

The Potential Role of the Pharmacist in Supporting Patients with Depression – A Literature-Based Point of View

This article was published in the following Dove Press journal:
Integrated Pharmacy Research and Practice

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Objective: The current article is aimed at identifying the best practice for counseling around depression in community and outpatient pharmacies, resulting in a draft guideline, proposing key steps and an algorithm for integration of community pharmacists into care for patients with depression.

Methods: A literature review was performed followed by a detailed analysis, for the purpose of creation a short draft document used as a basis for creation of a guideline for pharmaceutical care for patients with depression. The technological scheme PRISMA flow diagram was applied. The paper is based on current knowledge, taking into consideration already published articles, guidelines, and recommendations about pharmaceutical care for patients with depression, giving a basis for further studies.

Results: This paper includes two main sections: 1) depression – a short description of the main symptoms, risk factors and pharmacotherapy guidelines available in Bulgaria important for the purposes of ensuring qualitative community-based pharmaceutical care; and 2) the pharmacists' role in providing high-quality care – the main aspects of pharmaceutical care for patients with depression with specific examples.

Conclusion: The involvement of pharmacists in supporting depressive patients is crucial taking into account the specific characteristics of the pharmacological treatment: delayed onset of clinical results, risks in case of sudden pharmacotherapy abruption without physician consultation, multiple adverse drug reactions and drug–drug, drug–food and drug–alcohol interactions, etc. The current article could also be used as an initial document for creating a methodological guideline for providing pharmaceutical care services for patients with depression.

Keywords: depression, drug-related problems, pharmaceutical care, pharmacists, guideline

Background

Pharmaceutical care is a responsible provision of drug therapy for the purposes of achieving definite outcomes and improvement of patient's quality-of-life.¹ The main responsibilities of the pharmacists are defined as a result of long-term studies: 1) to ensure that all medications are appropriate, effective, and safe for a particular patient, and 2) to identify, solve, and prevent various drug-related problems (DRPs).² In 2013 a working group formed by investigator members of the Pharmaceutical Care Network Europe (PCNE) preformulated the definition so as to respond to the current expectations and views: "Pharmaceutical Care is the pharmacist's contribution to the care of individuals in order to optimize medicines use and improve health outcomes".³

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Depression is a common psychiatric illness, which is associated with several specific symptoms such as depressed mood, markedly diminished interest or pleasure in activities, psychomotor retardation, weight loss or weight gain, fatigue or loss of energy, feelings of worthlessness or guilt, recurrent thoughts of death, or recurrent suicidal ideation, etc.⁴ Being chronic in nature and affecting people of working age, depression leads to great economic and financial burden, which is also evaluated in a number of studies.^{5,6,7} Moreover, the World Health Organization (WHO) reports that depression will be the second leading cause of disability in the world by 2020.⁸ Non-adherence to antidepressants, which is defined as being over 75% after 6 months, could lead to a lack of effect, to higher costs and significant burden for the patient, family, and society.⁹

Pharmacists may play a significant role in the primary care for patients suffering from depression, giving advice, recommendations, counseling about medicines, following up the patients for drug-related problems, and assessing patients' adherence on the basis of their skills and knowledge about the medicines.¹⁰ The community pharmacist is recognized as a crucial member of the multidisciplinary primary care team for all patients with chronic and acute diseases.¹¹ Pharmacist-provided patient care services are proved to bring significant benefits on patient health outcomes.¹² Gomes et al¹³ evaluated the effectiveness of pharmaceutical care services and their influence on the patients' quality-of-life. As a result of ensuring various interventions for increasing the level of compliance and educational programs, the depressive symptoms were reduced and the quality-of-life was improved ($P < 0.05$). Another study among patients with depressive disorder demonstrated quality-of-life improvement, improved adherence, and effectiveness of the therapy as a result of pharmaceutical care services.¹⁴ In comparison with the standard care, pharmaceutical care provides a reduction in the number of hospitalizations and emergency visits not only in patients with depression, but also in patients with bipolar disorder.¹⁵ Rubio-Valera et al⁹ found a probability of 0.71–0.75 for community pharmacy intervention vs usual care in depressed patients initiating treatment in terms of improved adherence level and Quality Adjusted Life Years (QALYs) to be cost-effective.

Searching in the literature we identified only review papers, a pharmacist guided protocol for improved of monitoring patients treated with antidepressants, and physician-focused clinical practice guidelines or some local implemented instructions regarding pharmaceutical services for this group of

patients.^{16,17,18,19} In 2018, the Royal Pharmaceutical Society highlighted the need for implementing the pharmacists' potential for supporting people with mental disorders without presenting any specific and concrete guidance.²⁰ Moreover, the role of the pharmacists and their unique skills in medication management, provision of drug information, and counseling patients with mental diseases is clearly identified in a recent study by Rubio-Valera et al.²¹ Therefore, pharmacists all around the world need a detailed guideline providing algorithms and instructions on how and when pharmaceutical care should be provided to patients with depressive disorders.

The current article aimed at identifying the best practice for counseling around depression in community and outpatient pharmacies, resulting in a draft guideline, proposing key steps and algorithms. The article gives a short description of the main symptoms, risk factors, and pharmacotherapy guidelines important for the purposes of ensuring qualitative community-based pharmaceutical care for patients with depression. It also highlights the pharmacists' role in providing a high-quality care presenting the main aspects of pharmaceutical care for patients with depression presenting the most common identifiable drug-related problems among the observed group of patients.

Methods

A literature review of the published literature regarding pharmaceutical care, depression treatment, and role of the pharmacist in the care for patients with depressive disorder was performed. A detailed analysis for the purpose of creating a short guideline for pharmaceutical care for patients with depression was made. The discussion about the guideline's structure and further validation of the drafted guideline are planned to be the next steps. The paper is based on the current knowledge taking into consideration already published articles, guidelines, and recommendations about pharmaceutical care for patients with depression.

A search was conducted in the Internet based scientific data base PubMed as well as in other sources, such as paper-based journals and scientific books. The key words used were depression, pharmaceutical care, pharmacists, and pharmacy services. A particular consistency was followed:

1. Defining the study question: What are the best practices for counseling around depression in community and outpatient pharmacies?
2. Input the key words in the database PubMed Clinical Queries – “depression” AND “pharmaceutical care”

- OR “pharmacy services “AND “pharmacists” AND “community pharmacy” OR “outpatient pharmacy”.
3. Other relevant sources of information were also reviewed, and suitable studies were selected.
 4. The search for the available studies in PubMed was initiated and the details shown by the system were subdivided into three categories: clinical studies, systematic reviews, and medical genetics.
 5. The studies were analyzed following the PRISMA flow diagram. The duplicated studies were withdrawn from the analysis. Studies were selected only if they met the following inclusion criteria: 1) The studies were free full text systematic reviews, government documents, reports, comments, classical articles, or guidelines; 2) The objects in the studies were patients with depression (no limitation regarding the age); 3) Studies were in English; and 4) Studies including specific drug-related problems and ways for overcoming and preventing them. The exclusion criteria were: 1) duplicated studies; 2) language different from English; 3) studies focusing mainly on efficacy of specific therapies for depression; and 4) studies which covered patients who did not suffer from depression but from other mental disorders;
 6. The technological scheme PRISMA Flow Diagram was applied.

