ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 8| Issue: 8| August 2022|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2022: 8.205 || ISI Value: 1.188

THE EXISTING LANDSCAPE OF DEPRESSION.REVIEW

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Article DOI: https://doi.org/10.36713/epra11089
DOI No: 10.36713/epra11089

ABSTRACT

Introduction: *Depression is a global health problem that has been increasing in recent years, but it is still underdiagnosed and it's not taken seriously enough. For this reason, it is vital for health workers to know their correct diagnosis and treatment to prevent patients from reaching their worst outcome, which is suicide.*

Objective: *To examine how these patients have been approached and managed, and the effectiveness of both pharmacological and non-pharmacological therapies, based on review articles from the last five years.*

Methodology: *a total of 43 original and review articles, collected from the Cochrane Library, PubMed and Google Scholar databases, were searched for the term "Depression". The documents were found in Spanish and English. Some articles were excluded due to lack of updated information and lack of relevance for our literature review.*

Results: *there is a fundamental pillar for the treatment of depression, based on psychological therapies (primary and fundamental element), pharmacotherapy and, as a last line, electroconvulsive therapy. The drugs generally used are serotonin reuptake inhibitors and serotonin and noradrenaline reuptake inhibitors. There are other therapies such as acupuncture, music therapy, which have shown some benefit.*

Conclusions: *throughout this time, it has been determined that current diagnostic modalities have made it possible to diagnose early and a greater number of people suffering from depression, starting with psychotherapy, and administering antidepressant drugs in the absence of response to psychotherapy.*

KEY WORDS: *depression, dysthymia, psychotherapy, Serotonin Uptake Inhibitors, Serotonin and Norepinephrine Reuptake Inhibitors.*

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INTRODUCTION

This review seeks to improve the knowledge of general physicians regarding depression, since it has become a global health problem that grows day by day. It is vitally important to master strategies in the correct diagnosis and treatment of this disease from the primary care health level.

According to the world health organization, depression is a disease characterized by persistent sadness and lack of interest or pleasure in activities that were previously rewarding and pleasurable. It is quite common throughout the world and is estimated to affect 3.8% of the global population, including 5% of adults and 5.7% of adults over 60 years old.

Depression has been become a serious health problem, especially when it is recurrent and has a moderate to severe intensity, affecting and altering the life quality of patients and in the worst case, it can trigger in suicide, which is the fourth cause of death in the age group 15 to 29 years.

Nowadays, we can find treatments for this disease, but they are hampered by a lack of resources and qualification in healthcare providers. That is why, the WHO is developing programs and strategies that serve to mitigate the barriers that exist in the prevention, diagnosis and treatment of this disease, which already constitutes a pandemic (WHO, 2021).

METHODOLOGY

This review focused on summarizing the most relevant aspects of the diagnosis and treatment of depression in the last 5 years. A total of 43 articles were analyzed, including reviews and original articles. Only 30 of the total bibliographies were used, because the remaining 13 were not relevant. Resources such as PubMed, Google Scholar, Elsevier, ScienceDirect and Cochrane were used as support; the keywords for the research were: "depression", "depressive symptoms" and "new trends in the treatment of depression".

RESULTS AND DISCUSSION

In the past it was believed that depression occurred only in older adults; however, over the years it has been shown that the prevalence in people over 65 years of age is only 1 to 4%, a similar or even lower prevalence than other groups. It is necessary to clarify that some groups of older adults have high rates of depressive symptoms; such is the case of those with chronic diseases at 25%; even older adults in nursing homes have a prevalence from 25 to 50% (Casey, 2017).

It would be important to talk about minor depression, which is a subsyndromal depression, which is characterized by presenting one of two main depressive symptoms plus one of three additional symptoms and it is associated with levels of disability similar to major depression. Another relevant concept to take into consideration is Dysthymia (previously known as Persistent Depressive Disorder in the DSM-5); this is a chronic form that is less severe than major depression that lasts two or more years and tends to start early in life, persisting into old age (Wilkinson et al, 2018)(Haigh, 2018).

