



Cogitare Enfermagem

ISSN: 1414-8536

ISSN: 2176-9133

Universidade Federal do Paraná

Oliveira, Priscilla Caroliny de; Deta, Felipe Pires; Paglione, Heloísa  
Barboza; Mucci, Samantha; Schirmer, Janine; Roza, Bartira de Aguiar  
ADESÃO AO TRATAMENTO NO TRANSPLANTE DE FÍGADO: REVISÃO INTEGRATIVA  
Cogitare Enfermagem, vol. 24, e58326, 2019  
Universidade Federal do Paraná

DOI: <https://doi.org/10.5380/ce.v24i0.58326>

Disponível em: <https://www.redalyc.org/articulo.oa?id=483660296014>

- Como citar este artigo
- Número completo
- Mais informações do artigo
- Site da revista em [redalyc.org](http://redalyc.org)

UABEM [redalyc.org](http://redalyc.org)

Sistema de Informação Científica Redalyc

Rede de Revistas Científicas da América Latina e do Caribe, Espanha e Portugal

Sem fins lucrativos acadêmica projeto, desenvolvido no âmbito da iniciativa  
acesso aberto

## REVIEW

**ADHERENCE TO LIVER TRANSPLANTATION TREATMENT: AN INTEGRATIVE REVIEW**

Priscilla Caroliny de Oliveira<sup>1</sup>, Felipe Pires Deta<sup>2</sup>, Heloísa Barboza Paglione<sup>3</sup>, Samantha Mucci<sup>4</sup>, Janine Schirmer<sup>5</sup>, Bartira de Aguiar Roza<sup>6</sup>

**ABSTRACT**

**Objective:** to evaluate the interventions of the multidisciplinary team that provide improvements in adherence to treatment after liver transplantation.

**Method:** integrative review of the literature. The inclusion criteria were articles published between 2012 and 2017, in the Portuguese, English and Spanish languages, performed with the adult population that had undergone liver transplantation.

**Results:** the initial search resulted in 84 publications, with 10 studies being selected. The data were tabulated according to the relevance of the content, objectives, type of intervention, number of patients and level of evidence. Four analytical categories were found: educational interventions; adoption of an individual therapeutic plan; change in the immunosuppressive regimen; emotional and psychological support and strengthening of the support network.

**Conclusion:** the multidisciplinary team should provide information about the transplantation process, perform appropriate management of immunosuppression, regularly assess the patients for signs of depression and anxiety, investigate their beliefs and values, and institute an individualized care plan.

**DESCRIPTORS:** Liver transplant; Patient compliance; Adherence to medication; Patient care team; Review.


**HOW TO REFERENCE THIS ARTICLE:**


Oliveira PC de, Deta F, Paglione HB, Mucci S, Schirmer J, Roza B de A. Adherence to liver transplantation treatment: an integrative review. Cogitare enferm. [Internet]. 2019 [access "insert day, month and year"]; 24. Available at: <http://dx.doi.org/10.5380/ce.v24i0.58326>.





This work is licensed under a [Creative Commons Attribution 4.0 International License](https://creativecommons.org/licenses/by/4.0/).


<sup>1</sup>Registered Nurse. PhD Candidate in Nursing. Federal University of São Paulo. São Paulo, SP, Brazil. 

<sup>2</sup>Nursing Student. Federal University of São Paulo. São Paulo, SP, Brazil. 

<sup>3</sup>Registered Nurse. MSc in Health Sciences. Federal University of São Paulo. São Paulo, SP, Brazil. 

<sup>4</sup>Psychologist PhD in Health Sciences. Psychologist of the Paulista School of Medicine. São Paulo, SP, Brazil. 

<sup>5</sup>Registered Nurse. PhD in Maternal and Child Nursing. Professor of Nursing of the Federal University of São Paulo. São Paulo, SP, Brazil. 

<sup>6</sup>Registered Nurse. PhD in Nursing. Professor of Nursing of the Federal University of São Paulo. São Paulo, SP, Brazil. 

## ADESÃO AO TRATAMENTO NO TRANSPLANTE DE FÍGADO: REVISÃO INTEGRATIVA

### RESUMO

**Objetivo:** avaliar as intervenções da equipe multiprofissional que proporcionam a melhora da adesão ao tratamento após o transplante de fígado.

**Método:** revisão integrativa da literatura. Os critérios de inclusão foram artigos publicados entre 2012 e 2017, nos idiomas português, inglês e espanhol, realizados na população adulta submetida ao transplante hepático.

**Resultado:** a busca inicial resultou em 84 publicações sendo selecionados 10 estudos. Os dados foram tabulados de acordo com a relevância do conteúdo, objetivos, tipo de intervenção, número de pacientes e nível de evidência. Foram encontradas quatro categorias analíticas: intervenções educativas; adoção de um plano terapêutico individual; alteração do regime imunossupressor; suporte emocional, psicológico e fortalecimento da rede de apoio.

**Conclusão:** a equipe multiprofissional deve prover informações sobre o processo de transplantação, realizar o manejo adequado da imunossupressão, avaliar regularmente o paciente quanto aos sinais de depressão, ansiedade, crenças e valores, e instituir um plano de cuidados individualizado.

**DESCRIPTORIOS:** Transplante de fígado; Cooperação do paciente; Adesão à medicação; Equipe de assistência ao paciente; Revisão.

## ADHESIÓN AL TRATAMIENTO EN EL TRASPLANTE DE HÍGADO: REVISIÓN INTEGRATIVA

### RESUMEN

**Objetivo:** evaluar las intervenciones del equipo multiprofesional que promueven la mejoría de la adhesión al tratamiento tras el trasplante de hígado.

**Método:** revisión integrativa de la literatura. Se publicaron los criterios de inclusión entre 2012 y 2017, en los idiomas portugués, inglés y español, y estos se aplicaron en población adulta sometida al trasplante hepático.

