Solving the problem of antidepressant selection in Lithuania

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Abstract

Purpose: To ascertain the opinion of psychiatrists of the factors those determine antidepressants selection.

Material and methods: An original questionnaire of 30 questions, which deals with reliance of antidepressants selection according to the subtype of depression, was represented for a quarter of all Lithuanian psychiatrists.

Results: Respondents for depression with obsession – 36% chose paroxetine. It is interesting that despite the controversial opinion about the TCA prescribing according to their side effects profile and safety to use, our respondent chose amitriptyline for the melancholic depression with suicidal thoughts (50.2%) and for the anesthetic depression (28%). In some cases there is no unanimous opinion among the psychiatrists – data scattering was received in selection, the respondents chose different antidepressants from different groups in similar frequency. For the treatment of the adynamic depression – 7.6% – amitriptyline, 12.1% – citalopram, 10.6% – reboxetine, 10.6% – venlafaxine, for the anxious depression – 15.2% – amitriptyline, about 20% – citalopram, 15.2% – mirtazapin, for the anesthetic depression – 14.3% – escitalopram, 9% – sertraline, 8.3% – venlafaxine. There is no clear tendency or prevailing antidepressant.

Conclusions: Psychopathological peculiarity of depression can be one of the most important criteria in antidepressant selection. However, in many cases, the subtype of depression is ascertained empirically and based solely on the personal experience and clinical practice of the psychiatrist. There are no clear diagnostic criteria or practical guidelines for the reliable verification of the psychopathological subtype of depression, which would allow for the selection of a more adequate and prompt treatment for the patient.

Key words: depression, type of depression, selection of antidepressants.

Introduction

There are more than two tens of registered antidepressants in Lithuania and all of them are indicated as effective drugs for depression treatment. A new dual-action antidepressant has appeared recently as well as several novel antidepressants have been presented for the Drugs Control Agency that are at different research stages now. It is estimated that there will be more antidepressants generated during the next decade that will have different mechanism of action from those of the current ones [1,2].

There is a quite wide spectrum of antidepressants nowadays. However, a big assortment of pharmaceuticals results in various problems that the physicians must take into consideration while selecting an optimal treatment [3]. This appears to be a difficult task, though the identification of treatment failures is quite an easy one. Often do physicians and their patients ask themselves as to which one is the best choice, whether other pharmaceuticals bring better results, how to make a decision, if there are no clear guidelines for treatment? Unfortunately, practicing therapists have poor experience-based references for a proper choice of antidepressant. The majority of reviews of theoretical approach and practical guidelines relating to antidepressant consumption conclude that each sort of these pharmaceuticals is equally efficient, thus the recommendations for a certain antidepressant is based on the aspects of side effects, tolerance, patient opinion, and price. Patients react differently to antidepressants. Many of them go through trial after trial with little or no improvement at all. Eventually, some people

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find antidepressants that help them achieve remission; however, others do not. Some practical guidelines detect a quite diverse response to treatment depending on a clinical profile. For example, American Psychiatric Association (APA) set Practice Guideline for the Treatment of Major Depressive Disorder claim that the atypical symptoms and those of anxiety, melancholia, and border person disorder typical of non-psychosis, unipolar depression disorder might be related to a different response to the antidepressant. According to this guideline, it is recommended to give preference for the selective serotonin reuptake inhibitors (SSRI) and avoid of bupropion while treating depression with high anxiety, whereas, in case of obsessive--compulsive symptoms, SSRI with clomipramine are preferred, as well as tricyclic antidepressants (TCA) are recommended in case of a severe and melancholic depression; atypical depression is typically treated by SSRI or monoamine oxidase inhibitors (MAOI) while avoiding TCA [4].

Unfortunately, the data of these practical guidelines that guide the psychiatrists' selection of an antidepressant is quite limited in its scope and utility. The majority of the depressed patients are treated in outpatient settings. Melancholia and the episode of severe depression are comparatively rare in a current outpatient psychiatry practice [5]. Generally, anxiety disorders are comorbid conditions in depression [6,7]; the APA practical guide states that bupropion might act as an *anxiogenic* and therefore it should not be given to patients. Though MAOI and TCA can be useful for patients with anxious depression, other pharmaceuticals are given the preference. Practical guide does not cover possible impact of a specific symptom and type of depression on the selection of antidepressant.