Results and Discussion

There were 77 papers relevant to our research question: 47 in PubMed and 30 from other sources (books, paper-based reports, guidelines, and articles). The study selection process is presented in [Figure 1](#). No potentially relevant studies after duplicates were removed. After reviewing the titles, abstracts, and the full publications, 39 of the articles meeting exclusion criteria were excluded and only 38 were summarized.

The characteristics of the included studies are initially analyzed, summarized, and combined for the purposes of presenting initial ideas for creating a guideline. They are presented in the current part of the article as we are planning to present a discussed and validated version of the guideline in a further more detailed paper.

Depression – Symptoms, Epidemiology, and Treatment

Depression is a common psychiatric disorder affecting more than 300 million people worldwide. It causes

significant distress, limitations in personal and social functioning, and worsens the quality-of-life of those affected.^{22,23} The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) outlines specific criteria for the diagnosis of depression. Some of the most specific symptoms are depressed mood, loss of interest or pleasure, significant weight loss or weight gain, a slowing down of thought and a reduction of physical movement, fatigue or loss of energy, feelings of worthlessness or excessive or inappropriate guilt, diminished ability to think or concentrate, recurrent thoughts of death or suicidal thoughts.^{24,25} Among all mental disorders, depression is related to the highest risk of suicide, followed by schizophrenia and alcohol abuse.²⁶ The main causes for depression are genetic factors, personal predisposition, concomitant diseases, family history, huge life changes (negative or positive events), or social determinants (stress, isolation, loneliness, unemployment).²⁷ Depression might be in mild, moderate, or severe form, which is defined after complex clinical evaluation based on the number, type, and severity of the symptoms. According to the monoamine hypothesis, depression is characterized by diminished activity of monoamine neurotransmitters (predominantly norepinephrine, dopamine, and serotonin) in the brain. The amygdala, the thalamus, the hippocampus, and the prefrontal cortex play significant roles in depression, where the low levels of monoamines cause the symptoms of dysthymia, anhedonia, lack of motivation, lack of activity, fatigue, insomnia, and cognitive effects. Depression is associated with chronic stress, which overactivates the hypothalamic–pituitary–adrenal axis, causing elevated levels of cortisol, induction of fight-or-flight response, and overactivation of the autonomous nervous system with somatic symptoms (tachycardia, palpitation, shortness of breath, and diaphoresis by overactivation of the sympathetic nervous system and gastrointestinal symptoms by overactivation of the parasympathetic nervous system). Chronic stress also changes the immune response and causes reduced neuroplasticity. Early losses and trauma experiences significantly increase the risk of depression later in life through their effect on the limbic system.^{28,29}

Pharmacotherapeutic guidelines for treatment of psychiatric disorders present the main principles of depression treatment on the basis of severity, age, and concomitant diseases



PRISMA 2009 Flow Diagram

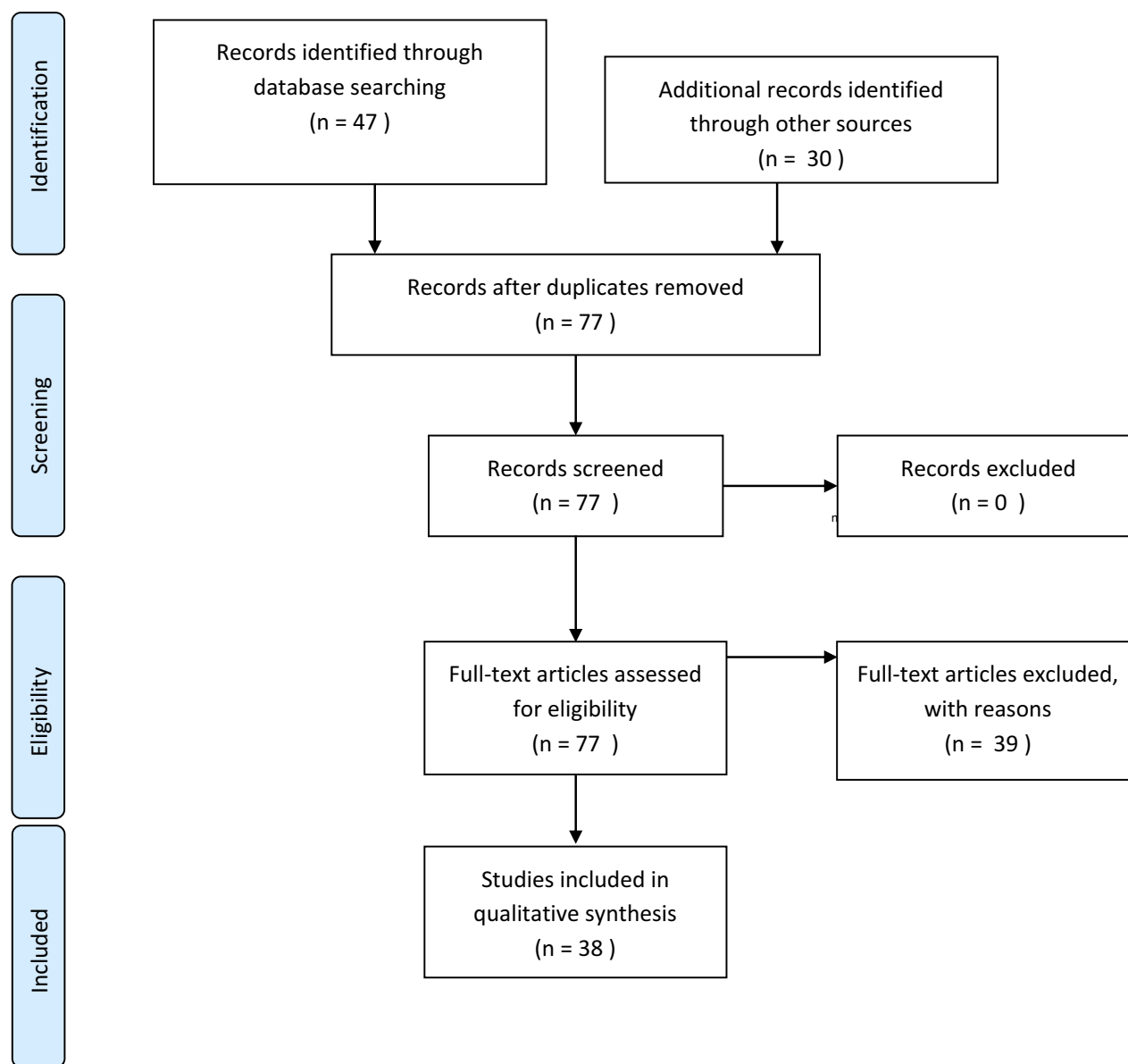


Figure 1 PRISMA flow diagram. Adapted from: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 6(6): e1000097. doi:10.1371/journal.pmed1000097.

