggest a relationship between body weight loss and reduced risk of cancer. The results of 16 out of 34 studies included in this review confirmed this relationship. This correlation was clearly visible only in women and it was present for all types of cancers considered obesity-related (colorectal cancer, breast cancer in postmenopausal women, cancers of the endometrium, kidney, oesophagus and pancreas) [68].

The relationship between abnormal body weight and the risk of developing certain cancers is supported by high-quality scientific evidence. It has been repeatedly confirmed in metaanalyses of the results of available research. Importantly, however, the correlation between obesity and certain malignancies is still not entirely clear, or remains unknown, and thus requires further studies.

## Conclusions

Both obesity and type 2 diabetes mellitus and cancer are among the most common chronic diseases today. The data collected by global organisations for the protection and promotion of health indicate a sharp increase in the incidence of these diseases in the past few decades. This is due, on one hand, to the constantly increasing human life expectancy, and on the other hand, to changes in lifestyle, consisting in decreasing level of physical activity and the consumption of highly processed foods in quantities exceeding the caloric needs of the body.

The epidemiological studies presented above and concerning the prevalence and the relationship between abnormal body weight and type 2 diabetes and cancer often differ in the selection criteria of the study groups, their sizes, age ranges of the included populations, as well as their timeframes. These factors may slightly affect the results of these studies. However, on this basis, it is apparent that there are some tendencies and trends in the occurrence and the mutual relationships between obesity, type 2 diabetes and cancer.

Importantly, the results of epidemiological studies allow concluding that the epidemic of obesity is becoming a major problem not only in developed countries but also in developing countries with low and middle income. They also point to a significant correlation between excess body weight and the risk of type 2 diabetes. This risk appears to be greatest in those with the highest values of BMI and abdominal type of obesity (central obesity).

The significantly higher incidence of certain cancers in patients with abnormal body weight identifies an important modifiable risk factor for carcinogenesis, which is obesity. This is extremely important from the cancer prevention point of view. This relationship further underscores the importance of obesity as a disease of civilisation, which is a major threat to public health, and points to the need for further research focused on identifying pathophysiological links between obesity and cancer, and type 2 diabetes.

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## Statement on conflict of interest

Prof. Med. Waldemar Karnafel, MD, PhD — participates in advisory board of AstraZeneca Pharma Poland as an external expert in the field of diabetes.

Barbara Możejko-Pastewka, MD, PhD — is an employee of AstraZeneca Pharma Poland.