It would be interesting to explore the criteria of antidepressant prescription that Lithuanian physicians use, as there is no exact information that would elucidate the selection of antidepressant. There have been only a few researches on the practice of the psychiatrists' prescription of antidepressants. The majority of articles focus on the tendencies of prescription rather than the argument for the prescription of certain pharmaceuticals [8-12]. The research of the factors that have influence on psychiatrists' choice of antidepressant can disclose the spheres for further scientific research in order to confirm or deny the tendencies of selection. Now, the information that would prove the significance of clinical criteria for the choice of antidepressant is lacking. Presumably, the non-clinical aspects, such as the economic factors of market, will have more impact on the choice of pharmaceuticals. Therefore, it is difficult to contradict the restrictions of the pharmaceutical guidelines.

This research is based on the opinion of Lithuanian psychiatrists of the antidepressants and the factors that determine their selection. It has been conducted by giving them a questionnaire. This article focuses on the discussion as to what factors affect the selection of antidepressant for treatment.

Methods

The survey had been conducted from January till March, 2005. The psychiatrists from different regions of Lithuania participated therein. The stratified sample was chosen; first, the biggest Lithuanian hospitals were chosen and 20 per cent of psychiatrists who worked therein were questioned pro rata in incidental order, independently of gender, age, occupation, work experience, etc. When the questionnaires were given to the respondents, they were informed about the objective of this survey. The respondents filled in the questionnaires anonymously.

In the questionnaire, there were 30 questions that included the respondents' demographic information, their opinion of 14 the most popular antidepressants in Lithuania and of the factors that have influence on the selection of antidepressant. They were asked to evaluate the efficiency of antidepressants, their tolerance in the scale from 1 to 5, where 1 means very low efficiency or tolerance and 5 means very good efficiency or tolerance; and, according to their significance, to rank 5 factors that have the most significant impact on the selection of depression treatment. The statements from the questionnaire are displayed in the tables of **Result** part of this article. These statements were formulated on the basis of the review articles, manuals and the clinical experience of the authors. Data analysis was performed with Statistical Package for the Social Sciences (SPSS) 10 for Windows software.

Results

The sample group consists of 133 psychiatrists, which approximately covers a quarter of all the Lithuanian psychiatrists. The answers of 18 respondents were excluded; 9 questionnaires were not sent back to the researchers.

The working experience of more than a half of psychiatrists exceeded 20 years (50.4%). The number of patients treated from depression distributed quite evenly among the respondents, which means that approximately 29 per cent of the respondents treat from 20 to 50 patients annually, the same percentage of the respondents treat from 50 to 100 patients, as well as more than 100 patients yearly; only 13 per cent of the respondents treat less than 20 patients during the mentioned period.

Generally, Lithuanian psychiatrists chose the following groups of antidepressants: SSRI, TCA, and noradrenergic and specific serotonergic antidepressants (NaSSA).

The respondents ranked the following antidepressants as the best ones: mirtazapin, escitalopram, citalopram, amitriptyline according to the efficiency and escitalopram, citalopram, sertraline, mirtazapin according to the tolerance (*Tab. 1*). While estimating the antidepressants according to their efficiency, mirtazapin was acknowledged as very effective (5 points) by 58.5 per cent of the respondents; within the same group, escitalopram was acknowledged as very effective by 55.3 per cent and citalopram by 48.9 per cent of them. While estimating the antidepressants according to the tolerance 66.4 per cent of the respondents acknowledged escitalopram as very good (5 points); within the same group, 51.6 and 50 per cent of the respondents claimed citalopram and sertraline as fully tolerated respectively.

Research data confirm that, in general, the selection of antidepressant was influenced by the complexion of depression symptoms, the tolerance of the pharmaceutical and the comor-

Table 1. **Evaluation of the antidepressants by the efficiency and tolerability. Mean efficiency points (from 1 – very low up to 5 – very good) and mean tolerability points (from 1 – very low up to 5 – very good)**

	Mean efficiency points	Mean tolerability points
Mirtazapin	4.45	4.24
Escitalopram	4.42	4.63
Citalopram	4.13	4.45
Amitriptyline	4.13	2.56
Paroxetine	4.04	4.13
Sertraline	3.94	4.39
Venlafaxine	3.9	3.95
Clomipramine	3.56	3.17
Nortriptyline	3.4	2.64
Tianeptine	3.21	4.08
Imipramine	3.19	2.67
Fluoxetine	3.17	3.68
Bupropion	3.06	3.64
Doxepine	3.03	3.19

bid disorders (*Tab. 2*). According to the frequency, the patient's previous response to the treatment was the second factor that influenced the choice of practitioners. Some other factors, such as sexual dysfunction, patient opinion and co-operation during the consumption of the pharmaceuticals, that are often discussed in literature rarely did make any influence on the selection of antidepressant.