**Resultado:** la búsqueda inicial resultó en 84 publicaciones, seleccionándose 10 estudios. Se tabularon los datos de acuerdo con la relevancia del contenido, objetivos, tipo de intervención, número de pacientes y nivel de evidencia. De eso, resultaron cuatro categorías analíticas: intervenciones educativas; adopción de un plan terapéutico individual; alteración del régimen inmunosupresor; soporte emocional, psicológico y fortalecimiento de la red de apoyo.

**Conclusión:** es necesario que el equipo multiprofesional provea informaciones acerca del proceso de trasplantación, realice el manejo adecuado de la inmunosupresión, evalúe regularmente el paciente cuanto a las señales de depresión, ansiedad, creencias y valores, e instituya un plan de cuidados individualizado.

**DESCRIPTORIOS:** Trasplante de hígado; Cooperación del paciente; Adhesión a la medicación; Equipo de asistencia al paciente; Revisión.

## INTRODUCTION

Liver transplantation allows patients with terminal liver disease the opportunity to increase their survival, together with the improvement of their quality of life. However, the results are directly related to the patient's regular commitment to the treatment, including immunosuppressive therapy and lifestyle adjustments<sup>(1-3)</sup>.

Survival of liver recipients in the first five years after the procedure ranges from 60% to 80%, depending on the type of disease responsible for the transplant indication and other variables, such as associated morbidities, access to healthcare, and ability to develop and manage the self-care<sup>(3-4)</sup>.

Transplantation involves the inherent risk of graft rejection with consequent organ dysfunction. To minimize this risk, patients are submitted to immunosuppressive regimens and should be monitored for signs of graft failure<sup>(5)</sup>. Therefore, non-adherence to treatment strongly influences the clinical outcomes in transplants, also contributing to increased costs for the health system<sup>(6-7)</sup>.

A meta-analysis that included 147 studies published between 1981 and 2005, which addressed adherence to immunosuppressive therapy after solid organ transplants, found that only 20% of these studies were related to liver recipients. Nevertheless, it was evidenced that one in 10 deaths of patients submitted to liver transplantation was related to non-adherence to the immunosuppressive medications. Non-adherence rates were 36.0% among kidney recipients, 14.5% in heart recipients and 6.7% among liver recipients<sup>(8)</sup>.

Several factors may influence adherence to the therapeutic regimen<sup>(9)</sup>. The World Health Organization (WHO) listed five dimensions that interfere with adherence, considering the multidimensionality of the process: factors related to the patient, the treatment, the socioeconomic situation, the health systems, and the disease<sup>(10)</sup>.

Patients present different adherence to treatment barriers, therefore it is important to implement interventions adapted to their risk factors<sup>(11)</sup>. In 2009, a systematic review evaluated 12 intervention studies that were conducted to improve adherence rates in patients who underwent organ transplantation. Three of them specifically addressed adherence in patients after liver transplantation, with only one with adult recipients<sup>(12)</sup>. These studies investigated interventions with the health care provider and in the health environment, however, showed limited improvements in the adherence rate. They also showed that no single intervention was superior in improving the adherence to treatment<sup>(12)</sup>.

Since then, many refinements have occurred to help keep patients engaged in the treatment. Innovative health technologies and the establishment of policies for the management of patients with chronic disease have been shown to be effective in increasing patients' adherence to treatment<sup>(13-14)</sup>. However, there is little evidence regarding the most effective strategies for managing adherence to treatment in specific populations. Thus, the investigation of interventions that can contribute to adherence in liver transplantation is of great value, possibly providing a base for the actions of the multidisciplinary team with these patients.

Considering the above, the aim of this study was to map, through an integrative review, the existing evidence on interventions proposed by the multidisciplinary team to avoid or reduce the lack of adherence to pharmacological and non-pharmacological treatments in patients that had undergone liver transplantations.

## METHOD

An Integrative Review (IR) of the literature, to identify and analyze the studies available

in the databases and provide the synthesis of knowledge produced on a particular topic, allows the visualization of evidence gaps in the professional practice and enables the contextualization of the research on a given theme<sup>(15-16)</sup>.

The steps that constituted the IR were: identification of the theme and definition of the guiding question; literature search or sampling; extraction of study data and compilation of the findings; evaluation of the studies and interpretation of the results; and finally, synthesis of the knowledge or presentation of the integrative review itself<sup>(16)</sup>.

The identification of the topic began with the definition of the keywords used for the initial search: Liver transplantation, Adherence to treatment, and Interventions of the multidisciplinary team. For the definition and elaboration of the research question, the PICO research strategy<sup>(17)</sup> was used, an English language acronym, used to select the Population: "adult patients (>18 years of age) undergoing liver transplantation"; the Intervention: "interventions to improve adherence to treatment after liver transplantation"; Comparison: "level of adherence to treatment before and after adoption of strategies to improve adherence"; and Outcomes: "adherence to treatment after the transplantation". Next, the research question was identified: What interventions that contribute to improved adherence to liver transplantation treatment are performed by the multidisciplinary team?

The study was carried out in June of 2017 in five databases: Latin American and Caribbean Health Sciences Literature (LILACS), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Medical Literature Analysis and Retrieval System Online (Medline/PubMed), Scientific Electronic Library Online (SciELO) and Virtual Health Library (VHL), through the controlled descriptors "Medication Adherence/Adesão à Medicação", "Liver Transplantation/Transplante de Fígado" and "Patient Compliance/Cooperação do Paciente" in different combinations in Portuguese and English, selected from Medical Subject Headings (MeSH) and Descriptors in Health Sciences (DeCS).

Inclusion criteria were full text articles published between 2012 and 2017, in English, Portuguese or Spanish, carried out with adult patients (aged 18 years and over) that had undergone liver transplantation, regardless of the type of donor (live or deceased donor) and the etiology of the hepatic impairment. Any pharmacological or non-pharmacological intervention applied to keep patients following the prescribed treatment was considered. Table 1 presents the search.

