Trends in depression diagnosis and consumption of antidepressants in Lithuania in 2004–2009

Liubov Kavaliauskienė*,

Rimantas Pečiūra,

Virginija Adomaitienė

Medical Academy,
Lithuanian University
of Health Sciences,
Kaunas, Lithuania

Background. One in five people affected by depression will not recover fully from a first episode, and in 70–80% of those achieving remission, depression will recur. The aim of this study was to evaluate the consumption of antidepressants during six years (2004–2009) in Lithuania, to analyze the trends in the diagnosis of depression and its compliance with the use of antidepressants for the future investigation of rationalizing medicamentous depression treatment costs in Lithuania opportunities.

Materials and methods. Data on the total sales of antidepressants were obtained from the IMS (Intercontinental Marketing Service) Health Incorporated. The data were calculated by the DDD (Defined Daily Dose) methodology and expressed in DDDs per 1.000 inhabitants per day. Data on depression diagnosis were obtained from the National Psychiatric Health Centre and expressed as the number of diagnoses in total and by depression types and gender.

Results. The total consumption of antidepressants increased from 10.17 DDD / 1000 inhabitants / day in 2004 to 15.0 DDD / 1000 inhabitants / day in 2009. The number of total depression diagnoses increased by 12%. The number of first time diagnosed depression increased not as significantly as relapsed depression diagnoses – by 27%. In 2009, women were diagnosed with depression 4.5 times more frequently than men. Moreover, depression relapse numbers grew up by 33% during the six study years among women.

Conclusions. During the study period, the consumption of antidepressants increased by 48%. Women were diagnosed with depression more frequently than men. The results of our study show that the number of depression diagnoses are growing because of depression relapse in women.

Key words: antidepressants consumption, depression relapse, pharmacoeconomics

INTRODUCTION

Depression is common, costly, treatable, and has a major influence on the quality of life (1). As far back as 1997, the World Health Organization considered depression as the second greatest cause of disability in the world (2).

Medical conditions like depression, which are chronic or follow a pattern of remission and relapse, are associated with illness-related burdens that fall into two broad categories. The first is the burden of ill-health experienced by the person affected, including discomfort, pain or distress, or difficulties in carrying out the activities of daily life. The second is the wider economic burden which includes the cost of providing health and social care, loss of productivity and time off work, the burden on caregivers, and loss of wages or reliance on state benefits. In this context, depression has been described as a condition that is "chronic and recurrent in nature, impairs family life, reduces social adjustment, and is a burden on the community" (3). The burden of depression is high partly because it is very

Correspondence to: Liubov Kavaliauskienė, Lithuanian University of Health Sciences, Medical Academy, Faculty of Pharmacy, Department of Drug Technology and Social Pharmacy, A. Mickevičiaus 9, LT-44307 Kaunas, Lithuania. E-mail: liuba@kavaliauskai.lt

common. The National Institute for Health and Clinical Excellence estimates that 9.8% of presons 16 to 65 years old in the UK are suffering from mixed depression and anxiety (4). One in five people affected by depression will not recover fully from a first episode, and in 70–80% of those achieving remission, depression will recur at least once. The long-term recurring nature of depression magnifies its wider economic burden (5, 6).

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 of people killed themselves because of the impact of depression in 2006 in the whole Europe (7).

The use of antidepressants has increased in all Western countries during the past 15–20 years. The defined daily dosages were developed as a tool for presenting drug consumption figures and have been used for many years in drug utilization studies where they are useful for both national and international comparisons of drug consumption and the evaluation of long-term trends in drug use. In Finland, the increase between 1990 and 2006 was nearly 8-fold (8), i. e. from 7.09 defined daily doses (DDD) expressed for 1 000 inhabitants a day in 1990 to 55.47 DDDs in 2006. Similar trends have been reported elsewhere (9). Although the consumption of antidepressants 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 (10).

The aim of this study was to assess the antidepressant consumption patterns in six years (2004–2009) in Lithuania, to analyze their use within different antidepressant groups, trends in the diagnosis of first-time and relapsed depression and their compliance with antidepressant sales for the future investigation of the possibilities to rationalize the costs of medicamentous treatment of depression in this country.

MATERIALS AND METHODS

Data on the total sales of antidepressant drugs in all Lithuanian regions over six years (2004–2009) were obtained from the IMS (Intercontinental Marketing Service) Health Incor-

porated. The data were retrieved as units of antidepressant drugs and their costs. The system and use were quantified in terms of defined daily doses (DDDs).

