

## PŮVODNÍ PRÁCE

**Depression relapse and antidepressants consumption in the quality of life aspect**KAVALIAUSKIENĖ L.<sup>1</sup>, PEČIŪRA R.<sup>1</sup>, ADOMAITIENĖ V.<sup>2</sup>, MASTEIKOVÁ R.<sup>3</sup><sup>1</sup>Lithuanian University of Health Sciences, Medical Academy, Faculty of Pharmacy, Department of Drug Technology and Social Pharmacy, Kaunas, Lithuania<sup>2</sup>Lithuanian University of Health Sciences, Medical Academy, Department of Psychiatry, Kaunas, Lithuania<sup>3</sup>University of Veterinary and Pharmaceutical Sciences, Faculty of Pharmacy, Department of Pharmaceutics, Brno, Czech Republic

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## SUMMARY

**Depression relapse and antidepressants consumption in the quality of life aspect**

Depression represents one of the most severe health problems. It belongs to the diseases which cause the largest amount of non-fatal disease burden worldwide, and greatly influences the quality of life. The frequency of this disease is connected with the consumption of antidepressants. This study thus aimed to overview the trends of antidepressants consumption in Lithuania, to assess the number of depression cases, when diagnosed for the first time and repeatedly with regard to demographic situation, and to evaluate the impact of this disease on women and the society. All prescribed antidepressants were divided into four groups, according to the ATC classification. Consumption of the preparations from single groups was expressed in defined daily doses (DDD), and utilization was expressed as DDD per 1000 inhabitants per day. The results demonstrate that each year there are more diagnosed cases of depression, which is related mainly with depression relapses. This increase is attended with the growth of antidepressants consumption: from 2004 till 2009 this indicator had increased even by 48%. At the same time, the character of pharmacotherapy has changed – the prescription of tricyclic antidepressants was markedly decreased, and the prescription of bicyclic derivatives (selective serotonin reuptake inhibitors – SSRI) and other more recent preparations increased. The demographic data show that women suffer from depression significantly more – in Lithuania this disease was diagnosed in women four times more than in men, the incidence of depression relapse was often more frequent.

**Key words:** depression – relapse – consumption of antidepressants – quality of life

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## SOUHRN

**Recidivující deprese a spotřeba antidepresiv s dopadem na kvalitu života**

Deprese představuje jeden z nejzávažnějších zdravotnických problémů. Patří mezi onemocnění, které je nejčastějším důvodem invalidity po celém světě, a značně ovlivňuje kvalitu života. Na výskyt tohoto onemocnění navazuje spotřeba antidepresiv. Proto cílem práce byl přehled spotřeby těchto přípravků v Litvě, sledování výskytu deprese diagnostikovaných poprvé a opakovaně s ohledem na demografickou situaci, a následně hodnocení dopadu onemocnění na ženu a společnost. Všechna předepisovaná antidepresiva byla rozdělena do čtyř skupin v souladu s ATC systémem. Spotřeby přípravků v jednotlivých skupinách byly stanoveny v definovaných denních dávkách (DDD) a údaje

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o spotřebách jsou uvedeny v počtu DDD na 1000 obyvatel a den. Výsledky ukazují, že počet diagnostikovaných depresivních onemocnění s každým rokem roste, za což odpovídá hlavně častější výskyt recidiv. Tento nárůst je doprovázen odpovídajícím zvýšením spotřeby antidepresiv – ta byla v roce 2009 při srovnání s rokem 2004 až o 48 % větší. Současně se za stejné období změnil charakter farmakoterapie – výrazně se snížila četnost předepisování tricyklických antidepresiv a zvýšilo se předepisování bicyklických derivátů a dalších novějších přípravků. Z pohledu demografického vyplývá, že depresi častěji trpí ženy – v Litvě toto onemocnění bylo diagnostikováno ženám přibližně 4× častěji než mužům, výskyt recidiv byl rovněž větší.