Table 1 - Electronic search details. São Paulo, SP, Brazil, 2018

Line	Search sequence
1	(adherence in liver transplant)
2	(interventions to improve adherence in liver transplant recipients)
3	(Medication Adherence) AND (liver transplant or transplantation)
4	(Patient Compliance) AND (adherence) AND (liver transplant or transplantation)
5	(databases LILACS or PubMed or CINAHL or VHL or SciELO)
6	(systematic or narrative or integrative or ethical or theoretical or literature or comprehensive or review or overview)
7	Date: 2012-2017
8	Language: English, Spanish and Portuguese.

The exclusion criteria considered were articles on adherence addressing other pathologies and therapies not related to liver transplantation.

No restrictions were imposed regarding the design of the included studies (controlled or uncontrolled). Thus, the studies considered were randomized controlled clinical trials (RCTs) and, in their absence, non-randomized clinical trials, cohort studies, case control or descriptive studies. Mixed studies, performed with other types of transplantation were also selected when they specified liver recipients. Secondary studies (abstract, letters to the editor, reviews, and book chapters) were not included. Recommendation guides and annals of congresses were excluded, aiming to avoid the potential risk of bias due to selective reporting.

The strategies adopted for each database described were organized in folders with the aid of the Endnote X6® program, which allows grouping of repeated references.

After removing all duplicates, the study titles and abstracts were read and those that did not fit the inclusion criteria were discarded. Intervention studies that did not address adherence to treatment as a result were considered ineligible. The data extraction was carried out using a validated instrument<sup>(17)</sup> and performed in two phases: a) evaluation of the titles and abstracts of all the studies selected, independently, by two evaluators; b) after selection of the abstracts, through the consensus of the evaluators, the evaluation of the full text followed. The critical analysis of the articles consisted of the reading of the study in its entirety, performed independently by two researchers. Next, the selected publications were retrieved in full so that they could have the methodological quality assessed.

The two reviewers independently assessed the level of evidence of the studies, according to the Oxford Center for Evidence-Based Medicine classification, which stratifies studies into 1A (Systematic Review, meta-analysis of RCTs), 1B (RCTs with confidence of 95%); 2A (Systematic Review of Cohort Studies), 2B (Cohort Studies, including Lower Quality Randomized Clinical Trials), 2C (Outcomes Research, observation of therapeutic results and Ecological Studies), 3A (Systematic Review of Case-Control Studies), 3B (Individual Case-Control Studies), 4 (Case Series, Cohort Studies, and Lower Quality Case Control Studies), and 5 (Expert Opinions)<sup>(18)</sup>.

Finally, the information obtained was synthesized, the results were interpreted through descriptive analysis and the analytical categories were constructed according to the aims of the review and guiding question.

## RESULTS

A total of 84 articles were identified in the databases searched, with 32 of these excluded due to repetition. Thus, 52 studies were eligible for the first selection, which was performed through the reading of the titles and abstracts, with another 38 excluded due to not fulfilling the inclusion criteria. A total of 14 articles were evaluated fully, of which 4 were excluded. Therefore, 10 articles composed the sample (Figure 1).



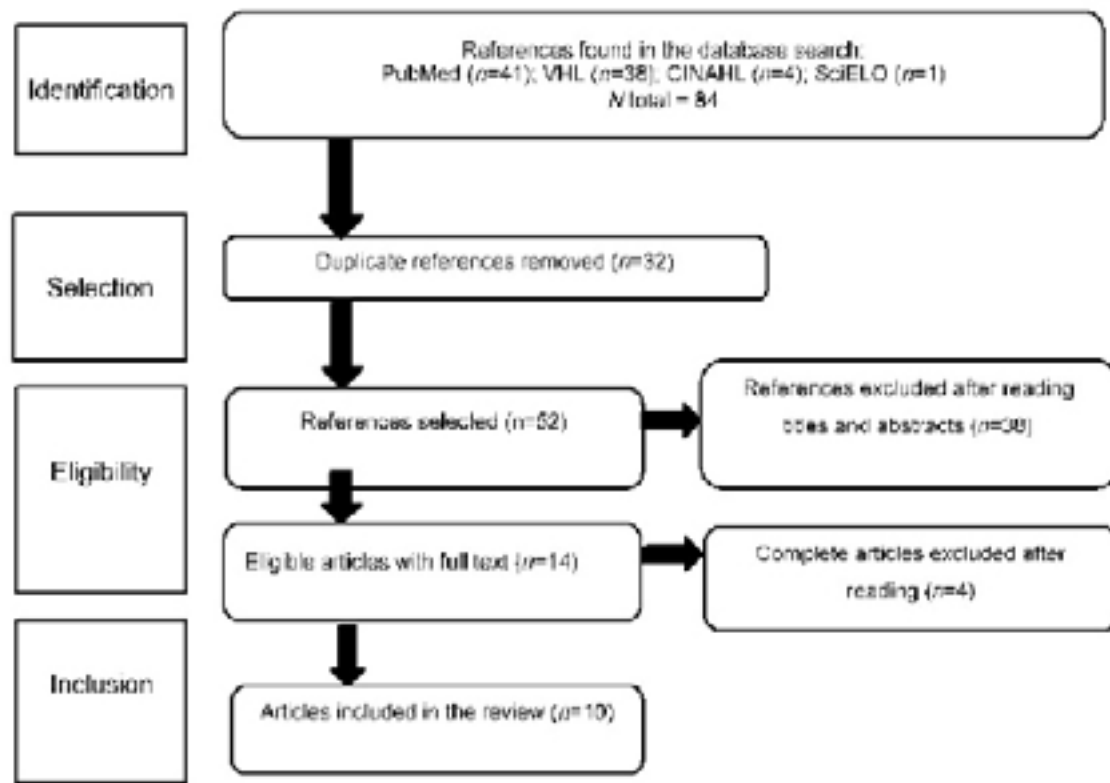


Figure 1 - Diagram of inclusion and exclusion of the articles found in the databases searched. São Paulo, SP, Brazil, 2018

Next, for the extraction of the data, a second complete reading of the 10 selected articles was carried out, which were organized in tables, considering the following topics: title and year of publication, authors and name of the periodical; objective, type of study/method, results and level of evidence. Chart 1 shows the studies according to title, year of publication, authors and periodical.