The most widely accepted method for measuring medicine consumption is the defined daily dose (DDD). This method was adopted by the World Health Organization (WHO) more than 20 years ago as a means to standardize drug utilization research among countries (11). The DDD theoretically corresponds to the average daily maintenance dose for a drug's major indication. The WHO has defined and periodically updates the DDD for most antibiotics available in the United States; these definitions are available free of charge on the Internet (12). The DDD / 1000 patient-days measurement has its limitations. For example, the DDD values are based on typical dosages for adult populations with the normal renal function. In institutions with large populations of children or patients undergoing dialysis, traditional DDD measurements may not accurately mirror the patient-level use of medicines (13). Occasionally, the DDDs do not reflect common dosages utilized in specific institutions or doses actually dispensed (14).

The defined daily dosages were developed as a tool for presenting drug consumption figures and have been used for many years in drug utilization studies where they are useful for both national and international comparisons of drug consumption and the evaluation of long-term trends in drug use (15). Drug consumption figures serve as a basis for the identification and evaluation of factors influencing the level of drug use.

Data were calculated by the DDD methodology and expressed in DDDs per 1.000 inhabitants per day. The DU95% was used as the quality indicator of drug prescribing. The number of drugs contributing to 95% of sales as a proportion of the total number was calculated for each year.

Data on depression diagnoses were obtained from the National Psychiatric Health Centre and expressed in total diagnoses and by depression types and gender.

RESULTS

The total consumption of antidepressant drugs in Lithuania increased by 48% in six years (from 10.17 DDD/1000 inhabitants / day in 2004 to 15.10 DDD / 1000 inhabitants / day in 2009) (Fig. 1).

Changes of consumption within antidepressant classes in six years (2004–2009) are the following (Fig. 1):

• the proportion of consumption of TCAs declined by 42% (from 2.03 to 1.18 DDD / 1000 inhabitants / day);

• the consumption of SSRIs showed a pronounced increase of 45% (from 6.38 to 9.25 DDD / 1000 inhabitants / day); therefore, SSRIs were the most widely used antidepressants;

• the consumption of newest drugs classified as "other antidepressants" increased significantly (almost three times) over the study period (from 1.61 to 4.63 DDD / 1000 inhabitants / day). However, this is associated with the expanded use of mirtazapine, tianeptine, buproprion and venlafaxine as in 2004 buproprion and venlafaxine have appeared in the antidepressants segment;

• there were modest changes in the consumption of lithium.

A comparison of the proportions of different antidepressant classes has shown that the proportion of SSRIs remained almost the same (62%), although their consumption has increased, while the proportion of other (newer) antidepressants increased almost two times and comprised 31% of the total market.

Over the study period, the consumption of sertraline remained on the top of the list. Besides, the results show that the proportion of sertraline consumption decreased from a quarter of all antidepressants (24.5%) to 22.6%, and in parallel the proportion of amitryptiline consumption declined more than by half – from 14.33% to 6.71%. The use of paroxetine, mirtazapine and escitalopram increased, whereas the use of other SSRIs (fluoxetine, citalopram, fluvoxamine) decreased.

The number of total depression diagnoses increased from 20.381 in 2004 to 22.821 in 2009.

The number of first-time diagnosed depression (F32) grew up not as significantly as the number of relapses (F33) – from 8 300 in 2004 to10 514 in 2009 (Fig. 2).