(Figure 2). The goal of treatment is achieving remission and full recovery of the patient's social functioning.²²

The first antidepressant (AD) was discovered in the 1950s, and several pharmacological groups are available now: monoaminooxidase inhibitors, selective inhibitors of serotonin reuptake (SSRIs) and/or noradrenaline (SNRIs),

tricyclic and tetracyclic antidepressants, SPARI, and - multimodal AD (Figure 3).^{30,31} The first line therapies are: SSRIs, SNRIs, and serotonin antagonist and reuptake inhibitors (SARIs), noradrenergic, and specific serotonergic antidepressant (NaSSA (mirtazapine)). Tricyclic AD, MAOIs, and others AD (tianeptine, agomelatine

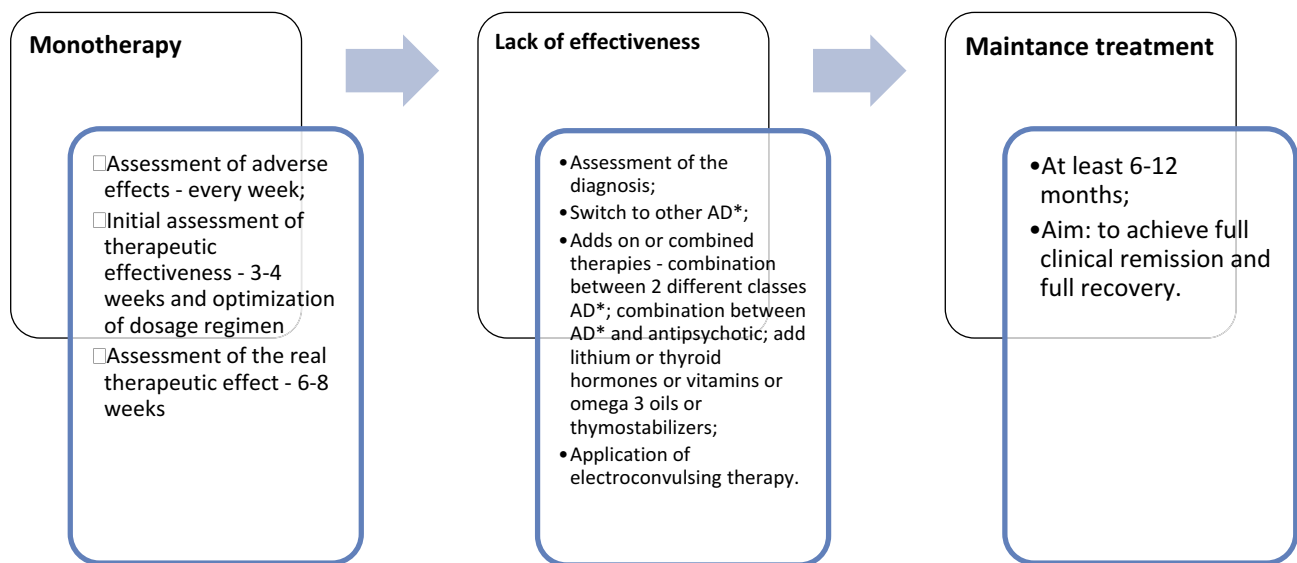


Figure 2 Pharmacotherapy principles for depression.
Abbreviation: AD, antidepressants.

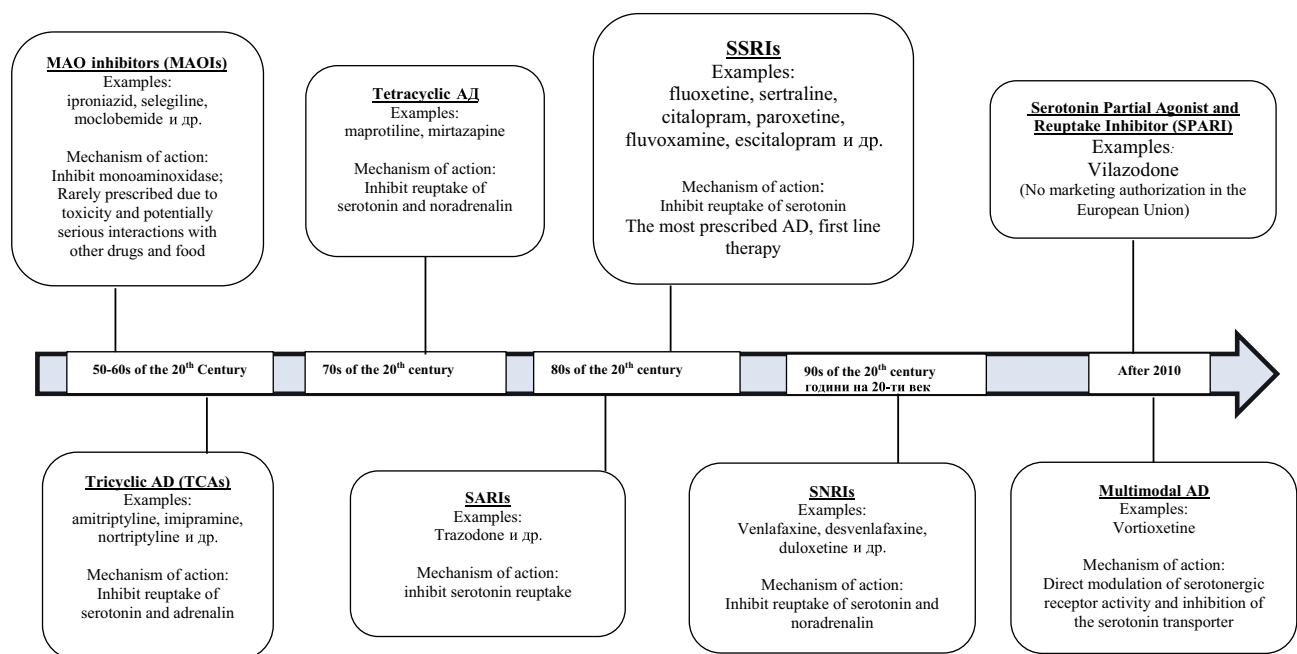


Figure 3 Main pharmacological groups antidepressants.