There was a possibility to indicate new criteria in the questionnaire concerning the factors that influence the selection of antidepressant but there were no records in the answered forms.

The results of the selection of antidepressant depending on the subtype of depression are displayed in the charts.

Discussion

The depressions are not the homogenous group in regard to their psychopathological structure. Nowadays classifications notice some peculiarities (subtypes) of depression – psychotic depression, depression with catatonic features, with or without somatic symptoms, agitated depression, etc. (ICD-10, DSM-IV TR). We uphold the view of some European and American psychiatrists that some forms of disturbances (symptoms) can markedly prevail over the picture of depression [13-18].

On that ground we have chosen some psychopathological "subtypes" of depressions in our survey: adynamic, anaesthetic, agitated (anxious), depression with obsessions and depression with clear suicidal thoughts. In common with clear diagnostic criteria for depression in all cases we note some specific peculiarities of psychopathological structure of each "subtype".

In the structure of adynamic depression there are prevailing psychomotor suppression, thinking process and movements are going slow, loss of energy, inability to make everyday social activities, strong feeling of disability and asthenia, gone sensation, sometimes – even inability to get up from the bed or get about. In case of anaesthetic depression the patients complain of prevailing loss of feelings, anhedonia, blur vision and weak perception of surroundings, inability to understand what is going on, depersonalization and derealization. In the structure of anxious depression there are marked prevailing feelings of inner tension, anxiety, trouble, angst, psychomotor agitation. In case of obsessive depression there were low self-esteem and prevailing obsessive thoughts of worthlessness, shoddy, booming around, picayune, contemptible, pathetic, pitiful and pygmy. In case of depression with strong suicidal thoughts there were prevailing feelings of hopelessness, purposeless, disability, things looking black, being at a deadlock.

The objective of the study was to explore and comprehend the criteria that guide psychiatrists in the selection of antidepressants for the patient with depression. As the number of the researches that assess the influence of clinical symptoms on different responses to the new generation antidepressants is relatively small, the scientific exploration of the psychiatrists' practice of prescription would be an interesting and useful one.

Most often were the SSRI, TCA and NaSSA groups of antidepressants selected; this might be due to the fact that many antidepressants of these groups are effective and well tolerated. The aspects of efficiency and safety are analyzed in much of clinical research. In this study, the authors try to analyze other factors possibly significant for the selection of antidepressants.

The results of the study reflect few significant factors that are important for the treatment of depression. According to the

Table 2. **The factors generally impacting antidepressant selection**

	Factors impacting antidepressant selection	N	Choice of practitioners (%)
1.	The character of symptoms, type of depression	128	96.2
2.	Tolerability and safety of the medication	102	76.7
3.	Comorbid physical disorders	92	69.2
4.	Preceding response to treatment	87	65.4
5.	Personal experience of treatment with specific antidepressant	69	51.8
6.	Patient's age	61	45.8
7.	Pharmacodynamic and pharmacokinetic characteristics of medicament	54	40.6
8.	Patient's opinion, motivation to use medication, compliance	20	15
9.	Price of the medication	19	14.3
10.	Sexual dysfunction	18	13.5
11.	Pharmacy concerns' influence	1	0.75