The results show that in 2009 women were diagnosed with depression 4.5 times more frequently than men. Moreover, depression relapse numbers grew up by 33% during the study years among women, while in men the number of relapsed depression cases was almost the same (Figs. 3, 4).
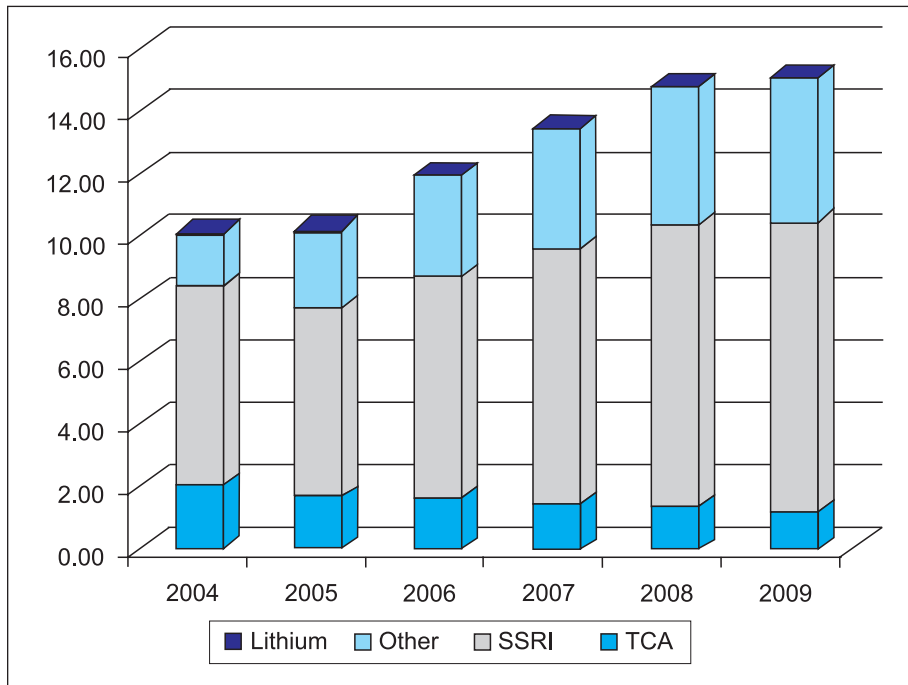

Fig. 1. Consumption of antidepressants (total and by classes) in DDD / 1000 inhabitants / day in 2004–2009
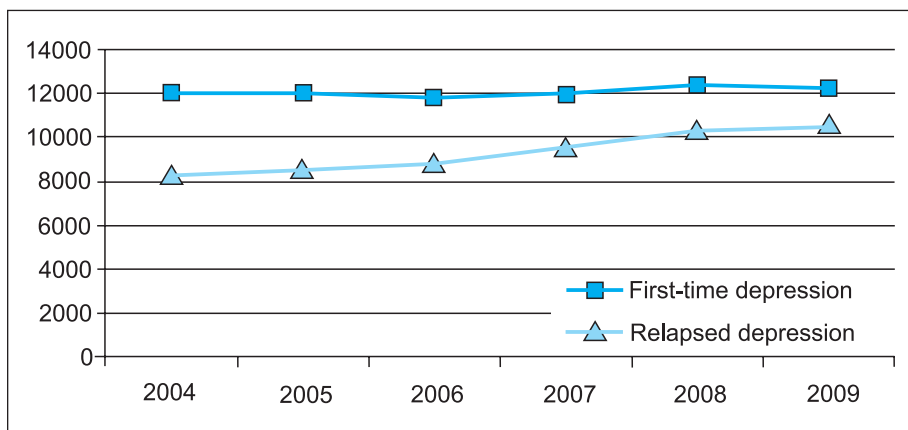

Fig. 2. First-time (F32) and relapsed (F33) depression diagnoses in Lithuania in 2004–2009