Chart 1 - Distribution of the studies according to title, year of publication, authors and periodical. São Paulo, SP, Brazil, 2018 (continues)

Title	Year	Authors	Periodical
1. Immunosuppressive Medication Adherence in Liver Transplant Recipients <sup>(19)</sup> .	2016	Promraja R, Dumronggittiguleb W, Sirivatanauksornb Y, Ruenroma A, Tovikkaib C, Limsrichamrernb S, et al.	Transplantation Proceedings
2. Systematic Pharmaceutical Educational Approach to Enhance Drug Adherence in Liver Transplant Recipients <sup>(20)</sup> .	2016	Asavakarna S, SirivatanauksornaY, Promrajb R, Ruenrom A, Limsrichamrerna S, Kositamongkola P, et al.	Transplantation Proceedings
3. Adherence and treatment satisfaction in liver transplant recipients <sup>(21)</sup> .	2016	Albekairy AM, Alkatheri AM Jarab A, Khalidi N, Althiab K, Alshaya A, et al.	The Saudi Journal of Gastroenterology
4. Conversion of twice-daily to once-daily Tacrolimus is safe in stable adult living donor liver transplant recipients <sup>(22)</sup> .	2015	Kim SH, Lee SD, Kim YK, d Park SJ.	Hepatobiliary & Pancreatic Diseases International

5. Influence of intention to adhere, beliefs and satisfaction about medicines on adherence in solid organ transplant recipients <sup>(23)</sup> .	2014	Hugon A, Roustit M, Lehmann A, Saint-Raymond C, Borrel E, Hilleret MN, et al.	Transplantation
6. An observational study evaluating Tacrolimus dose, exposure, and medication adherence after conversion from twice- to once-daily Tacrolimus in liver and kidney transplant recipients <sup>(24)</sup> .	2014	Bäckman L, Persson CA.	Ann Transplant
7. Increased Medication Compliance of Liver Transplant Patients Switched From a Twice-Daily to a Once-Daily Tacrolimus-Based Immunosuppressive Regimen <sup>(25)</sup> .	2013	Eberlin M, Otto G, Krämer I.	Transplantation Proceedings
8. Rurality and other factors associated with adherence to immunosuppressant medications in community-dwelling solid-organ transplant recipients <sup>(26)</sup> .	2012	Sankaranarayanan J, Collier D, Furasek A, Reardon T, Smith LM, McCartan M, et al.	Research in Social and Administrative Pharmacy
9. Psychosocial predictors of adherence after liver transplant in a single transplant center in Portugal <sup>(27)</sup> .	2012	Diogo Telles-Correia, António Barbosa, Inês Mega, Estela Monteiro	Progress in Transplantation
10. Immunosuppressant treatment adherence, barriers to adherence and quality of life in renal and liver transplant recipients in Spain <sup>(28)</sup> .	2012	Morales JM, Varo E, Lázaro P.	Clinical Transplantation

The articles were evaluated regarding the type of study, main aims, type of treatment adherence intervention studied and level of evidence. A total of 9 (90%) cross-sectional studies were found and 1 (10%) prospective multicenter study. Regarding the sample, this ranged from 50 to 1,479 transplant patients evaluated. In order to facilitate the comprehension of the results obtained, the investigations included in the review were grouped into analytical categories, as described in Chart 2.

Chart 2 - Distribution of the studies according to objective, type of study, sample size, results and level of evidence. São Paulo, SP, Brazil, 2018 (continues)

No.	Aim	Type of study	Sample	Results	Level of Evidence	Category
1	To evaluate the adherence to immunosuppressive medication in liver transplant patients <sup>(19)</sup> .	Cross-sectional, in a single center	50 patients	Education and explanation of the importance of the immunosuppressants to the patient and family/caregivers are essential for improved adherence.	2C	Educational interventions: non-adherence related to a deficit in information about the treatment.
2	To implement a pharmaceutical educational approach to improve adherence to immunosuppressive drug therapy at the Siriraj Hospital <sup>(20)</sup> .	Cross-sectional, in a single center	50 patients	Providing knowledge and care in relation to immunosuppressants and their use improves adherence.	2C	Educational interventions: non-adherence related to a deficit in information about the treatment.



3	To identify the factors that best predict adherence to medication and to explore the relationship between treatment satisfaction and adherence to medication in patients undergoing liver transplantation <sup>(21)</sup> .	Cross-sectional, in a single center	154 patients	Patients more satisfied with the treatment have better adherence to the therapy, an individual care plan that helps in improving patient satisfaction with the treatment and consequently the adherence is recommended.	2C	Adoption of an individual therapeutic plan: non-adherence related to not fulfilling the specific needs of the patient.
4	To assess the safety, efficacy and adherence to immunosuppression by converting the dose of Tacrolimus from twice daily to once daily in stable liver transplant (by live donor) adults <sup>(22)</sup> .	Cross-sectional, in a single center	229 patients	Change of dose (single).	2C	Change in immunosuppressive regimen: non-adherence related to the number of daily doses of immunosuppressive drugs.
5	To test whether the parameters of a model adapted from the planned behavior theory and, more specifically, attitudes that are influenced by beliefs and satisfaction with the medication can predict adherence in solid organ transplant patients <sup>(23)</sup> .	Cross-sectional, in a single center	153 patients	Emotional evaluation. The provider should identify negative beliefs regarding immunosuppression, since it is a factor that decreases adherence.	2C	Emotional and psychological support and help: non-adherence related to psychological and emotional factors, beliefs and values.
6	The primary objective was to investigate the effect of the conversion from a twice-daily dose of Tacrolimus to once-daily at 90 days after the substitution in stable renal and hepatic transplant patients in the routine clinical practice. A second objective was to evaluate the changes in medication adherence following the change of Tacrolimus dose <sup>(24)</sup> .	Prospective, multicenter observational	224 patients	Change of dose (single).	2B	Change in immunosuppressive regimen: non-adherence related to the number of daily doses of immunosuppressive medications.
7	To compare medication adherence rates among liver transplant patients with the Tacrolimus therapeutic regimen over time after transplantation <sup>(25)</sup> .	Cross-sectional, in a single center	63 patients	Change of dose (single) generated increased adherence.	2C	Change in immunosuppressive regimen: non-adherence related to the number of daily doses of immunosuppressive medications.