Depression incidents per year is around 15%, varying between countries. As examples we can mention: Sweden presents an incidence of 16.4%, Beijing 10.5%, Mexico between 26 and 66%, Peru with 9.8%, Colombia with 11.5% in women and 4% in men and Chile, between 7.6 and 16.3 %. In a 2018 report, Ecuador presented a prevalence of 39%, considering age over 65 years, presence of other diseases, social situation, marital status, among others, as risk factors (Calderón, 2018).

Other situations where the prevalence of depression increases, is the absence of a partner, living in foster care institutions and the lack of physical independence. About marriage and depression, they are associated depending on the social support and the type of relationship that the couple has. (Sjöberg et al, 2017).

A Singapore study in 2016 showed that this pathology was greater in patients between 75 and 84 years old; and there was an association with the presence of comorbidities, lack of life satisfaction and the presence of disability (Subramaniam et al, 2016).

A Colombian study from 2012 mentioned that the factors that can lead to depression are: being over 90 years old, living alone, being a woman, presenting dependency, loss of self-control and not having social resources. (Segura, 2015).

A mexican study in 2017, showed that depression was prevalent in the female sex, in a ratio of three to one with men and within the triggers there was the absence of social support, isolation, absence of family coexistence and dependency to perform activities of daily living. It was also observed that hospitalized patients have a higher risk of presenting early depression, due to the presence of chronic degenerative diseases, such as: diabetes, Parkinson's, Alzheimer's, arterial hypertension, hypothyroidism and arthritis (Martínez, 2007).

A 2008 study found that depression increased the risk of cancer, arthritis, cardiovascular diseases and neurological diseases (an effect produced by a decrease in the immune response); moreover, cardiac mortality is three times higher in patients with depression. Another effect caused by this pathology is the increased risk of suicide or the occurrence of violent acts, which are exacerbated by the presence of problems related to drug abuse, social isolation and lack of employment (Bousoño, 2022).

In another study conducted in 2019, it was shown that hearing loss doubles the risk of developing depression and increases the risk of anxiety and other mental disorders. Along with impaired vision, hearing loss is a determinant with a significant effect on communication and well-being, which can lead to isolation, reduced independence, cognitive impairment and even death in older adults (Leverton, 2019). Therefore, the presence of hearing and visual impairment leads to a reduced quality of life, which subsequently develops into depression.

Now, there are several elements that are taken into account when mentioning influential factors in the progression of depression. In previous chapters we mentioned that the presence of isolation leads to depression; however, a study carried out in 2017 showed that loneliness, by affecting the patient socially and emotionally, has a different impact. Being female, 50-65 years old, separated or divorced, unemployed,

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with low education and insufficient family income was also found to be associated with depression (Zhang et al, 2018). This study confirms the arguments mentioned in the 2012 study conducted in Colombia, which mentioned that these same factors were the elements that, when present, produced a higher probability of developing depression.

What happens in relation to risk factors?

- Biological: Depression and cardiovascular disease have been shown to be related, with depression manifesting first and increasing the incidence of hypertension. Some other studies have shown that positive emotions can reduce the 10-year incidence of cardiovascular disease. Another important element is cerebrovascular disease, which is referred to as Vascular Depression (depressive manifestations following a cerebrovascular event) (Sassarini, 2016).
- Functional aspect: One of the determinants is impaired mobility and gait. In a study conducted in Mexico, this effect was demonstrated, considering that a percentage of patients who were dependent due to some type of dysfunction (62 %) were depressed. There are 10 % of older adults who show symptoms of frailty (decreased muscle mass, strength, decreased energy and decreased physiological reserves) (Sassarini, 2016).
- Cognitive aspect: There is difficulty in social integration; and a link between Alzheimer's and depression has been identified (Sassarini, 2016).
- Sleep: It is not clear whether insomnia is a factor or a consequence, so those who suffer from insomnia are at greater risk of depression and aggravation of insomnia.
- Social aspects: Isolation and low socioeconomic status are strongly associated with depression (Sassarini, 2016).
- Economic aspects: Low income and decreased social cohesion (Sassarini, 2016).
- Demographics: Depression is higher in older women, the poor, those in nursing homes and in rural areas. Women are twice as likely to suffer a depressive episode, with higher risk in the peri- and post-menopausal state. Predictors of depression include vasomotor symptoms and smoking; however, their greatest risk factor is some past history. Treatment includes antidepressants, hormone replacement therapy, psychotherapy and lifestyle modification (Zis et al, 2017).
- Anatomical aspects: The size of the hippocampus, parahippocampus, amygdala and prefrontal cortex have been hypothesized. Another theory is the presence of altered secretion and action of neurotransmitters, such as serotonin; however, this theory has merit when affecting vulnerable individuals, such as those with chronic pain, where the pathogenesis of depression and pain is caused by neuroinflammation (Malhi et al, 2018).