Figure 1. **Antidepressants selection for the treatment of adynamic depression**

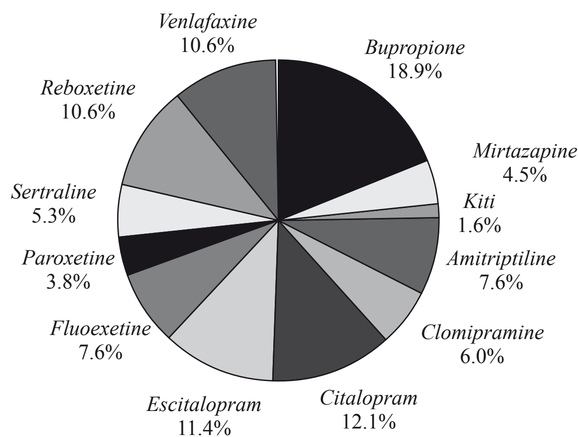
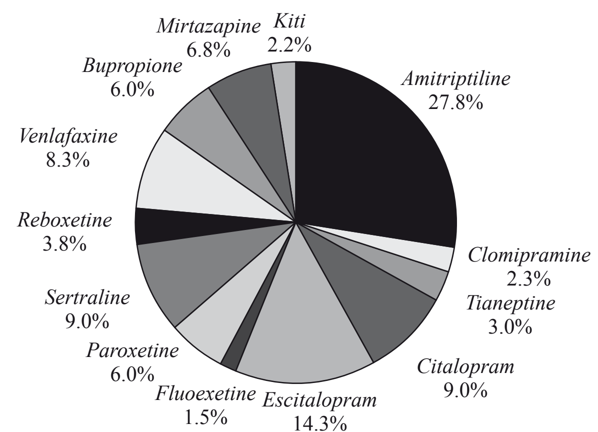


Figure 2. **Antidepressants selection for the treatment of anaesthetic depression**



respondents, one of the most important factors while selecting the antidepressant is the subtype of depression. In many cases (even 96.2%), the specialists noted that the character of depression symptoms has major influence on the selection of antidepressant. During the analysis of the selection of the antidepressant group by the subtype of depression, statistically significant results were retrieved (Monte Carlo χ^2=169, df=20, p<0.001). In authors' opinion, they are quite novel and important.

The factors of tolerance and safety were given the second place (76.7%). Given that the respondents treat a very wide contingent of patients in their practice, this is not strange. Comorbid physical disorders noted in the third place (69.2%) approved this assumption. The patient's opinion, the price of pharmaceuticals and sexual dysfunctions (as the side effect), in turn, were set for as the least significant factors for the selection of antidepressant. The relative costs of the antidepressants in Lithuania are pretty similar compared to one another with the exception of TCA group. These antidepressants are almost 3-4 times cheaper then other. For example, one month course of treating with SSRIs or NaSSA costs about 140-150 litas (40-44 EUR) and with TCA – about 20-60 litas (6-17 EUR). 80 per cent of prices are compensated by Lithuanian government.

Family histories of good medication response or bipolar affective disorder, comorbid psychiatric disorders (such as alcohol abuse, psychosis and others) were not included into the questionnaire. But there was possibility for psychiatrists to write it down in line "other" if the doctor seemed it important for the selection of the antidepressant. There were no notes about that.

In the authors' opinion, the most interesting results are retrieved during the analysis of the respondents' perspectives to treatment of a particular subtype of depression. In many cases, the respondents selected citalopram and escitalopram (23.5%) as well as bupropion (18.9%) for the treatment of adynamic depression (*Fig. 1*). In this particular case, the selection of bupropion is consequent, for its chemical structure is similar to that of amphetamine and stimulators. However, the selection of citalopram and escitalopram is clinically less grounded in the case of adynamic depression.

The anaesthetic subtype of depression was mostly treated with TCA (amitriptyline; 27.8%) or with citalopram and escitalopram (23.3%) (*Fig. 2*). The data about the adequate treatment strategies of this sort of depression is insufficient, which might be influenced by the complicated psychopathological structure of this subtype of depression. It has been proposed to use big or maximum doses of MAOI (this group of antidepressants is not reflected in the results of the study because it is not registered in Lithuania), SSRI, and TCA [19,20].

