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## The expectancy and quality of life in hypertension

### Długość i jakość życia w nadciśnieniu tętniczym

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#### Conflict of interest

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#### Summary

Hypertension is one of the most common diseases worldwide and still leading risk factor for cardiovascular mortality and disability. In Poland it affects about 32% of adult population, but blood pressure (BP) control is achieved only in every fourth patient. The review focuses on contemporary management of high blood pressure (BP) and underlines benefits of therapy for life expectancy in EU countries and in Poland. On the other hand we discuss the impact of high BP and its treatment on health-related quality of life (HRQoL). Recently performed studies showed a lower HRQoL in patients on antihypertensive treatment both with and without BP control, in comparison with hypertensives who did not receive treatment. Moreover, improvement of the HRQoL in patients with hypertension depends on numerous factors, not only BP control during antihypertensive therapy. Thus, the knowledge of the patient's well-being has considerable practical implications, especially in chronic diseases like arterial hypertension, which are associated with long-term or even lifelong treatment.

#### Streszczenie

Nadciśnienie tętnicze jest jednym z najbardziej rozpowszechnionych schorzeń na świecie, wiodącym czynnikiem ryzyka umieralności z powodów sercowo-naczyniowych oraz powodem niesprawności. W Polsce nadciśnienie dotyczy około 32% dorosłej populacji, a kontrolę ciśnienia tętniczego uzyskuje się tylko u 1/4 leczonych. Prezentowana praca dotyczy nowoczesnego leczenia nadciśnienia tętniczego, podkreślając jego korzystny wpływ na przedłużanie życia chorych w krajach Unii Europejskiej i w Polsce. Dyskutowany jest również wpływ wysokich wartości ciśnienia i farmakoterapii na jakość życia uwarunkowaną stanem zdrowia (HRQoL). Ostatnio prowadzone badania wskazują na niższą jakość życia chorych na nadciśnienie leczonych farmakologicznie, niezależnie od skuteczności leczenia, w porównaniu z chorymi, u których nie wdrożono leczenia. Ponadto wiadomo, że poprawa HRQoL u chorych na nadciśnienie jest uwarunkowana wieloma czynnikami, nie tylko kontrolą ciśnienia. Wiedza na temat samopoczucia pacjenta jest szczególnie istotna w chorobach przewlekłych, takich jak nadciśnienie tętnicze, w których leczenie trwa wiele lat, a często całe życie.

Hypertension is one of the most common diseases and its prevalence in adult population worldwide was 26% in the year 2000 and is estimated to reach 29.2% in the year 2025.

In Poland, according to the NATPOL epidemiological studies it occurs in 32% (35% males and 29% females) of population aged 18-79 years (1).

According to the CSO data (Health Status of the Polish Population in 2004), high blood pressure (BP) is reported by 20.7% men and 25.2% women as the second most common disease/chronic illness reported (CSO 2016).

According to WHO, high blood pressure is the most common risk factor of death in the world (fig. 1).

Currently, as in previous years, cardiovascular diseases, including hypertension and its complications such as stroke and myocardial infarction are the cause of more than 45% of all deaths in Poland (tab. 1).

Cardiovascular deaths in Poland increased steadily through the 1970s and 1980s, but from 1991 to 2005 the death rate decreased (2).

About 54% of the fall of mortality due to coronary heart disease (the most common cause of deaths among the diseases of circulatory system) was attributed to changes in risk factors but not BP (fig. 2). Blood pressure fall in women explaining about 29% of their decrease in mortality, but in men generating a negative influence – 8% increase in mortality (3).



Fig. 1. Mortality risk factor in middle-income countries in 2004 (World Health Statistics 2012, WHO 2012)

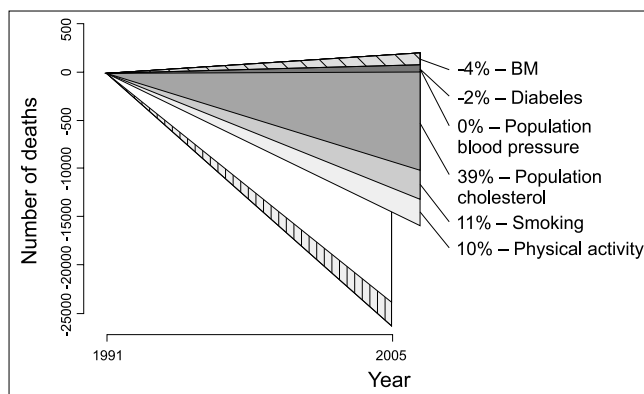


Fig. 2. Explaining the fall in coronary artery disease mortality in Poland between 1991 and 2005 (3)