What happens in relation to the diagnosis?

The importance of diagnosis is based on the use of diagnostic tests and the presence of symptoms; logically, it is necessary to have some expertise and intuition to be able to detect patients who do not have such obvious symptomatology. It should be mentioned that none of the symptoms are pathognomonic and are therefore found in other psychiatric pathologies. However, there are some symptoms that are more specific to psychiatric disorders, such as: anhedonia (decrease in pleasurable sensations) (the most important symptom for diagnosis), symptoms that are more evident at certain waking hours, feelings of guilt, fatigue, weight loss or gain and insomnia. Diagnosis should be made after an episode that has lasted two weeks or more. If this episode has not resolved and has extended over time, it is called Chronic Depression. If depressive symptoms are present for at least two years, without a period of remission, the condition is called Persistent Depressive Disorder or Dysthymia (Baader et al 2012).

Depression can manifest itself in various forms with a combination of symptoms, leading to difficulty in detection, especially in the presence of other illnesses. Being aware of the symptoms increases the likelihood of diagnosis, as there is a considerable proportion of people who are not detected. For this process, there is a questionnaire called the Patient Health Questionnaire (PHQ-9), with brief questions that are generally accepted by patients and help medical personnel to detect them; it is determined that the presence of 5 or more positive items determines the presence of major depression. Routinely, the patient should be asked about their feelings and the presence of symptoms (Baader et al 2012). The questionnaire is presented in table 1.

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Tabla 1. Patient Health Questionnaire (PHQ-9) (Sadler et al, 2018)

During the last 2 weeks, how often have you been bothered by the following problems?	**Never**	**Several Days**	**More than half of the days**	**Almost every day**
1. Having little interest or pleasure in doing things	0	1	2	3
2. Feeling discouraged, depressed, or hopeless	0	1	2	3
3. Problems falling or staying asleep, sleeping too much, sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Having a poor appetite or overeating	0	1	2	3
6. Feeling a lack of self-esteem, or that you are a failure or that you will disappoint yourself or your family	0	1	2	3
7. Having difficulty concentrating on things such as reading a newspaper or watching TV	0	1	2	3
8. Moving or talking so slowly that other people might notice, or otherwise being so agitated or restless that you move around a lot more than usual	0	1	2	3
9. Thoughts have occurred to you that you would be better off dead or that you would do harm in some way	0	1	2	3
If you identified yourself with any of the problems in this questionnaire, how difficult have you found it to do your job, take care of your home, or relate to other people because of these problems?				
Nothing at all	Somewhat difficult	Very difficult	Extremely difficult	

Source: BAADER M, Tomas et al. Validación y utilidad de la encuesta PHQ-9 (Patient Health Questionnaire) en el diagnóstico de depresión en pacientes usuarios de atención primaria en Chile. *Rev. chil. neuro-psiquiatr.*

What variations exist in relation to treatment?