(melatonergic)) as well as some antipsychotics are indicated as second line therapy.³²

Pharmaceutical Care Aspects for Patients with Depression

The pharmacist's obligations in the process of providing pharmaceutical care are: (1) collection of specific information for the patient's demographic data, history

of disease, medication therapy (current therapy, dose, therapeutic regimen, allergies, immunizations, previous drug therapy), current complaints; (2) analyzing the collected information so as to identify drug-related problems, to assess whether all medications are effective and safe for the patient as well as patient's adherence and compliance.^{33,34} Follow-up was aimed at defining the therapy effectiveness and long-term safety,

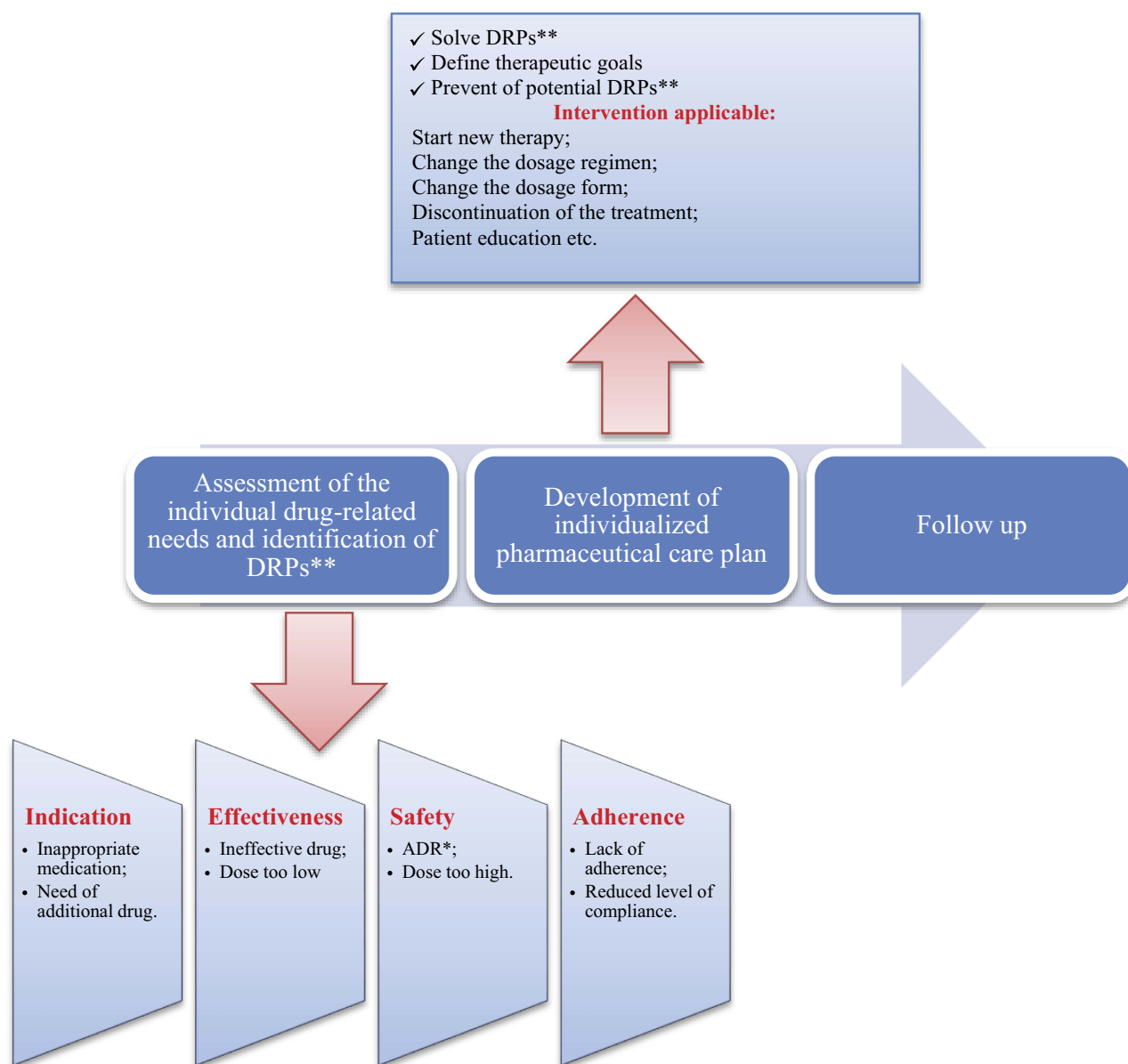


Figure 4 Steps and key element of pharmaceutical care.

Abbreviations: ADR, adverse drug reaction; DRP, drug-related problem.

assessing clinical results, defining the level of achieving the goals, level of adherence, and reassessing of new potential or actual DRPs (Figure 4).³⁵

The concepts and goals of provided pharmaceutical care could be based on the type of patient's visit: initial or follow-up (Figures 5 and 6).³⁶

Communication with the Patients and Their Family Members/Caregivers

Establishment of contact with the patient with depression, asking appropriate questions

Communication with patients with mental problems

presents a challenge for every pharmacist. Despite the various communication difficulties, the pharmacist should apply innovative strategies for overcoming them.³⁷ The pharmacist should play the dominant role during the conversation, applying appropriate voice tone, using simple and short sentences and body language without discussing several issues simultaneously – a focus should be made on a specific problem through a variety of technical and non-technical skills.³⁸ The consulting pharmacist should pay attention to and adapt the discussion towards patient's difficulties related to verbal speech and memorization.