**Klíčová slova:** deprese – recidivy – spotřeba antidepresiv – kvalita života

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## Introduction

Depression is a mood disorder with a significant impact on human life. It is noticed by specialists and society not only as a disease, which may be treated, but also as a serious condition of the person, depending on various psychological and social elements, and having an impact on the whole society <sup>1, 2</sup>. Depressive disorders were estimated to be the fourth leading cause of disease burden, accounting for 4.4% of total disability-adjusted life-years in the year 2000, and it causes the largest amount of non fatal burden, accounting for almost 12% of all total years lived with disability worldwide <sup>3</sup>. Depression was also associated with an increased

magazine “International Living” published a list of 194 countries, where they are listed according to the quality of-life index in January 2010. Lithuania was in relatively high, i.e., 22<sup>nd</sup>, position <sup>6</sup>.

Mental health is a key aspect of well-being and quality of life. Marked differences are found between countries when overall mental health is considered <sup>7</sup>. The highest scores for good mental health are seen in Norway, the Netherlands, Ireland, Germany, Denmark, and Sweden. Turkey comes at the bottom, at 47, followed by Malta, Romania, FYR Macedonia, and Latvia (all between 53 and 55). Lithuania got 58% of the mean mental health index and is not far from the lowest level countries (Fig. 1).

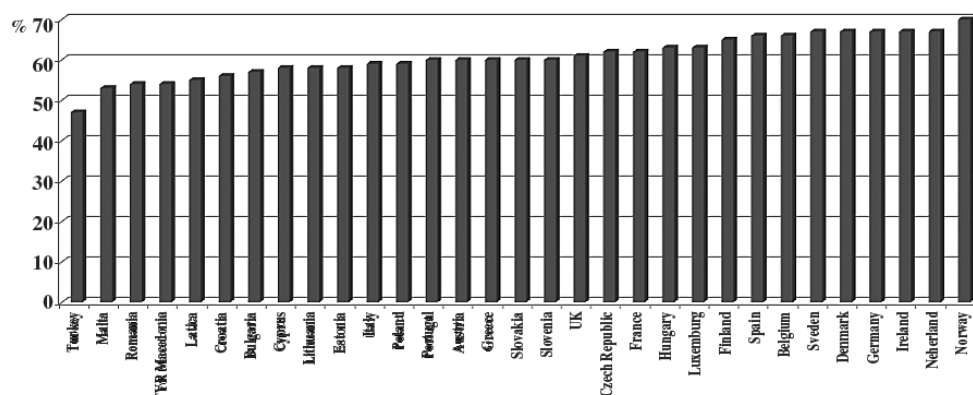


Fig. 1. Mean mental health index in some countries (from ref. 7)

mortality risk of 1.81 (1.58–2.07) in a meta-analysis of 25 community surveys involving more than 100,000 subjects <sup>4</sup>.

In recent years an increasing number of cases of recurrent depression is recorded, which greatly increases the overall number of patients with this disease. The number of suicides also increases together with the spreading depression, e.g. 59 thousand people killed themselves because of the impact of depression in 2006 in the whole Europe <sup>5</sup>.

When the study began to consider depression more broadly and looked for its other causes, the quality-of-life index began to be employed as well, in the formation of which the cost of living, culture and relaxation, economics, environment, level of freedom, health protection, safety and risk, climate are assessed. The

Use of antidepressants has increased in all Western countries during the past 15-20 years. In Finland, the increase between 1990 and 2006 was nearly 8-fold <sup>8</sup>, from 7.09 defined daily doses (DDD) expressed for 1000 inhabitants a day in 1990 to 55.47 DDDs in 2006. Similar trends have been reported elsewhere <sup>9</sup>. Although the consumption of antidepressant at the population level has increased notably, population-based studies with all psychotropics and antidepressants in particular suggest that increased prescribing may not have markedly improved the mental health of the population. In Scotland, for example, national development targets have already been made for reducing the increase in antidepressant use. On the other hand, underutilization of antidepressants among the depressed remains a constant concern since epidemiological evidence shows that

depressive individuals do not receive the care they need. Further, the impact of antidepressant utilization rates on suicides is discussed <sup>10)</sup>. Person-level and epidemiological data from Finland suggest that use of antidepressants decreases suicide rates; however, this association has not been found in all countries <sup>8)</sup>.