Psychotherapy:

Psychotherapy has been identified as the first-line intervention for mild to moderate depression. A response efficacy of 48% has been demonstrated. A 2019 study mentions that among the different techniques for non-pharmacological treatment of depression are: cognitive behavioral therapy, with 66% efficacy (identifying and modifying negative thoughts that affect emotions and behavior), behavioral activation, with 74% efficacy (managing positive activities and increasing positive interactions), and interpersonal psychotherapy (addressing interpersonal problems in a structured way). Whichever techniques are used, they should be used according to the patient's situation. Another 2018 study has shown that interpersonal psychotherapy helps when interpersonal problems are prominent; behavioral activation increases motivation and initiative, and cognitive behavioral therapy helps to modify distorted thoughts that lead to depression; in addition, improvements in sleep hygiene, significantly reducing insomnia, and promoting relaxation have been shown (Cuijpers et al, 2019). If there is no improvement after six weeks, pharmacotherapy should be initiated or referral to psychiatry.

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Problem-solving therapy, the patient learns to solve problems, based on the solutions found by the patient himself; the patient chooses the best one, a scheme is drawn up to carry it out and implement it to solve the problem. If it is not solved, the patient performs this procedure again (Azariah et al, 2019). Another therapy used is Problem Solving Therapy delivered by non-professional counselors, and these professionals teach strategies about better self-care and increased performance of pleasurable activities. This served to relieve interpersonal tensions (Gitlin et al, 2017) (Navas et al, 2016) (Park et al, 2019).

Study conducted in older adults in the parish of Sangolquí, Quito - Ecuador. 2015(Sailema & Mayorga, 2021).

Recommended activities for older adults with Depression	
The Lizards	The patient is given a box with a number of clamps, and is asked to place the pieces around the box using only the right hand; and then asked to switch hands.
Following the line	Defined strokes are placed, and the patient is asked to follow with coloured pencils.
Paint the figure	Paint the figure
Assemble the puzzle	Assemble the puzzle
Join the dots	It is an incomplete figure with dots, the aim of which is to join the dots with paints.
Tangram	It is about putting together new figures, using your creativity.
"Let's make balls"	Paper is used to form paper balls of various sizes.
"Make your favorite figure".	Plastiline is used to form various shapes
Draw your hand on paper	Draw the outline of your hand on the paper.
Pass the ball	A ball is handed out and passed to the other older adults without dropping it. Gradually increase the number of balls.
Repeat the figure	The patient has to replicate the figure in the air using only his or her lower limbs.
Step on the ball	Seated, the adults step on a ball with one foot and are told what movements to perform.
Assemble a pyramid	Patients are given ice cream sticks to form a pyramid.
" Classify them".	The patient is asked to sort a mixture of seeds, depending on whether it is peas, corn or beans.
"Cover the sheep".	A company sheep is handed out, and patients are asked to fill it with cotton wool.
Remember the figure	The patients are given cards with different models, and they have to look for the pairs among the cards.
Jenga	Remove pieces from the different levels and place them on top.
Cross the maze	They are given several mazes and must solve them.
"Who does your balloon look like?"	Each senior is given a balloon and asked to draw the faces of their classmates.
Origami	They are given sheets of paper on which they have to make origami figures.

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Consequences of doing these activities
- Positive changes in mood - Decrease in anxiety and tension levels. - Decrease in melancholy - Decrease in hostility and anger - Increased self-esteem - Decrease in depression

Source: Mencías JX, Ortega DM, Zuleta CW, Calero S. Mejoramiento del estado de ánimo del adulto mayor a través de actividades recreativas. Lecturas: educación física y deportes. 2015. Enero;20(212):1-13.

What are the pharmacological therapies currently being studied?