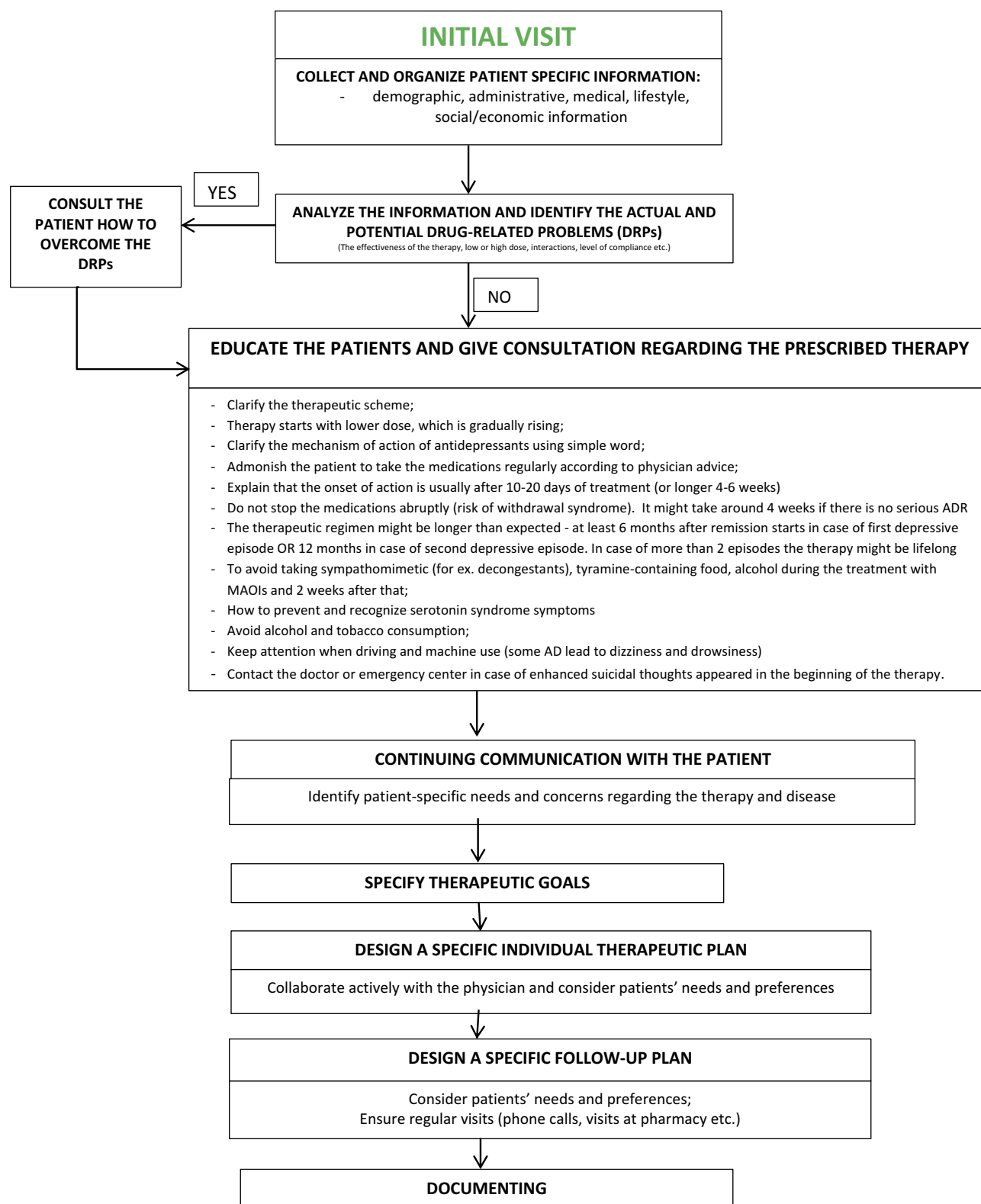


Figure 5 Algorithm for applying pharmaceutical care for patients with depression – initial visit.

The pharmacist as a health professional is able to recognize the initial symptoms, to identify the risky groups, and to target vulnerable people to join supporting groups, initiate

nonpharmacological treatment, or make an appointment with a psychiatrist for prescribing eventually of the most appropriate pharmacotherapy. Asking open-ended and closed questions,

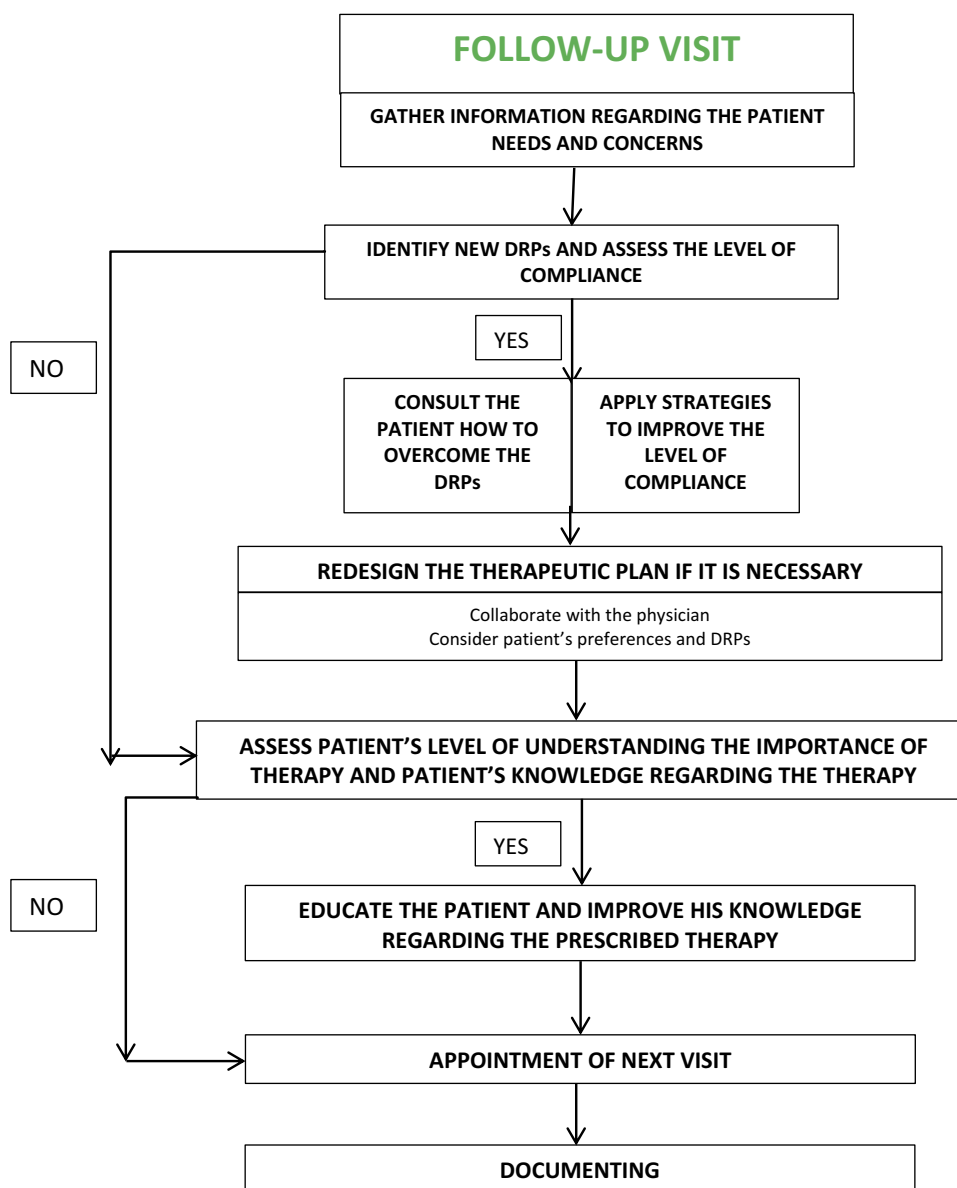


Figure 6 Algorithm for applying pharmaceutical care for patients with depression – follow-up visit.