The purpose of this article is to overview the trends of antidepressant drugs' consumption in Lithuania, to assess the number of depression cases, when diagnosed for the first time and repeatedly, demographically, evaluating the impact of this disease on women and the society as a whole, and linking with the quality of life.

## MATERIAL AND METHODS

Data of general sales of antidepressant drugs in Lithuania during 2004-2009 were obtained from IMS (Intercontinental Marketing Service) Health Incorporated. Data were selected as units and price of drugs. The consumption of drugs was measured as

3. Other (more recent) antidepressants: mirtazapine, bupropion, tianeptine, venlafaxine, trazodone, agomelatine, mianserin, reboxetine, duloxetine (ATC N06AX11, N06AX12, N06AX14, N06AX16)

4. Lithium (ATC N05AN01).

## RESULTS AND DISCUSSION

Each year there are more cases of depression diagnosed in Lithuania (Fig. 2). Moreover, depression prevalence each year is continuously growing up – during the last six years the increase was from 0.59% in 2004 to 0.69% in 2009. The statistics of diseases demonstrate a continuously increasing number of recurrent depression diagnoses (relapsed depression prevalence grew up from 0.24% to 0.32%), while the number of first time depressions rose minimally (prevalence grew up from 0.35% to 0.37%). Thus depression diagnosis numbers increase mainly because of depression relapse rates. According to the

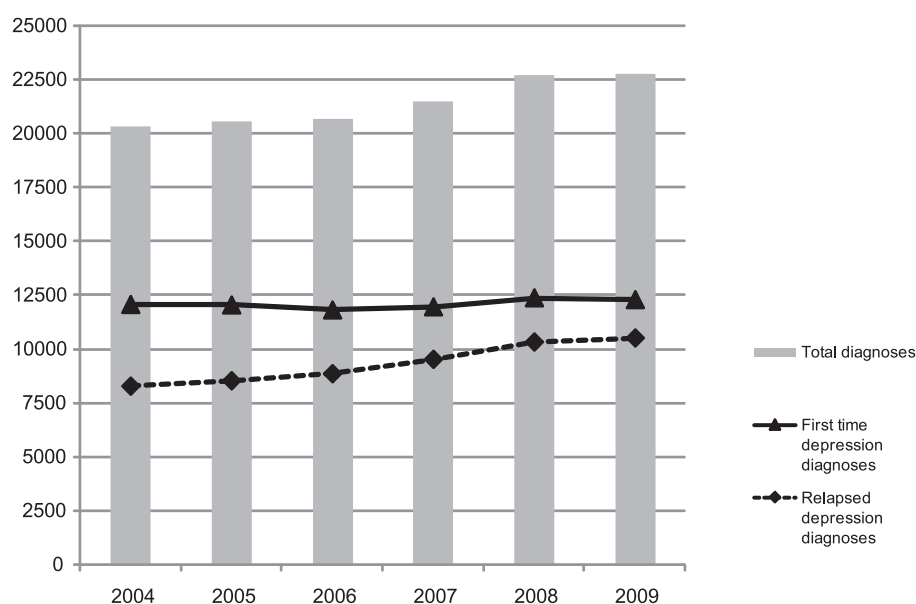


Fig. 2. Number of depression diagnoses in Lithuania in 2004–2009

defined daily doses (DDD). Data were calculated according to DDD methodology and expressed for 1000 inhabitants a day <sup>11)</sup>. Data of depression diagnoses were obtained from the State Mental Health Centre and expressed as the total number of diagnoses, and according to the type of depression and gender of the patients.