First of all, antidepressants have side effects, which are manifested based on severity; side effects are lower in mild depression and higher in moderate to severe depression. In a STAR*D trial treatment initiation was based on a four-level algorithm. Citalopram is prescribed in the first step. If treatment was unsatisfactory, alternative therapies are added as maintained at level one. At level two, a decision is made to switch from Citalopram to more commonly used medications (Sertraline, Venlafaxine or Bupropion); if this does not improve, another medication is added or cognitive-behavioral therapy is added. A multicentre study compared the efficacy of amitriptyline, mirtazapine, paroxetine, sertraline, venlafaxine and escitalopram, finding no significant differences over 8 weeks. For moderate to severe depression, first-line medication includes selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, bupropion and mirtazapine. There are three medications approved by the FDA for the management of depression: Vilazodone, Levomilnacipran and Vortioxetine. The Canadian Network for Mood and Anxiety Treatments guidelines include Vortioxetine and milnacipran as a first-line option and Vilazodone as a second-line option. Older classes of antidepressants, such as tricyclic antidepressants and monoamine oxidase inhibitors, have a higher risk profile than newer agents, so these newer drugs are usually used only if other agents are ineffective. Antidepressants should always be chosen based on the presence of adverse effects (the main goal is to minimize adverse effects), as well as the presence of other psychiatric disorders or specific symptoms. Therefore, drugs such as Paroxetine and Mirtazapine are not administered during the day in patients with daytime fatigue. Instead, if there is difficulty sleeping, sedative medications should be administered at night to promote sleep. When a medication is started, the lowest dose is always used, with adjustment every two weeks. Although improvement is not evident for up to two weeks, complete relief of symptoms is not evident for up to eight to twelve weeks. If substantial improvement is not evident, antidepressant medication should be rotated. If partial improvement is evident with the maximum tolerated dose of one medication, an antidepressant of another class should be added. Psychotherapy should be used in conjunction with antidepressant medication, as there is much clearer evidence of effectiveness than the use of medication alone. Once remission is evident, antidepressant treatment should be continued for at least another six months. If there is a high risk of recurrence (two or more past episodes, residual symptoms or the presence of severe symptoms), treatment should be maintained for two years or more. Recurrence of symptoms is common after an episode. In general, first-line antidepressants have manageable adverse effects. Serotonin reuptake inhibitors or noradrenaline and serotonin reuptake inhibitors should not be used with monoamine oxidase inhibitors, tricyclic antidepressants, tramadol, triptans, ondansetron or metoclopramide, because Serotonergic Syndrome (presence of agitation, confusion, fever, which can progress to seizures, coma and death) may occur (Jiang et al, 2021). The different types of antidepressant medications and their dosage are described in table 3. As a guide, an outline showing the general form of treatment of depression is presented in table 4.

Table 3. General scheme of drugs used and dosage

Drug	Doses
Selective serotonin reuptake inhibitors (SSRIs)	
Fluoxetine	20 - 80 mg/day
Sertraline	50 - 200 mg/day
Paroxetine	10 - 60 mg/day
Fluvoxamine	50 - 300 mg/day
Citalopram	10 - 40 mg/day

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Escitalopram	5 - 20 mg/day
Serotonin and noradrenaline reuptake inhibitors	
Venlafaxine	37.5 - 225 mg/day
Desvenlafaxine	50 - 100 mg/day
Duloxetine	60 mg/day
Other drugs	
Levomilnacipran	20 - 120 mg/day
Bupropion	50 - 450 mg/day
Mirtazapine	15 - 45 mg/day
Vilazodone	10 - 40 mg/day
Vortioxetine	10 - 20 mg/day
Agomelatine	25 - 50 mg/day

Source: Park LT, Zarate CA Jr. Depression in the Primary Care Setting. *N Engl J Med*. 2019;380(6):559-568. doi:10.1056/NEJMcp1712493

Table 4. General outline of treatment of depression

Objective			
The main goal of treatment is to complete remission of depression with full functional recovery and development of resilience.			
General Management			
- Discontinue any medications that potentially reduce mood. - Instilling good sleep hygiene and teaching the correct use of the medications you use - Implement appropriate lifestyle changes			
Interventions			
Genetics	***Psychological Therapies***	***Pharmacotherapy***	***Electroconvulsive therapy***
- Psycho education - Low intensity interventions - Support groups - Employment - Adequate accommodation	- Cognitive Behavioral Therapy - Interpersonal therapy - Mindfulness based cognitive therapy	First line - Selective serotonin reuptake inhibitors, serotoninand noradrenaline reuptake inhibitors, noradrenaline and dopamine reuptake inhibitors. - Melatonin agonist Second line - Tricyclic antidepressants - MAOis	Unilateral - Unilateral right Bilateral - Bitemporal - Bifrontal