## REFERENCES

1. Swinburn BA, Sacks G, Hall KD et al. The global obesity pandemic: shaped by global drivers and local environments. Lancet 2011; 378: 804–814.
2. WHO Fact Sheet No 311 Obesity and overweight 2015 http://www.who.int/mediacentre/factsheets/fs311/en/
3. Szymocha M, Bryła M, Maniecka-Bryła I. Epidemia otyłości w XXI wieku. Zdr Publ. 2009; 119: 207–212.
4. http://www.worldobesity.org/aboutobesity/world-map-obesity/
5. Global Strategy on Diet, Physical Activity and Health. Geneva: World Health Organization, 2004.
6. Australian Institute of Health and Welfare (AIHW) and National Heart Foundation of Australia. The relationship between overweight, obesity and cardiovascular disease. Cardiovascular Disease Series 2004; No. 23.
7. Rexrode KM, Buring JE, Manson JE. Abdominal and total adiposity and risk of coronary heart disease in men. Int J Obes Relat Metab Disord. 2001; 25: 1047–1056.
8. Field AE, Coakley EH, Must A et al. Impact of overweight on the risk of developing common chronic diseases during a 10-year period. Arch Intern Med 2001; 161: 1581–1586.
9. Wolin KY, Carson K, Colditzac GA. Obesity and Cancer. Oncologist 2010; 15: 556–565.
10. Cecchini M, Sassi F, Lauer JA, Lee YY, Guajardo-Barron V, Chisholm D. Tackling of unhealthy diets, physical inactivity, and obesity: health effects and cost-effectiveness. Lancet 2010; 376: 1775–1784.
11. Bianchini F, Kaaks R, Vainio H. Overweight, obesity, and cancer risk. Lancet Oncol. 2002; 3: 565–574.
12. OECD. Overweight and obesity among adults. Health at a Glance: Europe 2012, OECD Publishing.
13. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of Childhood and Adult Obesity in the United States, 2011-2012. JAMA 2014; 311: 806–814.
14. Podolec P, Karch I, Pająk A et al. Przegląd polskich badań epidemiologicznych w kardiologii. Kardiol Pol 2006; 64: 1031–1037.
15. http://www.pfp.edu.pl/download/Forum8.pdf
16. Zdrojewski T, Rutkowski M, Bandosz P et al. Prevalence and control of cardiovascular risk factors in Poland. Assumptions and objectives of the NATPOL 2011 Survey. Kardiol Pol 2013; 71: 381–392.
17. http://www.termedia.pl/Jaki-jest-stan-zdrowia-Polakow-wedlug-NATPOL-2011-,4624.html
18. Central Statistical Office. Health of the Polish population 2004.
19. Central Statistical Office. Health of the Polish population 2009.
20. Chief Sanitary Inspectorate. The problem of overweight and obesity in the Polish adult population — epidemiological data.
21. Central Statistical Office. Health and health care in 2011.
22. OECD Obesity Update 2014.
23. Monteiro CA, Moura EC, Conde WL, Popkin BM. Socioeconomic status and obesity in adult populations of developing countries: a review. Bull World Health Organ 2004; 82: 940–946.
24. Mendez MA, Monteiro CA, Popkin BM. Overweight exceeds underweight among women in most developing countries. Am J Clin Nutr 2005; 81: 714–721.
25. Devaux M, Sassi F. Social inequalities in obesity and overweight in 11 OECD countries. European Journal of Public Health 2013; 23: 464–469.
26. Dinsa D, Goryakin Y, Fumagalli E, Suhrcke M. Obesity and socioeconomic status in developing countries: a systematic review. Obes Rev 2012; 13: 1067–1079.
27. Kelly T, Yang W, Chen CS, Reynolds K, He J. Global burden of obesity in 2005 and projections to 2030. International Journal of Obesity 2008; 32: 1431–1437.
28. WHO Fact Sheets No 312 Diabetes 2015 http://www.who.int/mediacentre/factsheets/fs312/en/
29. World Health Organization. Prevention of diabetes mellitus. Report of a WHO Study Group. World Health Organization, Geneva 1994; 844.