All prescribed antidepressants in this study were grouped into four groups, according to the ATC classification, while defining DDD values:

1. Tricyclic antidepressants (TCAs): amitriptyline, clomipramine, doxepin, nortriptyline, imipramine, dosulepin (ATC N06AA);

2. Selective serotonin reuptake inhibitors (SSRI): sertraline, fluoxetine, paroxetine, citalopram, escitalopram, fluvoxamine (ATC N06AB);

data of researchers of the University of Virginia, USA, this disorder is recurring even for 50 percent of those with depression and those who have been treated. Other figures are more daunting – after repetitive treatment of depression, about 70 percent of patients fall into depression for the third time, and after three treatments – even 90 percent. Each recurring disease means that a previous treatment was unsuccessful <sup>12)</sup>.

The growth of patients with depression was followed by a corresponding increase in antidepressants use: over the years 2004–2009 the total consumption of these preparations in Lithuania was increased even by 48 percent (Fig. 3). However, the frequency of prescription of single preparations and

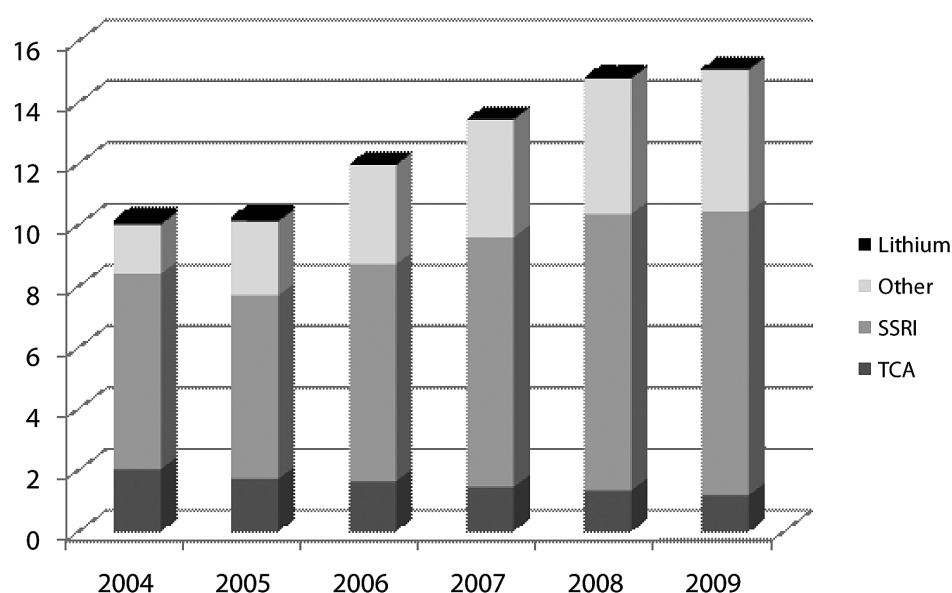


Fig. 3. The consumption of antidepressants in DDD/1000 inhabitants/day in 2004–2009