8	To examine the factors associated with the instrument "Immunosuppressant Therapy Adherence Scale" <sup>(26)</sup> .	Cross-sectional, in a single center	556 patients	Patient-centered interventions using technology to support decision making.	2C	Adoption of an individual therapeutic plan: non-adherence related to not fulfilling the specific needs of the patient.
9	To investigate which psychosocial and psychiatric factors determine adherence after liver transplantation <sup>(27)</sup> .	Cross-sectional, in a single center	150 patients	Individualized therapeutic plan in the pre-transplantation period improves post-transplant adherence.	2C	Adoption of an individual therapeutic plan: non-adherence related to not fulfilling the specific needs.
10	To evaluate adherence to immunosuppressive therapy and to identify the perceived barriers that affect adherence and the quality of life of patients undergoing kidney and liver transplantation <sup>(28)</sup> .	Cross-sectional, in a single center	1,479 patients	Adjusting the intensity of the treatment by reducing the dose frequency.	2C	Alteration of immunosuppressive regimen.

## DISCUSSION

The studies that compose this review, which deals with the issue of non-adherence to treatment among patients that had undergone liver transplantation, were predominantly produced in North America and Europe.

Regarding the methodological design, the sample was mainly composed of cohort studies. Of the 10 studies, 9 were classified as having a 2C level of evidence and only one as 2B.

It should be emphasized that the best evidence is obtained in studies with high methodological quality, since they are able to gather information that supports clinical decision making, such as randomized clinical trials. However, it is recognized that cohort studies are used in a classic way to evaluate the results of risk exposures<sup>(29)</sup>. Thus, considering the evaluation of the interventions adopted to reduce the risk of non-adherence to treatment after liver transplantation, this could be one of the possible study designs for investigating this type of phenomenon.

The data found in the studies included in this review were synthesized into four categories. The first, which included two articles, refers to "educational interventions - presence of non-adherence related to the deficit of information about the treatment".

The strategies adopted among the studies that compose this category suggest the optimization of the teaching and learning process as a useful tool to increase the level of adherence to treatment. The inclusion of family members in the teaching of medication use and the provision of information about the transplantation process associated with direct contact with the professional responsible for the clinical follow-up of the patient seems to have an impact on the adherence indices<sup>(19-20)</sup>.

It should be emphasized that adherence behavior should not be reduced to

compliance with professional recommendations, but rather to the result of exposure to learning situations (health education measures) and coping strategies developed by the patient and family based on these interventions, which impact on the quality of life and specifically on liver transplantation, graft and patient survival<sup>(4)</sup>.

Patients maintain the condition of chronic disease sufferers after the transplantation and, for this reason, the use of medications comprises part of their routine, leading to risks for health problems related to this condition.

It is critical that the patients and their family members are able to comprehend the circumstances surrounding the treatment after the liver transplantation; that they learn to deal with the medications; change hygiene habits in order to prevent infectious processes; adapt to the various changes, such as in the self-image, and deal with social issues, such as the return to work activities. In this way, it is essential to observe how the patient behaves and perceives the treatment. Recognizing patients' histories, habits and abilities places them as the focus of the intervention and healthcare<sup>(23,30)</sup>.

The category with the largest number of articles was "change of the immunosuppressive regimen - non-adherence related to the number of daily doses of immunosuppressive medications", which dealt with difficulties in adherence caused by the concomitant use of various medications.

The intervention adopted in the four studies included in this category was a change in dosage, with the reduction of doses (from two daily doses to one daily dose of immunosuppressant). From the adoption of this strategy, there was a significant reduction in non-adherence indices, stabilization of serum drug levels and absence of systemic-renal, cardiological and hepatic complications<sup>(22-25,28)</sup>. Therefore, the simplification of the therapeutic regimen is another useful recommendation, contributing to achieve the best results related to immunosuppressive adherence.

Another category was related to the "adoption of an individual therapeutic plan - non-adherence related to not fulfilling the specific needs of the patient", composed of three articles<sup>(21,26-27)</sup>.

Faced with the complexity of the patient that has undergone transplantation, it is fundamental that the team is prepared to fulfill the demands of the patients, at all levels of healthcare and holistically. Consideration should be given to the duration, diversity of care and nature of the recommendations made by the team as factors that intervene in the adherence<sup>(31)</sup>.

The final category consisted of only one study<sup>(23)</sup> and was associated with "emotional and psychological support and help - non-adherence related to psychological and emotional factors, beliefs and values". Several factors have been related to non-adherence to treatment, from diagnosis of depression and anxiety, to inadequacy of the new lifestyle and difficulties of reinsertion into the family and daily life after the transplantation<sup>(32)</sup>.

Other social issues or aspects associated with the patient's own characteristics, such as being male, with low social support<sup>(33)</sup>, or to the health system, such as the lack of medication, lack of access to the centers<sup>(34)</sup>, may be related to non-adherence to the post-transplant treatment.

In the majority of studies on adherence to health, there is a concern about the divergence between the healthcare providers' guidance and the patients' behaviors. Given this scenario, there are several attitudes, mechanisms and interventions to modify what are considered to be risk behaviors. The present review showed that, with regard to non-adherence to post-transplant treatment, the most studied area is non-adherence to immunosuppressive medications.