Tab. 1. Major death causes in Poland

Death causes (over 100 thousand inhabitants)	Year 2014		
	Total	Males	Females
Cardiovascular diseases including: coronary artery disease cerebrovascular disease	441.1	423.2	457.8
Diseases of arteries, arterioles and capillaries, including: atherosclerosis hypertensive disease	98.6	75.4	120.2
Total	978.2	1051.3	909.7

Small Statistical Yearbook of Poland, CSO, 2016 (4)

In recent years, trends in hypertensive disease mortality rates are favorable (tab. 2).

Trends in hypertensive disease mortality rates in Poland in the years 2008-2014 are presented in table 2.

Despite the continuous decrease, in Poland cardiovascular mortality is still higher than in 15 EU countries (fig. 3).

Data from Eurostat covering the period 2005-2014 prove that life expectancy for both men (tab. 3) and women (tab. 4) has increased.

However, similar to the most Central and East European countries, life expectancy at age of 45 years is

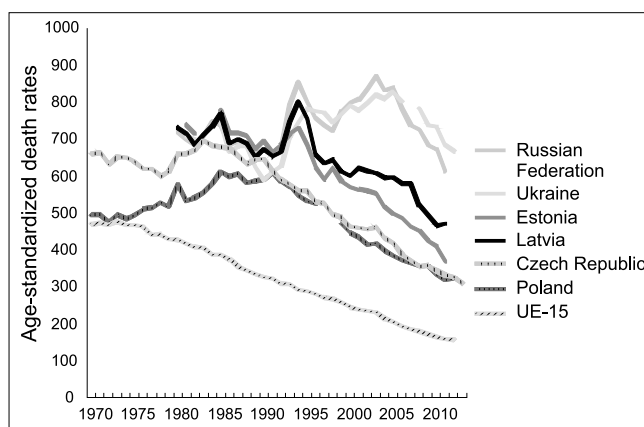


Fig. 3. Age-standardized cardiovascular disease mortality rates in 6 Central & Eastern European Countries and European Union (15 countries before May 2004). Source: Health for All Database, WHO Europe, 2015 (5)

still shorter in Poland in comparison with EU 15 countries from before 2004 (fig. 4).

Complications of hypertension, such as stroke, coronary heart disease, heart and renal failure influence the longevity of life in health.

In the years 2005-2014, the expectancy of life in good health in Poland has reduced (tab. 5).

Hypertension according to the 2012 World Health Statistic for middle-income countries in 2004 was the

Tab. 2. Trends in hypertensive disease mortality rate

Hypertensive disease as death cause (over 100 thousand inhabitants/year)	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Males	12.5	13.8	14.0	13.0	14.2	14.2	12.4	10.7	9.9	9.0
Females	16.6	17.4	17.0	16.4	18.1	18.4	15.9	13.0	12.3	11.4

Based on consecutive editions of the Small Statistical Yearbook of Poland, CSO 2007-2016 (4)

Tab. 3. Life expectancy for men at birth

Area/year	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
EU (28 countries)	75.4	75.8	76.0	76.3	76.6	76.9	77.3	77.4	77.8	78.1
Poland	70.8	70.9	71.0	71.3	71.6	72.2	72.5	72.6	73.0	73.7

Tab. 4. Life expectancy for women at birth

Area/year	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
EU (28 countries)	81.5	82.0	82.2	82.3	82.6	82.8	83.1	83.1	83.3	83.6
Poland	79.3	79.7	79.8	80.0	80.1	80.7	81.1	81.1	81.2	81.7