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Strategies
- Combined pharmacotherapy and psychological therapy - Increasing the dose of antidepressants if warranted - Addition of other antidepressant medication with lithium or antipsychotic medication - Combined antidepressants

Source: Malhi GS, Mann JJ. Depression. *Lancet*. 2018;392(10161):2299-2312. doi:10.1016/S0140-6736(18)31948-2

Depression in older adults in times of COVID-19

In a study carried out in Ambato - Ecuador in 2021, it evaluated how the COVID-19 pandemic affected 5374 older adults with depression; it was found that the average age was 71 years, with a higher prevalence in women, 51%. Predisposing factors for the development of this disease were confinement, fear of contracting the disease and loss of independence. The consequences of the pandemic were difficulty in falling asleep, sadness and decreased appetite. Finally, it was found that 1365 patients had severe depression, 1657 had moderate depression, 847 had mild depression and 1505 had no depression (Uphoff et al, 2020).

Outlooks to consider in the management of depression

People are sometimes resistant to treatment, which is a limiting element for the quality of life of those suffering from depression. However, a trial conducted in 2021 implemented the use of electroconvulsive therapies (despite presenting memory loss as an adverse effect) as an alternative for the treatment of depression; however, there is no evidence to date to support their use (Aalberts et al, 2017). In this same scenario, a trial conducted in 2020 also proposed the use of behavioral activation therapy, a therapy based on the performance of activities that seem pleasant to the patient, for symptom improvement, demonstrating considerably beneficial results (Smith et al, 2018). An interesting technique that was studied in a 2017 trial and has been used is music therapy; this therapy, when added to conventional medical treatment, decreases anxiety levels, decreases symptoms and increases functionality (Barbato et al, 2018). Also, it has been found that the use of acupuncture tends to decrease the severity of anxiety (Nieuwenhuijsen et al, 2020). Importantly, psychological therapy should not only be limited to the depressed patient, but also to the partner and family. This effect was found in a study in 2018, where it was shown to reduce symptoms and improve relationships (Wilkinson & Izmeth, 2016). Another important aspect is the presence of problems in the field of work. In this type of patients, a combination of clinical therapy and a work-oriented intervention is preferred, because it leads to a decrease in the number of days of absence due to depression; an additional effect is the increase of functionality at work (Van Leeuwen et al, 2021). Finally, it is of vital interest that medical therapy should always be maintained for at least 1 year to reduce the risk of a recurrence(30); in addition, caution should be exercised when discontinuing the antidepressant, as abrupt discontinuation may lead to a relapse (recurrence after improvement) (Moriarty et al, 2021). Finally, in those with psychotic depression, it is recommended that an antidepressant be given together with an antipsychotic, as it has been shown to be effective (Kruizinga et al, 2021).

CONCLUSIONS

- Depression is an illness that limits the quality of life of those who suffer from it, so its early diagnosis and treatment are of vital importance.
- The most beneficial initial therapeutic modality is psychotherapy, which can be complemented by group activities. In cases where psychotherapy is not sufficient, drugs such as selective serotonin reuptake inhibitors, noradrenaline and serotonin reuptake inhibitors, whose effectiveness has been well demonstrated when combined with psychotherapy, can be administered. Other therapies, such as acupuncture, music therapy, are used as an adjunct to the basic therapy.
- Therefore, depression can nowadays be diagnosed and managed appropriately if the resources available to us are used and we know how to take advantage of them.
- It is important that strategies and programmes continue to be developed worldwide to prevent, diagnose and treat this disease so that its cases do not continue to increase and also serve to generate a social focus of awareness regarding this major health problem.

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Volume: 8| Issue: 8| August 2022|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2022: 8.205 || ISI Value: 1.188

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ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 8| Issue: 8| August 2022|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2022: 8.205 || ISI Value: 1.188

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