Few studies address effective measures that promote behavioral changes related to the lifestyle desirable after the transplantation. It is emphasized that both interventions

are closely related to long-term results after the liver transplantation. Therefore, there is a need for the performance of studies that evaluate the interventions of the multidisciplinary team and promote adherence to the post-transplant treatment in a global way, not only covering the aspects inherent to immunosuppression.

It was identified that the studies presented make an analysis of adherence, based on the distribution of adherence and non-adherence in the transplanted population and propose the interventions and mechanisms that must be followed to achieve the best results. However, they do not discuss the values and contingencies related to the maintenance of risk behavior related to non-adherence. That is, the way patients face threatening situations, their beliefs and habits are variables that affect the responses of individuals, and this behavior must be taken into account when evaluating non-adherence to the liver transplantation treatment.

Perhaps this is related to the classic definition of adherence to treatment, which does not consider changes in the behavioral and cognitive repertoire of the patients, from the interventions implemented (quitting smoking and drinking, preventing stressful situations, adopting safe sex habits, adapting the routine to have a healthier diet with incorporation of physical activity), only considering whether the patient complies with the guidelines of a healthcare provider in an objective way (taking medications or following the consultation and examination routine)<sup>(35-36)</sup>.

It is believed that the issues addressed in this integrative review can help the decision-making of nurses and other healthcare providers with regard to mapping and recognizing the risk factors related to non-adherence to liver transplantation treatment, especially suggesting strategies and interventions that are associated with better patient monitoring and increased adherence to treatment<sup>(35,37)</sup>.

There is a lack of multicenter studies that assess adherence globally, including adherence to team recommendations and guidelines, and not only to aspects related to the immunosuppressive therapy. The majority of the studies discuss risk factors associated with non-adherence and do not address actions to improve their levels. In addition, different methods are used to measure adherence, which makes it difficult to compare the results in isolation.

The limitations of this study lie in the lack of investigations with more rigorously controlled methodological designs, which would allow greater comparisons and extrapolations of the results obtained through the IR.

## CONCLUSION

It was concluded that interventions that favor adherence to treatment among adult patients that have undergone liver transplantation, indicated by the studies analyzed, are of four types: a) educational interventions – non-adherence related to a lack of information about the treatment; b) adoption of an individual therapeutic plan - non-adherence related to not fulfilling the patient's specific needs; c) alteration of the immunosuppressive regimen - non-adherence related to the number of daily doses of immunosuppressive medications; and d) emotional, and psychological support and help - presence of non-adherence related to psychological and emotional factors, belief and values.

Therefore, the multidisciplinary team should provide information on the transplantation process to the patients and their families, perform the appropriate management of immunosuppression with a focus on simplifying the therapeutic regimen, regularly assess the patients for signs of depression and anxiety, investigate their beliefs and values, and establish an individualized care plan.

Accordingly, the incorporation of healthcare models that deal with the issue of "adherence to post-transplant treatment" should be comprehensive, multidisciplinary and

focused on the individual needs of each patient, incorporating the analytical behavioral perspective into the evaluation, so that it is possible to take into account individuals and their relationships with the world around them.

## ACKNOWLEDGMENTS

We thank the National Council for Scientific Development (CNPq), which financed, through the CNPq Universal Request for Proposals, the research project entitled "*Impacto do atendimento multiprofissional na adesão ao transplante de fígado*" that gave rise to this article. The lead author also thanks the National Council for Scientific Development (CNPq) Research Promotion Agency for the funding from the Social Demand Scholarships Program.

## REFERENCES

1. Martin P, Martini A, Feng S, Brown Jr RS, Fallon M. Evaluation for Liver Transplantation in Adults: 2013 Practice Guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. Hepatology [Internet]. 2014 [acesso 01 set 2017]; 59(3). Disponível em: [https://www.aasld.org/sites/default/files/guideline\\_documents/Evaluation\\_for%20LT\\_in\\_Adults\\_hep26972\\_0.pdf](https://www.aasld.org/sites/default/files/guideline_documents/Evaluation_for%20LT_in_Adults_hep26972_0.pdf).
2. Ming-Ming X, Brown RS Jr. Liver Transplantation for the Referring Physician. Clin Liver Dis. [Internet]. 2015 [acesso 23 set 2017]; 19(1). Disponível em: <https://doi.org/10.1016/j.cld.2014.09.008>.
3. Drent G, Moons P, Geest S, Kleibeuker JH, Haagsma EB. Symptom experience associated with immunosuppressive drugs after liver transplantation in adults: possible relationship with medication non-compliance? Clin Transplant. [Internet]. 2008 [acesso 22 ago 2017]; 22(6). Disponível em: <http://dx.doi.org/10.1111/j.1399-0012.2008.00864.x>.
4. Mendes KDS, Rossin FM, Ziviani LC, Castro-e-Silva O, Galvão CM. Necessidades de informação de candidatos ao transplante de fígado: o primeiro passo do processo ensino-aprendizagem. Rev. Gaúcha Enferm. [Internet]. 2012 [acesso 28 ago 2017]; 33(4). Disponível em: <http://dx.doi.org/10.1590/S1983-14472012000400012>.
5. Morrissey PE, Flynn ML, Lin S. Medication noncompliance and its implications in transplant recipients. Drugs [Internet]. 2007 [acesso 17 ago 2017]; 67(10). Disponível em: <https://doi.org/10.2165/00003495-200767100-00007>.
6. Pinsky BW, Takemoto SK, Lentine KL, Burroughs TE, Schnitzler MA, Salvalaggio PR. Transplant Outcomes and Economic Costs Associated with Patient Noncompliance to Immunosuppression. Am J Transplan. [Internet]. 2009 [acesso 18 ago 2017]; 11(9). Disponível em: <https://doi.org/10.1111/j.1600-6143.2009.02798.x>.
7. Chisholm MA, Mulloy LL, DiPiro JT. Comparing renal transplant patients' adherence to free cyclosporine and free tacrolimus immunosuppressant therapy. Clin Transplant. [Internet]. 2005 [acesso 19 ago 2017]; 19(1). Disponível em: <https://doi.org/10.1111/j.1399-0012.2004.00301.x>.
8. Dew MA, Martini AF, VitoDabbs A, Myaskovsky L, Steel J, Unruh M, et al. Rates and Risk Factors for Nonadherence to the Medical Regimen After Adult Solid Organ Transplantation. Transplantation. [Internet]. 2007 [acesso 19 ago 2017]; 83(7). Disponível em: <https://doi.org/10.1097/01.tp.0000258599.65257.a6>.
9. Johnson MJ. The Medication Adherence Model: A Guide for Assessing Medication Taking. Research Theory Nurs Pract. [Internet]. 2002 [acesso 17 ago 2017]; 16(3). Disponível em: <https://doi.org/10.1891/rtnp.16.3.179.53008>.
10. Sabate E. Adherence to Long-Term Therapies: evidence for action. Geneva: World Health Organization, 2003.