Many clinical studies discovered that anxiety is prevalent in half or sometimes even more than a half of depressed patients. Anxious depression is a frequent phenomenon and the anxiety as the symptom often influences the selection of antidepressant. Unfortunately, there is no research that demonstrates the advantage of any antidepressants for this large group of patients. On the contrary, several former studies were not successful in proving the difference of the response to various categories of antidepressants. For example, Rush et al. published the articles that disclosed no difference between bupropion and sertraline while treating the depressed patients and assessing the HAM-A scale [21]. Similar results were published by Akkaya et al. after they had conducted a comparative research of venlafaxine XR and reboxetine [22], Versiani et al. after the comparison of fluoxetine and amitriptyline [23]. The respondents' opinion of the selection of antidepressants is quite diverse (*Fig. 3*). One part of the psychiatrists preferred citalopram and escitalopram (34.3%), whereas others chose paroxetine (19.1%), mirtazapin (15.2%) or amitriptyline (15.2%). While in some sources, venlafaxine was chosen by only 3 per cent and sertraline by 8.4 per cent of the respondents. Thus there is no unanimous opinion among the respondents as to what antidepressant is the best one for treatment of anxious depression; however, there is a strong tendency to select SSRI, NaSSA and TCA.

The analysis of the respondents' opinion on the treatment of depression with suicidal tendencies has provided with interesting results. 50.2 per cent of the psychiatrists claimed that they would choose amitriptyline (*Fig. 4*). In such cases, 26.8 per cent of the respondents would choose citalopram and escitalopram. In the authors' opinion, the preference of TCA might be influenced by a strong and quick therapeutical effect, good

***Figure 3*. Antidepressants selection for the treatment of anxious depression**

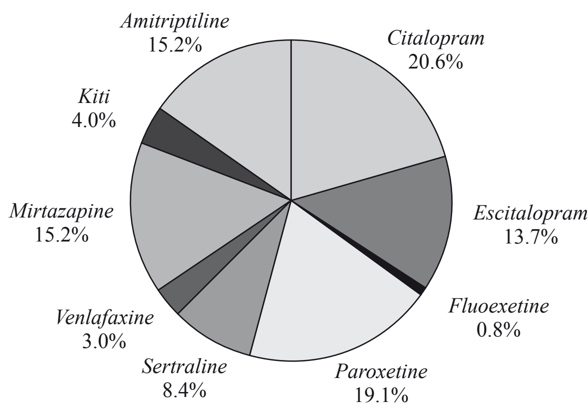
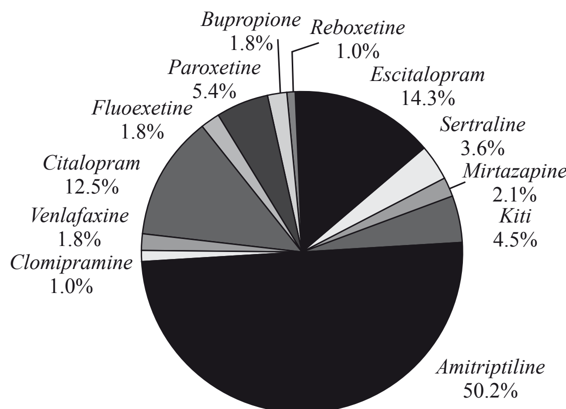


***Figure 4*. Antidepressants selection for the treatment of depression in prevalence of intense suicidal thoughts**



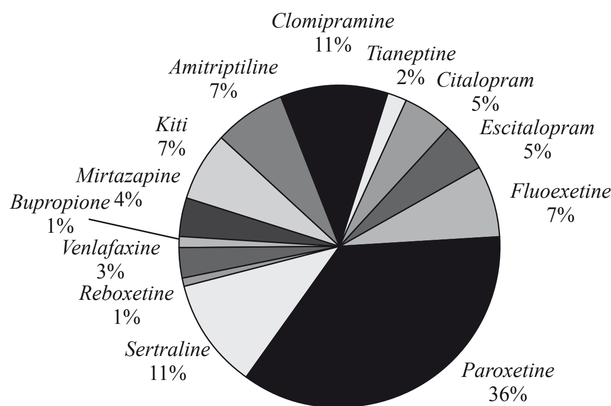
knowledge of pharmaceutical characteristics and a long clinical experience of treatment with TCA. In the case of a life-threatening situation (the danger of suicide), an acute side effect of TCA loses its significance. According to some researchers, the problem lies in that TCA themselves evoke the risk of suicide in case of overdose and are not recommended for the treatment of depression with suicide tendencies. It might be comment as patients with suicidal tendencies mostly are treated in inpatient settings in Lithuania. Suicidal tendency is the one of few cases when forced hospitalization can be considered according Lithuania's law. Treatment with TCA in inpatient department is not so dangerous for case of overdose on prescribed medication.