30. International Diabetes Federation. Diabetes Atlas, 6th edition 2014 Update http://www.idf.org/diabetesatlas
31. Danaei G, Finucane MM, Lu Y et al. Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group (Blood Glucose). National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2·7 million participants. Lancet 2011; 378: 31–40.
32. Boyle JP, Thompson TJ, Gregg EW, Barker LE, Williamson DF. Projection of the year 2050 burden of diabetes in the US adult population: dynamic modeling of incidence, mortality, and prediabetes prevalence. Population Health Metrics 2010; 8: 29.
33. Health Survey for England — 2012, Trend tables [NS] http://www.hscic.gov.uk/catalogue/PUB13219
34. Adult obesity: Public Health England, 2012. http://www.noo.org.uk/NOO_about_obesity/adult_obesity
35. Gatineau M, Hancock C, Holman N et al. Adult obesity and type 2 diabetes. Public Health England 2014.
36. Colditz GA, Willett WC, Stampfer MJ et al. Weight as a risk factor for clinical diabetes in women. Am J Epidemiol 1990; 132: 501–513.
37. Colditz GA, Willett WC, Rotnitzky A, Manson JE. Weight gain as a risk factor for clinical diabetes mellitus in women. Ann Intern Med 1995; 122: 481–486.
38. Vinciguerra F, Baratta R, Farina MG et al. Very severely obese patients have a high prevalence of type 2 diabetes mellitus and cardiovascular disease. Acta Diabetol 2013; 50: 443–449.
39. Chan JM, Rimm EB, Colditz GA, Stampfer MJ, Willett WC. Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men. Diabetes Care 1994; 17: 961–969.
40. Kodama S, Horikawa C, Fujihara K et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev 2014; 15: 202–214.
41. Wang Y, Rimm EB, Stampfer MJ, Willett WC, Hu FB. Comparison of abdominal adiposity andoveral adiposity in prediction risk of type 2 diabetes among men. Am J Clin Nutr 2005; 81: 555–563.
42. National Institute for Health and Care Excellence. PH46. Assessing body mass index and waist circumference thresholds for intervening to prevent ill health and premature death among adults from black, Asian and other minority ethnic groups in the UK, 2013.
43. Pontiroli AE, Galli L. Duration of obesity is a risk factor for non-insulin-dependent diabetes mellitus, not for arterial hypertension or for hyperlipidaemia. Acta Diabetologica 1998; 35: 130–136.
44. Sakurai Y, Teruya K, Shimada N et al. Association between duration of obesity and risk of non-insulin-dependent diabetes mellitus. The Sotetsu Study. Am J Epidemiol 1999; 149: 256–260.
45. Wannamethee SG, Shaper AG. Weight change and duration of overweight and obesity in the incidence of type 2 diabetes. Diabetes Care 1999; 22: 1266–1272.
46. Abdullah A, Stoelwinder J, Shortreed S et al. The duration of obesity and the risk of type 2 diabetes. Public Health Nutr 2010; 14: 119–126.
47. Wildman RP, Muntner P, Reynolds K et al. The Obese Without Cardiometabolic Risk Factor Clustering and the Normal Weight With Cardiometabolic Risk Factor Clustering Prevalence and Correlates of 2 Phenotypes Among the US Population (NHANES 1999-2004). Arch Intern Med 2008; 168: 1617–1624.
48. Iacobellis G, Ribaudo MC, Zappaterreno A, Iannucci CV, Leonetti F. Prevalence of Uncomplicated Obesity in an Italian Obese Population. Obes Res 2005; 13: 1116–1122.
49. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev 2014; 15: 504–515.
50. Prospective Studies Collaboration. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. Lancet 2009; 373: 1083–1096.
51. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 2008; 371: 569–578.
52. Lew EA, Garfinkel L. Variations in mortality by weight among 750,000 men and women. J Chronic Dis 1979; 32: 563–576.
53. Vainio H, Bianchini F. IARC Handbooks of Cancer Prevent–Weight Control and Physical Activity. Lyon, France: IARC Press; 2002.
54. World Cancer Research Fund and American Institute for Cancer Research. food, nutrition, physical activity, and the prevention of cancer: a global perspective, 2007. Washington, DC: American Institute for Cancer Research.
55. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Clark W. Body-Mass Index and Mortality in a Prospective Cohort of U.S. Adults. N Engl J Med 1999; 341: 1097–1105.
56. Keimling M, Renehan AG, Behrens G et al. Comparison of Associations of Body Mass Index, Abdominal Adiposity, and Risk of Colorectal Cancer in a Large Prospective Cohort Study. Cancer Epidemiol Biomarkers Prev 2013; 22: 1383–1394.
57. Renehan AG, Flood A, Adams KF et al. Body Mass Index at Different Adult Ages, Weight Change, and Colorectal Cancer Risk in the National Institutes of Health-AARP Cohort. Am J Epidemiol 2012; 176: 1130–1140.
58. Pischon T, Lahmann PH, Boeing H et al. Body size and risk of colon and rectal cancer in the European Prospective Investigation Into Cancer and Nutrition (EPIC). J Natl Cancer Inst 2006; 98: 920–931.
59. Ma Y, Yang Y, Wang F et al. Obesity and Risk of Colorectal Cancer: A Systematic Review of Prospective Studies. PLoS ONE 2013; 8: e53916.
60. Ning Y, Wang L, Giovannucci EL. A quantitative analysis of body mass index and colorectal cancer: findings from 56 observational studies. Obes Rev 2010; 11: 19–30.
61. Maruthur NM, Bolen S, Gudzune K, Brancati FL, Clark JM. Body Mass Index and Colon Cancer Screening: A Systematic Review and Meta-Analysis. Cancer Epidemiol Biomarkers Prev 2012; 21: 737–746.
62. Xia X, Chen W, Li J et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep 2014; 4: 7480.
63. Ursin G, Longnecker MP, Haile RW, Greenland S. A meta-analysis of body mass index and risk of premenopausal breast cancer. Epidemiology 1995; 6: 137–141.
64. Chan DSM, Vieira AR, Aune D et al. Body mass index and survival in women with breast cancer — systematic literature review and meta-analysis of 82 follow-up studies. Annals of Oncology 2014; 25: 1901–1914.
65. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers 2014; 29: e21–29.
66. Bergström A, Hsieh CC, Lindblad P, Lu CM, Cook NR, Wolk A. Obesity and renal cell cancer — a quantitative review. Br J Cancer 2001; 85: 984–990.
67. Wang F, Xu Y. Body mass index and risk of renal cell cancer: a dose-response meta-analysis of published cohort studies. Int J Cancer 2014; 135: 1673–1686.
68. Birks S, Peeters A, Backholer K, O'Brien P, Brown W. A systematic review of the impact of weight loss on cancer incidence and mortality. Obes Rev 2012; 13: 868–891.