11. Low JK, Williams A, Manias E, Crawford K. Interventions to improve medication adherence in adult kidney transplant recipients: a systematic review. *Nephrology Dialysis Transplantation*. [Internet.] 2015 [acesso 19 Jun 2017]; 30(5). Disponível em: <https://doi.org/10.1093/ndt/gfu204>.
12. Bleser L, Matteson M, Dobbels F, Russell C, Geest S. Interventions to improve medication adherence after transplantation: a systematic review. *Transplantation Internacional*. [Internet]. 2009 [acesso 26 ago 2017]; 22(8). Disponível em: <https://doi.org/10.1111/j.1432-2277.2009.00881.x>.
13. Cutler DM, Everett W. Thinking Outside the Pillbox – Medication Adherence as a Priority for Health Care Reform. *N Engl J Med*. [Internet]. 2010 [acesso em 16 set 2017]; 362(17). Disponível em: <http://www.nejm.org/doi/full/10.1056/NEJMp1002305#t=article>.
14. Patel S, Jacobus-Kantor L, Marshall L, Ritchie C, Kaplinski N, Khurana PS, et al. Mobilizing your medications: an automated medication reminder application for mobile phones and hypertension medication adherence in a high-risk urban population. *J Diabetes SciencTechn*. [Internet]. 2013 [acesso 28 ago 2017]; 7(3). Disponível em: <https://doi.org/10.1177/193229681300700307>.
15. Souza MT, Silva MD, Carvalho R. Revisão Integrativa: o que é e como fazer. *Einstein*. [Internet]. 2010 [acesso 15 ago 2017]; 8(1). Disponível em: <http://dx.doi.org/10.1590/s1679-45082010rw1134>.
16. Forrest JL, Kupiec LM. Evidence-based Decision Making: Introduction and Formulating Good Clinical Questions. [Internet]. 2014 [Acesso 17 jul 17]; 1(3). Disponível em: <https://www.dentalcare.com/en-us/professional-education/ce-courses/ce311>.
17. Santos CMC, Pimenta CAM, Nobre MRC. The PICO strategy for the research question construction and evidence search. *Rev. Latino-Am. Enfermagem*. [Internet]. 2007 [acesso 2017 ago 17]; 15(3) Disponível em: <http://dx.doi.org/10.1590/S0104-11692007000300023>.
18. Centre for Evidence-Based Medicine. Oxford centre for evidence-based medicine – levels of evidence (March 2009). [Internet]. 2009 [acesso 16 jun 2017]. Disponível em: <http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/>.
19. Promraj R, Dumronggittigule W, Sirivatanauskorn Y, Ruenrom A, Tovikkai C, Limsrichamrern S, et al. Immunosuppressive medication adherence in liver transplant recipients. *Transplant. Proc*. [Internet]. 2016 [acesso 13 jun 2017]; 48(4). Disponível em: <https://doi.org/10.1016/j.transproceed.2015.12.097>.
20. Asavakarna S, Sirivatanauksorna Y, Promrajb R, Ruenrom A, Limsrichamrerna S, Kositamongkola P, et al. Systematic pharmaceutical educational approach to enhance drug adherence in liver transplant recipients. *Transplant. Proc*. [Internet]. 2016 [acesso 13 jun 2017]; 48(4). Disponível em: <https://doi.org/10.1016/j.transproceed.2015.12.100>.
21. Albekairy AM, Alkatheri AM, Jarab A, Khalidi N, Althiab K, Alshaya A, et al. Adherence and treatment satisfaction in liver transplant recipients. *Saudi J Gastroenterol*. [Internet]. 2016 [acesso 20 jun 17]; 22(2). Disponível em: <http://doi.org/10.4103/1319-3767.164209>.
22. SH Kim, SD Lee, YK Kim, SJ Park. Conversion oft wice-daily to once-daily tacrolimus is safe in stable adult living donor liver transplant recipients. *Hepatobiliary Pancreat Dis Int*. [Internet]. 2015 [acesso 13 jun 2017]; 14(4). Disponível em: [https://doi.org/10.1016/S1499-3872\(15\)60378-2](https://doi.org/10.1016/S1499-3872(15)60378-2).
23. Hugon A, Roustit M, Lehmann A, Saint-Raymond C, Borrel E, Hilleret MN, et al. Influence of intention to ad here, beliefs and satisfaction about medicines on adherence in solid organ transplant recipients. *Transplant*. [Internet]. 2014 [acesso 13 jun 2017]; 98(2). Disponível em: <https://doi.org/10.1097/TP.0000000000000221>.
24. Bäckman L, Persson CA. An observational study evaluating tacrolimus dose, exposure, and medication adherence after conversion from twice- to once-daily tacrolimus in liver and kidney transplant recipients. *Ann Transplant*. [Internet]. 2014 [acesso 13 jun 2017]; (19). Dispovível em: <http://doi.org/10.12659/AOT.890101>.
25. Eberlin, M, Otto G, Krämer I. Increased Medication Compliance of Liver Transplant Patients Switched From a Twice-Daily to a Once-Daily Tacrolimus-Based Immunosuppressive Regimen.