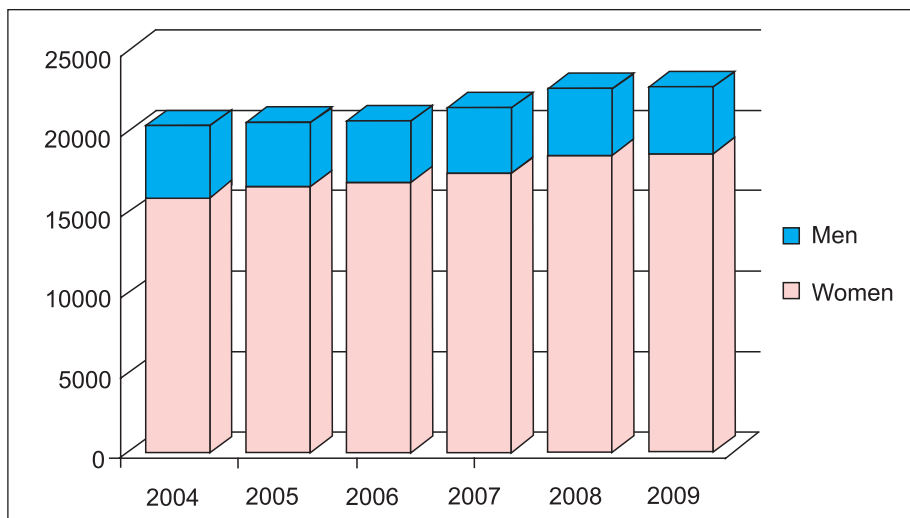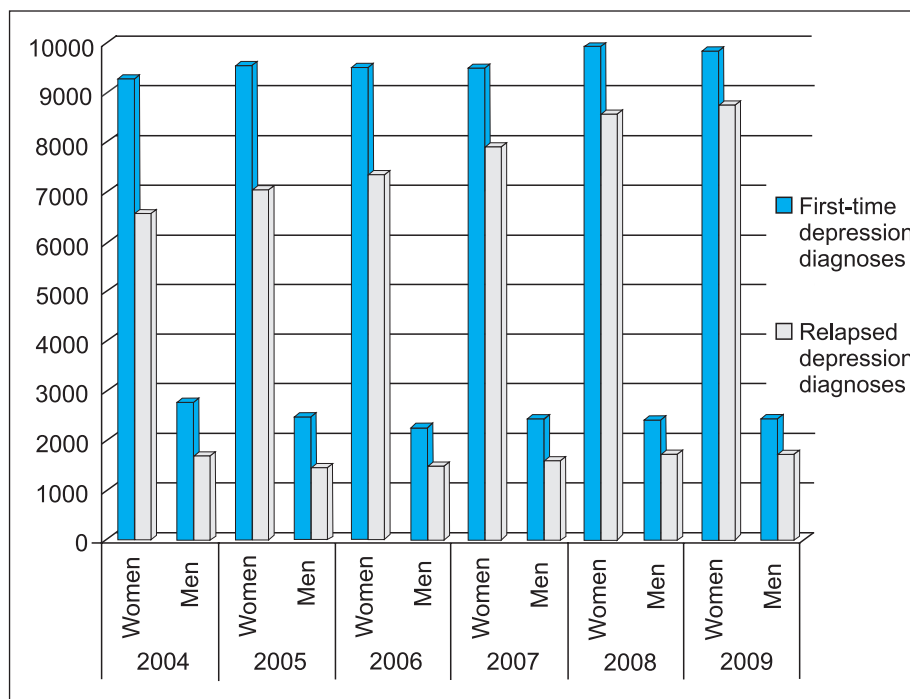**Fig. 3.** Total depression diagnoses by gender in Lithuania, 2004–2009

Fig. 4. First-time and relapsed depression diagnoses by gender in Lithuania, 2004–2009

DISCUSSION

Depression and especially its relapse have a great impact on the quality of life. The results of our study show an increase in the consumption of antidepressants during 2004–2009. Does this mean that if we go back to 2004 depression treatment schemes, we would save money and get a more effective treatment? Investigations should be performed in future to test this hypothesis.

Each year there are more cases of depression diagnosed in Lithuania. The statistics of diseases demonstrates a continuously increasing number of recurrent depression diagnoses.

According to data of researchers from the University of Virginia (USA), this disorder is recurrent even for 50% of those with depression and those who have been treated.

Other figures are more daunting: after a repetitive treatment of depression, about 70% of patients and after three treatments even 90% fall into depression for the third time. Each recurring disease means that a previous treatment was unsuccessful (16).

The biggest impact on consumption growth was made by the use of SSRIs and the newest "other antidepressants". The increased use of selective serotonin reuptake inhibitors and other nontricyclic antidepressants is probably related to their better tolerability, an improved risk-to-benefit ratio and lower toxicity in case of overdosage. The proportion of different antidepressants classes also surprises: during studied six years the proportion of SSRIs remained almost the same, while the proportion of newer "other" antidepressants grew up almost two times. Over the study period, the

consumption of sertralin remained on the top of the antidepressant consumption list, followed by the newest antidepressants such as paroxetine, mirtazapine and escitalopram. In this situation, a hypothesis arises that the reason for depression relapse growth may be the consumption of modern and newest medicines.

Also, the results show that women were diagnosed with depression more frequently than men. Moreover, depression relapse numbers in women increased drastically.

These data are consistent with data on a higher prevalence of depression in females (17–19). However, women do not experience more mental diseases than men; they are simply more prone to depression and anxiety, whereas men are more likely to have addictive disorders and personality disorders (20). 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 (21). 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 (22). Special considerations are required for analyzing the risk factors influencing the women's physical health (23).

Our results confirm the findings reported in the literature that there is a gender gap in depression across Europe. Socioeconomic 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 and in certain Eastern European countries (24).

The impact of depression on society has not yet been assessed in Lithuania. This disease carries a considerable epidemiological impact and is often both misdiagnosed and mistreated; depression imposes an enormous burden on society, resulting from its high prevalence, under-diagnosis and under-treatment. Depression implies many costs and consequences, including a decreased quality of life for patients and their families, high morbidity and mortality, and substantial economic losses (25).