avoiding confusing questions and interrupting patients while he/she is speaking, listening actively, demonstrating empathy and using the most appropriate body language (eye contact, smile, understanding look, etc.) could help the pharmacist to significantly improve the communication process (Table 1). Moreover, the community pharmacists have frequent contact with patients with depression and other mental health problems which gives them the possibility to engage the patients more actively in the therapeutic process.³⁹

Education of the Patient and His/Her Relatives/ Caregivers

Give Additional Information About the Disease and Symptoms
As one of the most accessible health professionals, the

pharmacists could assist the risk groups (postpartum women, geriatric patients, teenagers, etc.) to visit a psychiatrist. Participating in community-based health campaigns, assuring appropriate advice and information flyers including suitable directions for rational drug use, clarifying the importance of therapy adherence, nonpharmacological treatment approaches and lifestyle modification, the pharmacists could not only improve community health but also contribute in decreasing the stigma of depressive disorders.⁴⁰ Different studies confirmed the capability of the pharmacist to be involved in screening programs and risk assessment services for depression.^{41,42} Kondova et al⁴³ identified that 70% of all patients screened in a community

Table I Questions Asked by Pharmacists and Their Purposes

Question	Purpose
What medications do you take in what dose and when do you take them?	<ul style="list-style-type: none"> The purpose is to understand whether the patient understands the prescribed therapy and administers it properly
How long do you take these medications according to the current dosage regimen? When was the last time your therapy was changed?	<ul style="list-style-type: none"> The purpose is to clarify the effectiveness and appropriateness of the therapeutic regimen
How do you feel after taking your medication(s)?	<ul style="list-style-type: none"> The purpose is to clarify the effectiveness and appropriateness of the therapeutic regimen
Do you consider stopping abruptly the medications for depression? Do you think interrupting the therapy suddenly is appropriate?	<ul style="list-style-type: none"> In this way the pharmacist can identify the level of patient's knowledge regarding the medications and therapeutic regimen
Do you consult with a pharmacist when buying OTC medicinal products?	<ul style="list-style-type: none"> To identify timely drug-related problems
Would you like to ask some questions regarding the medications you take?	<ul style="list-style-type: none"> To assess the level of knowledge and to stimulate the patient to be an active partner in the process
Have you ever had suicidal thoughts?	<ul style="list-style-type: none"> To assess the severity of the disease
	<ul style="list-style-type: none"> To assess the history of condition
	<ul style="list-style-type: none"> To indicate worsening of the condition
Do you see your psychiatrist regularly?	<ul style="list-style-type: none"> To identify the level of adherence to therapy
	<ul style="list-style-type: none"> To identify the level of patient's involvement in the therapeutic process

pharmacy setting have positive results of PHQ-2 test, and 55% of them had indications of mild-to-moderate depression. One of the possible methods for timely diagnosis is through giving various depression screening tools (Patient Health Questionnaire (PHQ-2 and PHQ-9), Self-Rating Depression Scale (Zung scale (SDS)) or Von Zerssen scale).⁴⁴

A systematic review published in 2018 concluded that educational materials, outreach visits, and feedback can improve counseling in community pharmacy settings.⁴⁵ Therefore, additional information regarding the following topics should be given to patients with depression: what the first signs of depression are, how important the consultation with a psychiatrist is due to the risk of serious complications, how the medications should be taken, etc. The relatives and friends could also be involved in the team caring for patients with depression (Figure 7).

Understanding the Principles of Non-Pharmacological Treatment

There are a lot of nonpharmacological approaches which could be implemented in the individualized care plan for depressive patients: cognitive behavioral therapy [CBT] (the psychotherapist identifies irrational and dysfunctional patient's thoughts

and looks for new more realistic ones; the purpose is to overcome the negative thinking and to modify the existing behavioral models); physical activity – 3–5 times per week, 20–30 minute nature walks, etc.; light therapy – in case of seasonal depressive disorders; music therapy; acupuncture; food supplements (omega 3 oils, Hypericum perforatum); stress management practicing yoga, meditation; healthy eating and sleeping habits; cognitive bibliotherapy.^{46,47,48}

Assuring Effective, Safe, and Appropriate Pharmacological Treatment

Giving Instructions about Dosage Regimen and Therapeutic Scheme

Giving detailed guidance regarding pharmacotherapy by the provider of pharmaceutical care, the service pharmacist, is crucial. The educational process includes an explanation of the therapeutic scheme, the mechanism of action of antidepressant (AD), avoiding complex medical words, and clarification that the onset of action of the prescribed AD is usually after 10–20 days (or longer: 4–6 weeks) and the therapy is continuous (2–6 months) depending on the severity of the disease. The initial dose is lower and it increases gradually. The patient must adhere to the therapeutic scheme as long as it is prescribed knowing that there is no risk of addiction.⁴⁹ The therapy must