- Transplant. Proc. [Internet]. 2013 [acesso 13 jun 2017]; 45(6). Disponível em: <https://doi.org/10.1016/j.transproceed.2012.10.037>.
26. Sankaranarayanan J, Collier D, Furasek A, Reardon T, Smith LM, McCartan M, et al. Rurality and other factors associated with adherence to immunosuppressant medications in community-dwelling solid-organ transplant recipients. *Research Soc Admin Pharm*. [Internet]. 2012 [acesso 13 jun 2017]; 8(3). Disponível em: <https://doi.org/10.1016/j.sapharm.2011.04.001>.
27. Telles-Correia D, Barbosa A, Mega I, Monteiro E. Psychosocial predictors of adherence after liver transplant in a single transplant center in Portugal. *Progress transplant*. [Internet]. 2012 [acesso 14 jun 2017]; 22(1). Disponível em: <https://doi.org/10.7182/pit2012569>.
28. Morales JM, Varo E, Lázaro P. Immunosuppressant treatment adherence, barriers to adherence and quality of life in renal and liver transplant recipients in Spain. *ClinTransplant*. [Internet]. 2012 [acesso 14 jun 2017]; 26(2). Disponível em: <https://doi.org/10.1111/j.1399-0012.2011.01544.x>.
29. Lazcano-Ponce E, Fernández E, Salazar-Martínez E, Hernández-Ávila M. Estudios de cohorte. Metodología, sesgos y aplicación. *Salud Pública México*. [Internet]. 2000 [acesso 17 jul 2017]; 42(3). Disponível em: <http://doi.org/10.1590/S0036-36342000000300010>.
30. Jaarsma T, Nikolova-Simons M, Van Der Wal MHL. Nurses' strategies to address self-care aspects related to medication adherence and symptom recognition in heart failure patients: An in-depth look. *Heart Lung*. [Internet]. 2012 [acesso 2 ago 2017]; 41(6). Disponível em: <https://doi.org/10.1016/j.hrtlng.2012.03.003>.
31. Berben L, Dobbels F, Engberg S, Hill MN, De Geest S. Anecological perspective on medication adherence. *Western J Nursing Research*. [Internet]. 2012 [acesso 29 ago 2017]; 34(5). Disponível em: <https://doi.org/10.1177/0193945911434518>.
32. Bautista LE, Vera-Cala LM, Colombo C, Smith P. Symptoms of depression and anxiety and adherence to antihypertensive medication. *American J Hypertension*. [Internet]. 2012 [acesso 16 set 2017]; 25(4). Disponível em: <https://doi.org/10.1038/ajh.2011.256>.
33. Rodrigue JR, Nelson DR, Hanto DW, Reed AI, Curry MP. Patient-reported immunosuppression nonadherence 6 to 24 months after liver transplant: Association with Pretransplant Psychosocial Factors and Perceptions of Health Status Change. *Progress Transplant*. [Internet] 2013 [acesso 16 set 2017]; 23(4). Disponível em: <http://doi.org/10.7182/pit2013501>.
34. Bender BG. Can Health Care Organizations Improve Health Behavior and Treatment Adherence? *Population Health Management*. [Internet] 2014 [acesso 11 set 2017]; 17(2). Disponível em: <https://doi.org/10.1089/pop.2013.0045>.
35. Mendes KDS, Silva Junior OC, Ziviani LC, Rossin FM, Zago MMF, Galvão CM. Educational intervention for liver transplantation candidates. *Rev. Latino Am. Enfermagem*. [Internet]. 2013 [acesso 16 set 2017]; 21(1). Disponível em: <http://dx.doi.org/10.1590/S0104-11692013000100018>.
36. Moraes ABA, Rolim GS, Costa Jr AL. O processo de adesão numa perspectiva analítico comportamental. *Rev Bras De Ter Comp*. [Internet]. 2009 [acesso 10 jun 2017]; (02). Disponível em: <http://pepsic.bvsalud.org/pdf/rbtcc/v11n2/v11n2a09.pdf>.
37. Abedini S, Gøransson L, Cockburn E, Kilany S, Holdaas H. Immunosuppression Adherence in Stable Kidney Transplant Patients Converted From Immediate- to Prolonged-Release Tacrolimus in Clinical Practice: A Norwegian Study. *Transplant Direct*. [Internet]. 2018 [acesso 1 mar 2018]; 4. Disponível em: [https://www.researchgate.net/publication/322269209\\_Immunosuppression\\_Adherence\\_in\\_Stable\\_Kidney\\_Transplant\\_Patients\\_Converted\\_From\\_Immediate- to\\_Prolonged-Release\\_Tacrolimus\\_in\\_Clinical\\_Practice\\_A\\_Norwegian\\_Study](https://www.researchgate.net/publication/322269209_Immunosuppression_Adherence_in_Stable_Kidney_Transplant_Patients_Converted_From_Immediate- to_Prolonged-Release_Tacrolimus_in_Clinical_Practice_A_Norwegian_Study).

Received: 09/03/2018

Finalized: 18/01/2019

**Corresponding author:**

Priscilla Caroliny de Oliveira

Universidade Federal de São Paulo

R. Napoleão de Barros 754 - 04024002 – São Paulo, SP, Brasil

E-mail: pri.transplante@gmail.com

**Role of Authors:**

Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work - PCO, FPD, SM, JS, BAR

Drafting the work or revising it critically for important intellectual content - PCO, HBP, JS, BAR

Final approval of the version to be published - PCO, JS, BAR

Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved - PCO

---