According to the references, TCA (clomipramine) and SSRI group are the best means for treatment of depression with clear obsessive-compulsive component. Most often did the respondents of the study choose paroxetine (36%), clomipramine (11%), which partly complies with the references of previous sources, and sertraline (11%) (*Fig. 5*). The frequency rate of the selection of other TCA, SSRI, and NaSSA was relatively low.

Thus there have been no clearly defined criteria and recommendations for the treatment of depression that would be coherent with psychopathological structure of depression until now. Although a huge number of specialists would choose the treatment (antidepressant) depending on the psychopathologic structure of depression. It complies with the results of research that have been conducted recently and the articles that turn to the psychopathologic structure of depression and a possibly diverse response to the antidepressants, subject to the subtype of depression more and more often [24].

In this study, the antidepressants that were ranked highly by the psychiatrists partly reflect the pharmacy market. The data of IMS Health Inc database on sales of antidepressants in Lithuania during the period of 2002-2004 shows that the consumption of SSRIs increased by 27.82 per cent and the one of TCA declined by 10.78 per cent; the consumption of other antidepressants increased by nearly three times. The cost of antidepressants increased up to 26 million litas (approximately 10 million US dollars) in the year of 2004; 68.15 per cent of them were intended for the SSRI group. Gladly, the results

***Figure 5*. Antidepressants selection for the treatment of depression with obsessions**



of this study do not reflect any influence from the part of the pharmacy companies on the prescriptions made by the psychiatrists in Lithuania. Only one respondent noted that he takes into consideration the name, authority and the advertisements of a pharmacy company while he selects the antidepressant.

A contemporary policy of health seeks to reduce the number of hospitalized patients is based on a holistic attitude towards the patient and his/her partnership with the physician, whereas the paternalistic model of intercourse is being criticized. Various researches display that partnership between the physician and the patient based on mutual understanding and trust has influence on the results of a therapeutical process. The success of consultation depends on a mutual agreement to the etiology, diagnosis and the way of treatment. The higher the equivalence rate of partnership between the therapist and the patient is, the more the latter will be liable to follow the plan of the treatment [25-27]. During the study, it had been noticed that rarely did the patient's opinion and the partnership while consuming pharmaceuticals have any influence on the psychiatrists' selection. Only 15 per cent of the respondents take into consideration the opinion of the patients. Obviously, in Lithuanian psychiatry

the paternalistic aspect of the therapist – patient model is still strong.

In summary, a glance at the opinion of a part of psychiatrists on the antidepressants and the patterns of their prescription reflects national tendencies of pharmaceutical prescriptions. Often were the SSRI group antidepressants chosen as effective and well tolerated pharmaceuticals. Interestingly, according to studies performed in other states, the priority is given to other antidepressants. For instance, in France, clomipramine, paroxetine and amitriptyline are estimated as the most effective antidepressants and tianeptine, paroxetine and citalopram as well tolerated (28). In the United States, citalopram, bupropion and sertraline are prescribed most often. In some countries, there is an opinion that TCA is already history and the prescription of this pharmaceutical reflects the malpractice and negligence of the psychiatrist [29].

Conclusions

The results of the research disclose that the psychopathological peculiarities of depression can be one of the most important criteria in antidepressant selection. However, in many cases, the subtype of depression is ascertained empirically and based solely on the personal experience and clinical practice of the psychiatrist. There are no clear diagnostic criteria or practical guidelines for the reliable verification of the psychopathological subtype of depression. It has been assumed that it is expedient to maintain scientific research on drawing these guidelines, which would allow for the selection of a more adequate and prompt treatment for the patient.

Limitations and weaknesses

Limitations and weaknesses of the survey have mainly to do with the investigated group was generally inpatient departments' psychiatrists. Also, there were not included all types of depression. We were especially interested in these subtypes of depression with psychopathological anaesthetic, adinamic and anxious structure and different clinical features but with no guidelines on how to treat them. In this survey we discus on Lithuanian psychiatrists' opinion on treatment approach to make it clear if it is need in such practical guidelines that could help or make specialists work easier. That is why we do not discus on ECT and psychotherapy. Moreover, there is only one hospital where ECT is available in Lithuania. Therefore we attach importance to adequate antidepressant selection. We want to admit that psychotherapy is mostly provided by psychologists – psychotherapists in Lithuania.

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