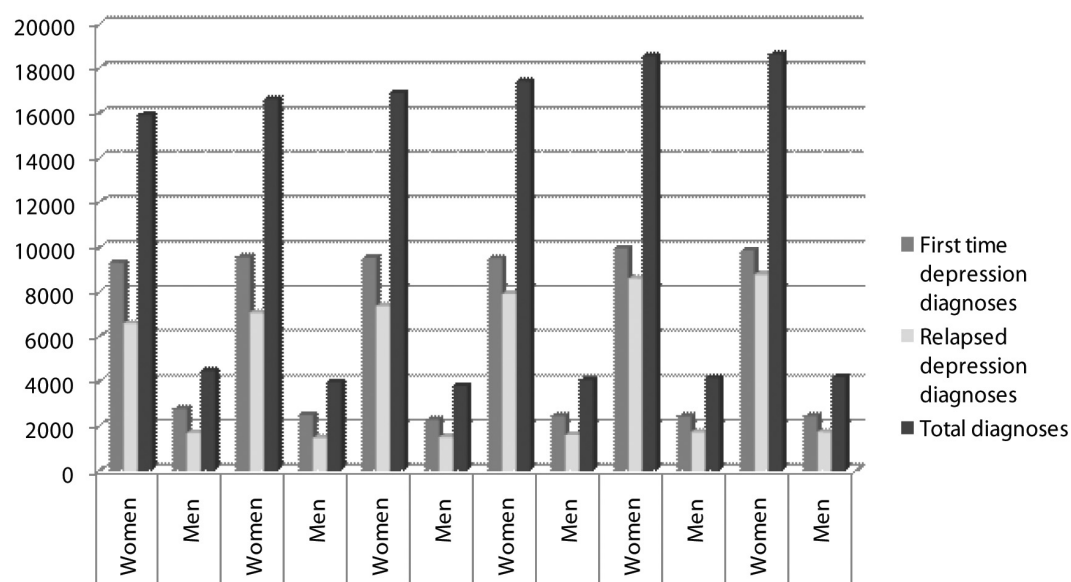


Fig. 4. Number of depression diagnoses by gender in Lithuania in 2004–2009

defined groups of antidepressants during this period changed.

For many years, tricyclic and tetracyclic antidepressants (TCAs) were the first-line treatment choice for depression in Europe, but recent studies indicate that some changes occur in the prescribing of antidepressants<sup>13)</sup>. In Lithuania the consumption of TCA group medicaments decreased by 42 percent (from 2.03 to 1.18 DDD/1000 inhabitants/day), apart from the fact that in accordance with recommendations and the priority of antidepressant selection in Lithuania, amitriptyline was the drug of choice for the treatment of depression<sup>14)</sup>. Evidently due to a relatively high toxicity of TCAs, these antidepressants are now used less frequently and for shorter periods than recommended.

On the contrary, the prescription of preparations from

the SSRI group increased significantly (by 45%), from 6.38 to 9.25 DDD/1000 inhabitants/day. This trend is in accordance with data from other European countries and the United States, where SSRIs belong to the first-line drugs<sup>15)</sup>. SSRIs are generally better tolerated than TCAs and are less likely to be discontinued due to the side effects<sup>13)</sup>. Early discontinuation of antidepressant therapy may increase the risk of relapse or recurrence of depression.

The consumption of other more recent antidepressants during the monitored period increased considerably likewise (from 1.61 to 4.63 DDD/1000 inhabitants/day). Over the past decade, there has been an increase in the number and types of antidepressants available. They have a wide range of mechanisms of action. Current practice guidelines recommend that physicians should choose an antidepressant drug based on the past

experience of treatment, side effects, patient preference and cost <sup>13)</sup>. The SSRIs and newer antidepressants consistently appear more cost-effective than TCAs in many patient groups <sup>16)</sup>.

Thus, increasing statistics of both depression diagnosis and consumption of antidepressants show that various factors must be assessed during the treatment of this disease.

When analysing the trends of consumption of antidepressants, the attention is paid to the gender of patients with this disease. It is assessed that generally women suffer from this disease twice more often than men <sup>17)</sup>. Besides physiological reasons, e.g., maturation difficulties, childbearing, menopause, etc., various social phenomena also influence the susceptibility to depression – inequality between men and women, cultural stereotypes, violence in family, high burden of responsibility, etc. Statistics shows that Lithuania does not differ overmuch in this term from the other countries in the world. Figure 4 shows that depression was diagnosed for women just about 4 times more often than for men. The cases of recurrent depression were recorded accordingly. The high incidence of depression in women must be taken into account. The statistics demonstrate only recorded diagnoses; however, there is no doubt that there are significantly more women who suffer from depression.

Among the aforementioned causes of incidence of depression in women, statistical indices of Lithuania only confirm quite poor social situation of women. In the beginning of the year 2010, 53.5 percent of women and 46.5 percent of men have resided in Lithuania, i.e., 1151 women for 1000 men. According to the data of 2009, women in Lithuania live approximately 12 years longer than men, till 78.6 and 67.5 years of age, respectively <sup>18)</sup>. Thus more women live in solitude. Nevertheless, a consideration of the association between family-related factors and depression reveals that, overall, married or those in a civil relationship have lower levels of depression than divorced, separated, widowed and single ones <sup>17)</sup>. Living with a partner seems to be an important buffer against depression for both genders.