Thus, as regards depression and other major chronic illnesses, it is important to consider the global disease management. Hence, a proper use of all the remedies available to date can really improve not only the clinical but also the economic component of the management of patients suffering from depression, thus producing global savings for the health system (26).

CONCLUSIONS

The increasing consumption of antidepressants and the growing numbers of depression diagnoses induce the necessity of a deeper analysis of the causes of this disease – physiological, psychological, social ones. Results of a comparison of the first-time and relapsed depression diagnoses are surprising: the level of first-time depression diagnoses remains almost the same, whereas relapsed depression numbers grow up significantly in all years of the study. The results of our study show that the number of depression diagnoses increases because of depression relapse in women.

Additional studies should be carried out in order to assess the true economic burden of depression treatment and especially the impact of its relapse on society.

References

1. Pirraglia P, Rosen A, Hermann R, Olchanski N, Neumann P. Cost-utility analysis studies of depression management: a systematic review. Am J Psychiatry. 2004 Dec; 161: 2155–62.

2. Murray C, Lopez A. Alternate projections of mortality and disability by cause 1990–2020: global burden of disease study. Lancet. 1997; 349: 1498–504.

3. Klerman G, Weissman M. The course, morbidity, and costs of depression. Arc Gen Psychiatry. 1992; 49: 831–4.

4. National Institute for Health and Clinical Excellence. Depression: managing depression in primary and secondary care. Clinical Guideline. 23; Full Guideline. London. British Psychological Society & The Royal College of Psychiatrists, 2004. http://www.nice.org.uk/guidance/index.jsp?action=download &o=29617 accessed 19/11/2007.

5. Wells K, Stewart A, Hays R, Burnam M. The functioning and well-being of depressed patients: results from the medical outcomes study. JAMA. 1989; 262: 914–9.

6. Hays R, Wells K, Sherbourne C, Rogers W, Spritzer K. Functioning and well-being outcomes of patients with depression compared with chronic general medical illnesses. Arc Gen Psychiatry. 1995; 52: 11–9.

7. Eurostat report on the causes of deaths in the EU (2006). http://epp.eurostat.ec.europa.eu/cache/ITY_OFFPUB/KS-NK-06-010/EN/KS-NK-06-010-EN.PDF (2010.08.14).

8. Sihvo S, Isometsa E, Kiviruusu O, Hamalainen J, Suvisaari J, Perala J et al. Antidepressant utilisation patterns and determinants of short-term and non-psychiatric use in the Finnish general adult population. J Affect Dis. 2008; 110: 94–105.

9. Nomesco (Nordic Medico Statistical Committee), 2004. Medicines consumption in the Nordic countries 1999–2003. Nomesco, Copenhagen. Online access: www.nomnos.dk (2010 08 06).

10. Isacsson G, Rich C. Antidepressant drug use and suicide prevention. Int Rev Psych. 2005; 17(3): 153–62.

11. World Health Organization. ATC classification index with DDDs. Oslo, Norway: World Health Organization Collaborating Centre for Drug Statistics Methodology, 2001.

12. World Health Organization Collaborating Centre for Drug Statistics Methodology. Home page. Available from www.whocc.no/atcddd/. Accessed August 2003.

13. Zagorski B, Trick W, Schwartz D, Tokars J, Weinstein R. The effect of renal dysfunction on antimicrobial use measurements. Clin Infect Dis. 2002; 35(12): 1491–7.

14. Natsch S, Hekster Y, de Jong R, Heerdink E, Herings R, van der Meer J. Application of the ATC/DDD methodology to monitor antibiotic drug use. Eur J Clin Microbiol Infect Dis. 1998; 17: 20–4.

15. Kiivet R, Bergman U, Rootslane L, Rago L, Sjoqvist F. Drug use in Estonia in 1994–1995: a follow-up from 1989 and comparison with two Nordic countries. Eur J Clin Pharmacol. 1998; 54(2): 199–224.

16. New Treatment Strategy for the Prevention of Recurrent Depression. ScienceDaily, Nov. 15, 2006. http://www.sciencedaily.com/releases/2006/11/061106144928.htm (2010 08 06).

17. Stewart D, Gucciardi E, Grace S. Depression. BMC Womens Health. 2004; 4 (Suppl 1): S19.

18. Lawrenson R, Tyrer F, Newson R, Farmer R. The treatment of depression in UK general practice: selective serotonin reuptake inhibitors and tricyclic antidepressants compared. J Affect Disord. 2000; 59(2): 149–57.