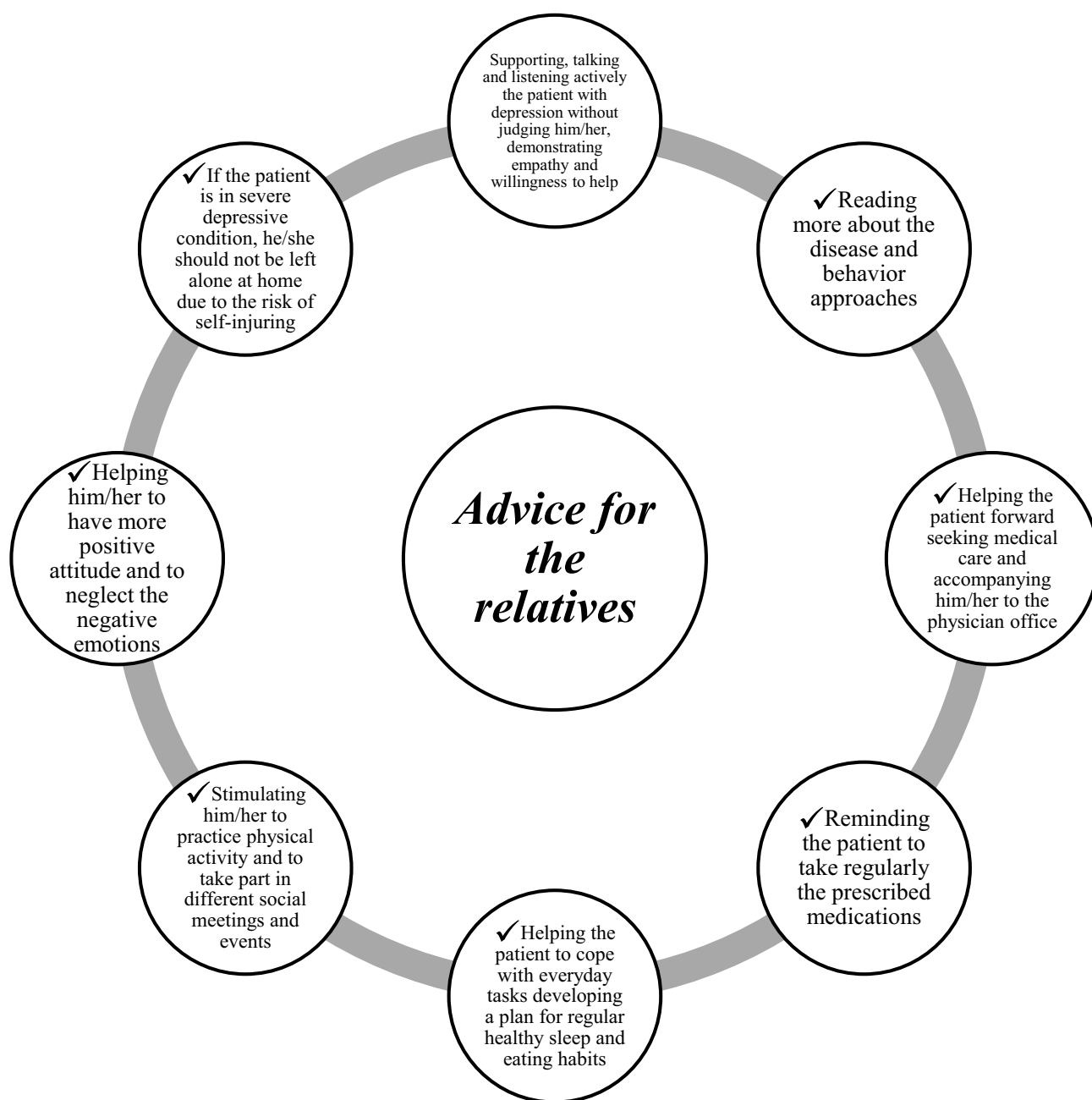


Figure 7 Pharmacists' advice for the relatives of those affected by depression.

not be stopped suddenly – a period of 2–3 weeks is required. Even if the symptoms relieve the therapy must be continued and not stopped without the physician's recommendation due to the risk of withdrawal syndrome (irritability, headache, insomnia, palpitations, sweating, and others lasting several days). Regular monitoring should be provided to every patient with depression in order for suicidal thoughts to be identified in a timely manner. Depressive symptoms are assessed every week or every other week. So, the pharmacist should remind the patient to consult with his/her physician regularly.

Identification and Prevention of Drug-Related Problems

Understanding the Most Common Adverse Drug Reactions (ADRs) and Giving Advice for Overcoming Some ADRs

Informing About the Possible Drug–Drug and Drug–Food Interactions. An essential element of pharmaceutical care services is the so-called medication review aimed to optimize medicines use and improve health outcomes.⁵⁰ Therefore, serious drug-related problems (DRPs) could be identified or prevented, and specific interventions for

the prevention and overcoming of the revealed DRPs could be recommended. PCNE developed a detailed guideline of DRPs, classifying them into several groups according to the type of problems, the causes, planned interventions for overcoming, level of acceptance, status, etc. (Table 2). According to the causes, DRPs are related to prescribing, dispensing, and drug use (Table 3).⁵¹

Identification and prevention of actual and potential DRPs is one of the main tasks of the pharmacists in the process of providing medication management services. The patient who suffers from depression should be acquainted with the possible adverse drug reactions related to the therapy with antidepressants. The most frequent ADRs are dryness in mouth, tachycardia, tremor, vomiting, sedation, weight gain, arrhythmias, insomnia, skin reactions – photosensitization, reduced sexual functions, etc. Some of them are dose-dependent and decreasing over time. Tobacco consumption might influence the effect of antidepressants – there are several studies showing evidence regarding the reduction of plasma concentration of fluvoxamine, duloxetine, mirtazapine, and trazodone in smokers in comparison with non-smokers. The therapy choice should be based on the status of the patient – whether he is a smoker

Table 3 Classification of DRPs on the Basis of the Causes⁵¹

	Group of DRPs	Examples
Related to prescribing	Drug selection	Inappropriate drug; contraindications; duplication of drugs; too many drugs for one indication, etc.
	Drug form	Inappropriate drug form
	Dose selection	Dose too low or too high; wrong instructions for dosing, etc.
	Treatment duration	Too short or too long
Related to dispensing	Dispensing	No availability of the drug; no provision of the required information; wrong drug, wrong instructions, etc.
Related to drug use	Drug use process (administered by the health specialist or by the patient)	Inappropriate time dosing; patient abuses drug; takes too high or too low dose; wrong way of administration; inability to use the drug correctly, etc.

Table 2 Classification of DRPs According to PCNE⁵¹

	Code 8.01	Groups of DRPs
Problems	P1 P2 P3	Effectiveness (therapeutic failure, lack of effect, Untreated symptoms) Safety (ADRs) Others (inappropriate drug, etc.)
Causes	C1 C2 C3 C4 C5 C6 C7 C8	Drug selection Drug form Dose selection Treatment duration Dispensing Drug use Patient related Other
Planned interventions	I0–4	No intervention; at prescribing, patient, drug level; other
Intervention acceptance	A1 A2 A3	Intervention accepted Intervention not accepted Other
Status of the DRP	O0 O1 O2 O3	Unknown Solved Partially solved Not solved

or non-smoker, due to the risk of pharmacokinetics interactions.⁵² Alcohol consumption is also contraindicated during the therapy with antidepressants. The pharmacist should clarify that antidepressants might lead to drowsiness and disturbances in concentration and therefore may influence the ability to drive and use machines. The appearance or enhancing of suicidal thoughts might be reported in the beginning of the therapy with AD, but it could not be a reason for interrupting the therapy – the patient and their caregivers should be advised to contact their psychiatrist or emergency center for more information.