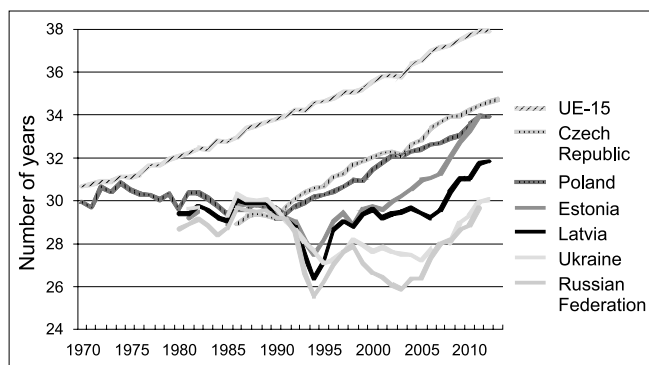


Fig. 4. Life expectancy at age 45 in 6 Central & Eastern European Countries and European Union (15 countries before May 2004) (5)

second risk factor of DALY (disability-adjusted life years) (fig. 5). By contrast, in Poland at that time smoking was the first risk factor. Elevated blood pressure was responsible for 10.4% of all lost life years.



Fig. 5. Risk factors of disability adjusted life-years (DALY) in middle-income countries in 2004 (World Health Statistics 2012, WHO 2012)

According to Rahim et al. (6) elevated BP is the leading risk factor for mortality and morbidity accounting for 7% of global disability adjusted life years and 9.4 million deaths in 2010. Global age-standardised BP has decreased during the past 30 years, however the number of individuals with uncontrolled hypertension increased from 605 to 978 million because of population growth and ageing. As a result, high BP increased from the fourth ranked risk factor for burden of disease in 1990 to the leading risk factor in 2010.

In Poland, the control of blood pressure in the last decade (in the years 2004/2005-2014/2015) has largely improved; from 10 to 23% in men and from 16 to 35.3% in women (unpublished data from WOBASZ I and II studies). Still, compared to the US, Canada and Western European countries, it is lower. Hypertension is in Poland and in the world the major cause of DALY loss.

The benefits of BP lowering treatment for prevention of cardiovascular disease are well established. In late 1960's the Veteran Affairs Cooperative Study based on pharmacological treatment provided the first strong casual evidence the BP lowering reduces the risk of death.

Over the next decades clinical studies on the treatment of hypertension and other cardiovascular risk factors were conducted and target blood pressure values for the population of patients were determined.

Recently several randomised trials compared the effect of a more versus less intensive BP lowering strategy on the risk of major cardiovascular events and death, including the SPRINT Trial initiated by National Health Institutes of USA (7, 8). The results of the meta-analyses published by Xie et al. (9), Ettehad et al. (10), Verdecchia et al. (11) (the latter included the results of SPRINT trial) confirmed the evidence supporting the benefits from more intensive BP lowering strategies.

### HEALTH-RELATED QUALITY OF LIFE

The effectiveness of antihypertensive therapy in daily clinical practice in Poland is not satisfactory. Blood pressure (BP) control is achieved only in every fourth patient, and there is still a discrepancy between a wide selection of modern antihypertensive drugs and a low percentage of patients achieving target BP values. One of the major reasons behind the low effectiveness of antihypertensive therapy is noncompliance with treatment recommendations, which may be associated, among others, with multiple adverse effects of drugs affecting the patient's well-being.

The assessment of so called health-related quality of life (HRQoL) allows patient-oriented monitoring of treatment outcomes, namely, a monitoring that involves the individual experience and expectations of a patient. Modern therapy of chronic diseases focuses on maximizing the efforts to prolong life expectancy, and significant achievements have been observed in this field. However, it is important not only to know whether a drug prolongs the life of patients, but also how it affects their well-being, their ability to perform daily activities and social roles, their satisfaction with their current health status, their physical and mental condition, as well as other areas of life (12). From the patient's perspective, whether and how the patient will comply with treatment recommendations depends on the above aspects of health, which today can be carefully measured (13).

The knowledge of the patient's HRQoL has considerable practical implications, especially in chronic diseases, which are associated with long-term or even lifelong treatment (14). In clinical practice, we often encounter patients who display symptoms of low intensity, or even no symptoms, at early stages of their dis-

Tab. 5. Life expectancy in good health in Poland

Poland/year	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Males	61.2	58.4	57.6	58.6	58.3	58.5	59.1	59.1	59.2	59.8
Females	66.9	62.9	61.5	63.0	62.5	62.3	63.3	62.8	62.7	62.7

eases (e.g., mild or moderate hypertension). In these patients, lifestyle modification is usually recommended at the initial stage, with a number of patients requiring long-term pharmacological treatment. This treatment usually does not bring an immediate, direct effect felt by a patient; nevertheless, it should be instituted and continued to prevent complications that reduce life expectancy (15).