Unemployment statistics show that there were significantly more employed women than men during the first quarter of 2010 – unemployment level of men was 23.2%, women – 13.1% <sup>18)</sup>. However, although women are noticeably more educated than men, earn significantly less: the gross average salary in 2009 was 1990 Litas for women and 2349 Litas for men <sup>18)</sup>.

However, women do not experience more mental illnesses than men; they are simply more prone to depression and anxiety, whereas men are more likely to have addictive disorders and personality disorders. The effects of stress, violence, poverty, inequality, sexism, care giving, relational problems, low self-esteem, and ruminative cognitive styles probably increase vulnerability to depression in women. Predictive factors for depression include previous depression, feeling out of control or overwhelmed, chronic health problems, traumatic events in childhood or young adulthood, lack

of emotional support, lone parenthood, and low sense of mastery. Special considerations are required for analysing the risk factors influencing the women's physical health <sup>14)</sup>.

Our results confirm the findings in international research that there is a gender gap in depression across Europe. Socioeconomic-related factors as well as family-related characteristics moderate the relationship between gender and depression. The largest gender differences in depression were found in a number of Southern European countries and in certain Eastern European countries <sup>17)</sup>. Until recently, many studies would have characterized Southern European countries as traditional, male breadwinner systems. In contrast, the Eastern European countries, especially the former Soviet Union countries, have a history of socialist policy that encourages dual-breadwinner households <sup>19)</sup>. However, both Southern and Eastern European countries are currently in transition. During the past decade, the Southern countries have been confronted with a rapid expansion of women's employment, which has forced them to be innovative in how they manage household responsibilities. Changes in men's behaviour, especially in relation to the unpaid work of care giving, have nevertheless been relatively small <sup>20)</sup>. For example, in Portugal, where we found the largest gender gap in depression, there is a relatively large number of mothers who are employed full time and of dual full-time income earners, along with relatively low levels of formal childcare provision <sup>21)</sup>.

Depression is often considered as a mental disease, thus, many people simply avoid talking about it. It is likely that men with the symptoms of depression do not take medical advice precisely because of the fear of society opinion – more often they choose suicide.

Since at least 1990, some have claimed that the SSRIs may induce suicide <sup>22)</sup>. Since the increased use of antidepressants in the past 15 years has mostly consisted of SSRIs, one should expect increasing suicide rates if they induced suicide. Increases have been found in some countries among younger men <sup>10)</sup>. Younger men, however, may be least likely to take antidepressants <sup>23)</sup>. They are probably also most likely to have substance abuse as a contributing factor to suicide <sup>24)</sup>. The dominant international picture is an overall decrease in suicide rates. Epidemiological studies comparing the suicide risk among patients treated with newer antidepressants with the risk in those who are treated with tricyclic antidepressants have found no difference between them <sup>25)</sup>.

The impact of depression on society has not yet been assessed in Lithuania. This impact is related not only with the lost ability of patients to work, unavailable income, social services provided, but also with the influence on the quality of life of the whole family and each of its member individually. Economic aspects of depression treatment (as well as of improper treatment, untimely diagnosis) must also be assessed to calculate how much the state pays for the patients with depression and what preventive means must be taken.



## CONCLUSIONS

Depression, in particular the recurrent one, severely affects the patient's quality of life. Increasing consumption of antidepressants and a growing number of depression diagnoses stimulate the need to have a closer look at the causes of the disease – the physiological, psychological, and social ones.

Considering the data presented in this article, one might conclude that the high incidence of depression in women in Lithuania is directly critical for the development of society as a whole. It is also worth noting that a proper diagnosis of depression and complete cure is not only the critical task for medics, but a necessity as well – besides psychological and social loss, high expenses of depression treatment are experienced too. Proper prescription of drugs and observation of the progress of the disease are the factors the common depression treatment management depends on. Individually selected treatment, which is started in due time, can help the person suffering from depression to become active and productive again more rapidly, and thus, to improve the quality of life.

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