Information regarding serotonin syndrome symptoms (SSS) and their prevention and recognition should be provided by the consulting pharmacist. SSS (hyper-reflexion, tremor, dizziness, parasympathetic reactions, confusion, etc.) can be a result of simultaneously taking serotonin agonist and serotonergic medicinal products.²⁴

Other DRPs which could be identified by the pharmacist are: lack of effectiveness of the prescribed medicines, dose too high or too low, drug-drug, drug-food supplements or drug-food interactions (Table 4), and low level of adherence.⁵³ The pharmacist is able to give practical advice for overcoming ADRs reported as a result of AD treatment (Table 5).^{54,55}

Table 4 Most Common Adverse Drug Reactions and Interactions Described for AD

Medication (INN)	ADRs	Interactions
Amitriptyline	Arrhythmias, heart arrest, photo dermatitis, constipation, dryness in mouth, sexual dysfunctions	+Clonidine ≤ hypertonic crisis; +MAO inhibitors ≤ high blood pressure, hyperthermia, convulsion
Citalopram Escitalopram Fluoxetine Fluvoxamine Paroxetine Sertraline	Nausea, vomiting, insomnia, dryness in mouth, headache, hypotension, tremor, etc.	+MAO inhib.; +serotonergic medications (triptans) ≤ SSS +H. perforatum ≤ increased risk of ADRs; +NSAIDs; p.o. anticoagulants ≤ risk of bleeding
Venlafaxine	Dryness in mouth, headache, sweating, nervousness, drowsiness, dizziness, etc.	+serotonergic medications (triptans, SSRIs) ≤ SSS
Tianeptine	Tachycardia, insomnia, headache, dryness in mouth, myalgia, insomnia, etc.	+MAOinhibitors ≤ collapse, hyperthermia, convulsions

Notes: Some ADRs like nausea, diarrhea, and anxiety appear only in the beginning of the therapy. A consultation with a physician is required in cases of lack of improvement. Tricyclic antidepressants (TCA) are not indicated in cases of recent myocardial infarction. Dose adjustment or switch to another medication in the case of lack of effectiveness at a minimum 6 weeks is required.

Table 5 Some ADRs and Advice Given by Pharmacists for Overcoming Them

Adverse Drug Reactions (ADRs)	Advice for Overcoming the ADRs
Dryness in mouth	Application of artificial saliva products, sugar free gum, vitamin c tablets (short-term use in order to prevent tooth erosion)
Antimuscarinic effects (blurred vision, sedation, confusion, etc.) caused by TCA	A strict monitoring in elderly patients as well as taking medications at bed time in order to prevent falls and fractures are recommended
Constipation	Advice for regular healthy eating habits: more fiber, liquids, warm water in the morning, abdominal massage, laxatives
Sedation	Taking the medications at bed time; otherwise – dose reduction
Nausea	Avoiding sweet, salty, or fatty food; taking the medicine after a meal, taking smaller portions of food during the day
Insomnia	Taking the medications in the morning
Sexual disturbances caused by SSRIs	Dose reduction or change therapy; inclusion of sildenafil at a pinch
Hypertension caused by venlafaxine	Blood pressure monitoring regularly; reduction of venlafaxine dosage; change the therapy
Tachycardia caused by TCA	Dose reduction or change the therapy
Weight gain	Dose reduction or change the therapy
Orthostatic hypotension	The patient should avoid standing up abruptly, reduce caffeine intake, drink more water, practice more physical exercise to strengthen the leg muscles
Headache	Dose reduction or change the therapy
Photosensitization caused by TCA, SSRIs, venlafaxine	Applying sun cream every 2 hours and avoiding sunbathing between 10 a.m. and 4 p.m.

Creation of Individualized Therapeutic Plan and Defining of Specific Goals

The main therapeutic goal in patients with depression is overcoming the symptoms with reducing as much as possible the adverse drug reactions, prevention of suicidal thoughts, and improving the remission rates. The

pharmacist may be actively involved in achieving the goals through realization of various educational programs for clarifying how important the therapy is. Development of an individualized therapeutic plan in collaboration with the psychiatrist and the affected patient and his family members/caregivers, taking into consideration the

individual needs and preferences could significantly optimize the therapy and improve the level of adherence.

Assuring Adherence and Assessment of Adherence Level

Literature data shows that 56% of patients taking antidepressants do not adhere to the prescribed therapy for different reasons such as patients' beliefs, side-effects, or cost.⁵⁶ The patient should be convinced that the disease is curable, the therapy is based on the severity of the disease, and only strict adherence, psychotherapy provided by a specialist, and support of family and friends may lead to improvement and full recovery. Assessment of the level of adherence might be made during the regular patient's visits on the basis of the number of dispensed packages and the number of executed prescriptions, after a conversation with the patient regarding his attitude toward the therapy and the therapeutic plan. A study revealed that patients suggest several pharmacy services to improve the adherence to antidepressants such as: a reminder e-mail before each refill or a small group education session.¹⁰ Studies concluded that the pharmacists' role is crucial for improving the level of adherence to antidepressants.^{57,58} A systematic review found that pharmacist interventions could be effective in improving the adherence level to antidepressants by 15–27%.⁵⁷ The individualized plan might be optimized on the basis of the reported adverse drug reactions and other DRPs so as to increase the level of adherence – for example to take the medication in the evening in order to avoid sedation during the day or to take the medication in the morning so as to prevent insomnia.

Follow-Up and Reassessment of DRPs

Patients should be aware of the possible ADRs accompanying AD therapy and be reminded to report all ADRs that occur. Tracking the status and reassessment of DRPs is essential and can be performed on the basis of a predefined plan at the pharmacy during the next visit or through telephone calls.⁵⁹ A published study highlights the importance of clinical pharmacists as he/she is able to improve mild-to-moderate mental health conditions, promote interdisciplinary collaboration between various medical specialists, and to improve the process of documentation and follow-up.⁶⁰

Conclusion

Application of pharmaceutical care services for patients with depression is effective and leads to condition improvement, reduction of the side-effects, timely identification of and the overcoming of potential or actual DRPs, and

improvement of patients' quality-of-life. Collaboration between psychiatrists, pharmacists, and the active inclusion of the affected and their relatives in the therapy could optimize and improve the complex care for patients with depression and achieving the targeted therapeutic outcomes.

The current article could be used as an initial proposal for creating a methodological guideline for providing pharmaceutical care services for patients with depression. A number of follow-up studies are needed to assess the feasibility of implementing community-based pharmaceutical care for patients with depression, the level of knowledge of pharmacists on depression, the effect of pharmaceutical care on this patient group, and the economic benefits from the point of view of society.

Acknowledgment

This work was supported by the Bulgarian Ministry of Education and Science under the National Program for Research 'Young Scientists and Postdoctoral Students'.

Ethical Approval

This article does not contain any studies with human participants or animals performed by any of the authors.

Compliance with Ethical Standards

The tables and figures are original. No ethical issues exist.

Disclosure

All authors declare that they have no competing interests.

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