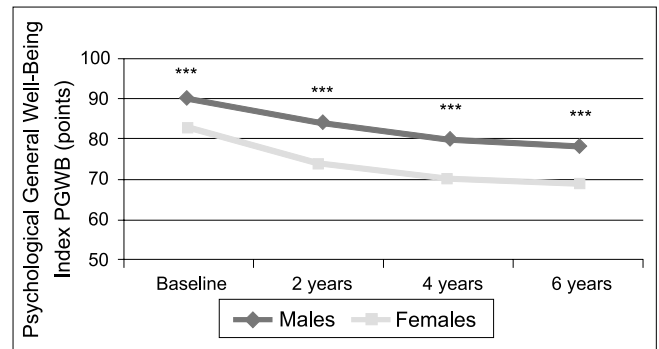
### FACTORS MODIFYING THE QUALITY OF LIFE IN PATIENTS WITH HYPERTENSION

In studies on HRQoL, mild or moderate hypertension is used as a model for all asymptomatic cardiovascular diseases that require chronic treatment. Most patients with hypertension do not experience symptoms, especially at early stages of the disease, and yet, their quality of life (QoL) is lower than that of healthy individuals matched for age. The difference ranges from 5 to 15%, depending on assessment methods and age of study participants (16). Some researchers claim that the lower QoL results from the specific effect of hypertension itself, while others attribute it to the effect of diagnostic labeling (i.e., after diagnosis patients experience anxiety, stress, and symptoms not experienced before). Even lower QoL is observed in hypertensive patients with concomitant coronary artery disease, arrhythmias, and, particularly, with heart failure. The presence of cardiovascular risk factors, such as lipid disorders, obesity, and low physical activity, is also associated with a reduced QoL. The higher the number of risk factors in a patient, the lower his or her HRQoL. It is estimated that the quality-adjusted life expectancy (QALE) in middle-aged and elderly patients with hypertension is approximately 6 years shorter than that in individuals without hypertension, and this is specifically attributed to a reduced QoL (17). The effect of hypertension on the reduction in QALE can be observed already in younger adults. Long-term population-based studies cited earlier showed that QALE is shorter by 2.2 years in 18-year-old patients with hypertension, as compared with age-matched healthy controls. It is also known that in patients older than 50 years of age increased BP values account for 15% of disability measured by disability-adjusted life years (DALYs), and in those older than 70 years of age – for 20%. Of note, the definition of DALY also includes QoL (18). A recent large prospective trial showed that low QoL in normotensive individuals is associated with the development of hypertension, independently of the presence of traditional risk factors, at least in women (19).

It is known that a reduced HRQoL in middle-aged hypertensive patients (by 10 to 20% in comparison with normotensive individuals) is associated with higher mortality from cardiovascular causes, independently of the presence of traditional risk factors. According to population-based studies, HRQoL in hypertensive women is lower than that in age-matched hypertensive men (20). A similar difference in QoL between men and women can be observed in the general population,

and the reasons for this phenomenon are complex. Nevertheless, in hypertensive women, the QoL starts to deteriorate earlier (often already after 35 years of age) and more rapidly than in healthy women. The above factors affecting HRQoL indirectly contribute to a wide prevalence of resistant hypertension by hindering its treatment and worsening prognosis (21).

Apart from sex-related differences, one of the most important factors affecting the QoL is age. Elderly people have a significantly lower HRQoL than young individuals. In our study including 1000 outpatients with hypertension, reduced QoL was observed in a 6-year follow-up in both sexes (fig. 6). At the same time, an improvement in BP control was observed, from 31% of patients at baseline to 51% at 6 years. However, even in patients with good BP control, the QoL at 6 years was reduced. This observation suggests that achieving BP control is not equivalent to improved QoL and that other conditions have to be met for the QoL to improve during treatment.



**Fig. 6.** Changes in the quality of life in men (age,  $46.0 \pm 14.6$  years) and women ( $49.6 \pm 12.4$  years) treated for hypertension on an outpatient basis for 6 years

\*\*\* $p < 0.001$  males vs females

Other factors that lead to a considerably reduced QoL in patients with hypertension include low educational and socio-economic status, disability, social isolation, and low level of social support. These factors directly affect the effectiveness of treatment because such patients are characterized by poor compliance with treatment, lower awareness of the importance of self-care, and, as shown by epidemiological studies, by increased cardiovascular risk. The presence of comorbidities, which are a source of negative physical and emotional symptoms, is another reason for an age-related reduction in QoL.