19. Poluzzi E, Motola D, Silvani C, De Ponti F, Vaccheri A, Montanaro N. Prescriptions of antidepressants in primary care in Italy: pattern of use after admission of selective serotonin reuptake inhibitors for reimbursement. Eur J Clin Pharmacol. 2004; 59(11): 825–31.

20. Stewart D, Rondon M, Damiani G, Honikman J. International psychosocial and systematic issues in women's mental health. Arch Women's Mental Health. 2001; 4: 13–7.

21. Mazure C, Keita G, Blehar M. Summit on women and depression: proceedings and recommendations. Washington, DC: American Psychological Association 2002. Available from: URL: http://www.apa.org/pi/wpo/women&depression.pdf

22. Danilevičiūtė V, Sveikata A. Šiuolaikinis požiūris į farmakologines ir klinikines naujų antidepresantų savybes. (Contemporary approach to pharmacological and clinical aspects of novel antidepressants). Medicina (Kaunas). 2002; 38(12): 1147–56.

23. Jakimavičius M, Sveikata A, Vainauskas P, Jankūnas R, Mikučionytė L, Sapolienė A et al. Analysis of antidepressant prescribing tendencies in Lithuania in 2003–2004. Medicina (Kaunas). 2007; 43(5): 412–8.

24. Velde S, Bracke P, Levecque K. Gender differences in depression in 23 European countries. Cross-national variation in the gender gap in depression. Soc Sci Med. 2010; 71: 305–13.

25. Mendlevicz J. The social burden of depressive disorders. Neuropsychobiology. 1989; 22: 178–80.

26. Stoudemire A, Frank R, Hedemark N, Kamlet M, Blazer D. The economic burden of depression. Gen Hosp Psychiatry. 1986; 8: 387–94.

Liubov Kavaliauskienė, Rimantas Pečiūra, Virginija Adomaitienė

DEPRESIJOS DIAGNOZAVIMO IR ANTIDEPRESANTŲ SUVARTOJIMO TENDENCIJOS LIETUVOJE 2004–2009 M.

Santrauka

Pagrindas. Vienas iš penkių depresija sirgusių žmonių po pirmojo ligos epizodo visiškai nepasveiksta, o 70–80 % remisiją pasiekusių žmonių depresija pasikartoja. Šio darbo tikslas buvo įvertinti antidepresantų suvartojimą per šešerius metus Lietuvoje (2004–2009), išanalizuoti depresijos diagnozavimo tendencijas ir jų atitikimą antidepresantų suvartojimui, kad ateityje būtų galima numatyti medikamentinio depresijos gydymo kaštų racionalizavimo galimybes Lietuvoje.

Medžiaga ir metodai. Bendri antidepresantų pardavimo duomenys Lietuvoje buvo gauti iš IMS (*Intercontinental Marketing Service*) „Health Incorporated" ir suskaičiuoti remiantis DDD (*Defined Daily Dose*) metodologija; gauta išraiška – DDD 1 000 gyventojų per dieną. Iš Valstybinio psichikos sveikatos centro gautų duomenų apie depresijos diagnozę išskirtas bendras diagnozių skaičius, taip pat jos suskirstytos pagal depresijos tipą ir lytį.

Rezultatai. Bendras antidepresantų suvartojimas padidėjo nuo 10,17 DDD / 1000 gyventojų per dieną (2004) iki 15,10 DDD / 1000 gyventojų per dieną (2009). Bendras depresijos diagnozių skaičius išaugo 12 %. Pirmą kartą diagnozuojamos depresijos skaičius padidėjo nedaug, tuo tarpu pasikartojančios depresijos diagnozių skaičius išaugo 27 %. 2009 m. moterims depresija buvo diagnozuota 4,5 karto dažniau nei vyrams. Be to, tiriamuoju laikotarpiu depresijos pasikartojimų skaičius moterų grupėje išaugo 33 %.

Išvados. Tiriamuoju laikotarpiu antidepresantų suvartojimas padidėjo 48 %. Moterims depresija buvo diagnozuota dažniau negu vyrams. Tyrimo rezultatai rodo, kad depresijos diagnozių skaičiaus didėjimą tarp moterų lemia pasikartojanti depresija.

Raktažodžiai: antidepresantų suvartojimas, depresijos pasikartojimas, farmakoekonomika