An important problem associated with pharmacological treatment of hypertension is the presence of adverse effects, which contribute to the low effectiveness of therapy. Some of the symptoms are non-specific (e.g., headache), others are clearly related to a drug class (e.g., cough during treatment with angiotensin-converting enzyme inhibitors), or, for example, bradycardia occurring during treatment with  $\beta$ -adrenolytics. It is commonly believed that antihypertensive drugs produce only few or nonserious adverse effects.

There are several reasons for this. First, in the methodology of clinical trials, it is the researcher and not the patient that assesses so called drug tolerance. Second, the subjective opinion of a patient on the effectiveness of treatment is not treated as valuable information and is usually neglected. Third, researchers focus more on so called hard endpoints (e.g., mortality) rather than on patients themselves and their problems (such as well-being, physical and mental condition, ability to perform social roles). Finally, clinicians lack experience in the measurement and interpretation of data on QoL and self-reported health status.

Studies, including those conducted in Poland, have long shown that only from 20 to 25% of patients on antihypertensive treatment spontaneously report adverse effects to their physicians, while more than 70% of patients actually experience them (22). Trevisol et al. (23) showed a lower QoL in patients on antihypertensive treatment both with and without BP control, in comparison with hypertensive patients who did not receive treatment. The number of drugs used is a clinically useful marker of the QoL. In outpatients with hypertension, an inverse correlation was observed between the number of antihypertensive drugs used and HRQoL.

### IMPROVEMENT OF THE QUALITY OF LIFE IN PATIENTS WITH HYPERTENSION

Improvement of the HRQoL in patients with hypertension depends on numerous factors, one of which is BP. Prospective studies have shown that BP reduction slightly slows down the process of lowering of the QoL, as it exerts a positive effect on cognitive function, well-being, physical condition, and vitality of patients. Studies on the treatment of isolated hypertension in elderly patients have also revealed that antihypertensive therapy may reduce the incidence of dementia. However, it is unknown whether these beneficial effects are permanent, because most data come from studies lasting from 12 weeks to 4 years. In addition, some of the more important studies, especially those in elderly people (Syst-Eur, HYVET), did not show an improvement in QoL during antihypertensive treatment despite improving BP control and prolonging the life of patients (24, 25).

According to numerous studies on large populations, modern antihypertensive drugs, irrespective of a drug class, significantly prolong life expectancy (26).

However, from the perspective of the patient's HRQoL, the choice of a particular treatment is of key importance. Recently, Thomopoulos et al. have reported that in every 1000 patients, a reduction of 33 major cardiovascular events is related to as many as 89 patients discontinuing treatment due to these adverse effects (27).

The analysis of individual drug classes revealed that angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers (sartans), newer  $\beta$ -blockers, and long-acting calcium channel blockers are associated with a minor improvement in the QoL, while centrally acting antihypertensive drugs and direct-acting arteriolar vasodilators have no beneficial effects on HRQoL. In addition, the use of  $\beta$ -blockers, thiazide diuretics, and older centrally acting drugs is associated with a reduction in sexual activity in men. Most studies assessing HRQoL in patients with hypertension concerned monotherapy. Combination therapy, which involves the use of several drugs, is more effective in achieving BP control but is rather associated with a reduction in HRQoL, although to an extent depending on the effect of individual drugs. It has also been shown that there are clear differences between antihypertensive drugs within each particular drug class. Moreover, the duration of drug action has been shown to be important: long-acting drugs are rated higher by patients than drugs with short half-lives. Since the HRQoL of untreated patients with hypertension is lower than that of healthy individuals, once initiating the treatment, it is necessary to consider the choice of a drug that would potentially improve the particular aspects of HRQoL.

### CONCLUSIONS

To summarize, the improvement in HRQoL during antihypertensive treatment may be expected in relatively young patients, with rather short disease duration and higher educational status, as well as who are currently employed and have no comorbidities. In order to obtain improvement, it is necessary to achieve and maintain BP control with at least 1 or 2 long-acting antihypertensive drugs. However, despite a careful drug selection to meet individual patients' needs and address their mental, physical, and social condition, the improvement in the QoL of most hypertensives is still a challenge for physicians.

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