

# The importance of educational interventions for adherence to the immunosuppressant treatment program to kidney-transplanted patients

## *Importância de intervenções educativas para adesão ao tratamento imunossupressor em pacientes transplantados renais*

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### Abstract

**Introduction:** the non-adherence to the immunosuppressant treatment program is frequent in kidney transplanted patients. To promote the adherence to this therapeutic, specific educational interventions for every learning style, can help create better results. **Objective:** verify the relevance of educative interventions adjusted to different learning styles for immunosuppressive treatment adherence in kidney transplant patients. **Methods:** cohort study. Fifty-nine (59) kidney transplanted patients took part in the study. To evaluate adherence was used the Basel Assessment of Adherence Scale for Immunosuppressives (BAASIS) instrument. The learning styles were identified by the VARK questionnaire. Results: significant differences were observed in the second ( $p<0,001$ ), third ( $p<0,001$ ) and fourth ( $p=0,009$ ) evaluate of the adherence, when compared with the first one. There wasn't found significant differences when related. They didn't go find differences significant when related the adhesion with the learning styles and too much demographic and clinical data. Conclusion: the adhesion to the immunosuppressor doesn't seem to be associated to the specific interventions for each learning style.

**Keywords:** Medication Adherence; Kidney Transplantation; Learning.

### Resumo

**Introdução:** A não adesão ao tratamento imunossupressor é comum nos pacientes transplantados renais. Para promover a adesão à esta terapêutica, intervenções educativas específicas para cada estilo de aprendizagem, podem propiciar melhores resultados. **Objetivo:** Verificar a importância de intervenções educativas ajustadas ao estilo de aprendizagem com a adesão ao tratamento imunossupressor de pacientes transplantados renais. **Métodos:** Estudo de coorte. Participaram 59 pacientes transplantados renais. Para avaliar a adesão foi utilizado o instrumento Basel Assessment of Adherence Scale for Immunosuppressives (BAASIS). Os estilos de aprendizagem foram identificados pelo questionário VARK. **Resultados:** Foram observadas diferenças significativas na segunda ( $p<0,001$ ), terceira ( $p<0,001$ ) e quarta ( $p=0,009$ ) avaliação da adesão, quando comparadas à primeira. Não foram encontradas diferenças significativas quando relacionada a adesão com os estilos de aprendizagem e demais dados demográficos e clínicos. **Conclusão:** A adesão ao imunossupressor não parece estar associada às intervenções específicas para cada estilo de aprendizagem.

**Descritores:** Adesão à Medicação; Transplante de Rim; Aprendizagem.

## Introduction

The kidney transplant is considered the best alternative of treatment to the patients with stage five of chronic kidney disease, when compared to dialysis therapies. This therapy is associated to a decrease in mortality rates. It also eliminates patients' dietary restrictions, improves their quality of life, and is more cost-effective for health services<sup>1</sup>. However, for treatment to be sustainable, patients must be acquainted with decisive factors, for example, information on the need for uninterrupted and strict use of medication, knowledge on adverse effects that may be caused by immunosuppressive drugs, as well as on symptoms of rejection<sup>2</sup>.

The immunosuppressives have an important role in preventing the rejection, especially in maintenance of the graft. But, the non-adherence of the immunosuppressant treatment is relatively common in kidney transplanted and this behavior can be linked to various factors, for example: age, sex, and not understanding the benefits of the treatment<sup>2</sup>.

There are different methods for assessing adherence, for example: pill count, drug concentration levels, dispensation, electronic monitoring, and self-report. As it is simple and low-cost, the latter is most widely used by health<sup>3</sup>. An instrument used specifically to evaluate the immunosuppressive adherence is the Basel Assessment of Adherence Scale With Immunosuppressive Medication (BAASIS). This is already validated and translated to Portuguese of Brazil evaluates the adherence in the last four weeks and consists in four questions, which the patient can choose to answer through a scale like Likert, five alternatives, that are: never, once a month, every two weeks, every week, more than once a week and every day. The issues raised in the instrument are: 1) Do you recall not having taken your immunosuppressive medications (give name of drugs) some times in the past four weeks? 2) Have you skipped several consecutive doses of your immunosuppressive medications in the past four

weeks? 3) Do you recall having taken your immunosuppressive medications with more than two hours time difference from the prescribed dosing time, in the past four weeks? 4) Have you reduced the prescribed amount of your immunosuppressive medications during the four weeks? The non-adherence by this instrument is characterized when the patient answers at least one "yes" to any question<sup>4,5</sup>.

The repetitive orientation to the patient is a way to promote the immunosuppressive adherence, but the education in front of this therapy brings the best results when it is performed in an individualized manner<sup>6</sup>. Also, the sum of education, interventions and social support contributes for positive outcomes of the treatment<sup>7</sup>. The same way, programs of education that contemplate contents on the aspects of transplant to patients that are still in waiting list and the others that are under evaluation to join, are also alternatives to improve the adherence<sup>8</sup>.

In this same perspective, a European study showed that patients reported the need for information about the treatment of kidney transplant not only in the hospitalization, but in the long-term too, demonstrated the importance of the implementation of the programmes of education to promote the self-care<sup>9</sup>. For this reason, it is important to consider the learning style and the difficulties found by the patients<sup>10</sup>. Classifying the learning styles to the promotion of the self-care of the kidney transplanted patients, can be an alternative to improve the adherence to the immunosuppressant treatment<sup>11</sup>. Furthermore, the first step is to identify the learning styles and, afterwards, develop education strategies in accordance with the respective styles. An instrument that represents the predominant learning style of people is the VARK (visual, aural, Read/Write, Kinesthetic) questionnaire, which classifies the styles in visual, aural, Read/Write, Kinesthetic<sup>12</sup>. Therefore, the objective of this study was to verify the relevance of educative interventions adjusted to different learning styles for immunosuppressive treatment adherence in kidney transplant patients.

## Methods

Cohort study, prospective with quantitative approach, performed in Nephrology and Transplant Service from the São Lucas Hospital from PUCRS, in Porto Alegre/RS (Brazil).

It was included patients over 18 years of age, kidney transplanted from deceased and living donors, with the minimum time after the transplantation of three months and 12 months at the most.

The sample that was defined for convenience included kidney transplanted patients, which were invited by telephone and, afterwards, combining an individual meeting in random dates, as scheduled days to the routine medical consultations. The research was held between October 2016 and April 2017, in the multi-professional service room, in the same days of the routine medical consultations of the participants.

To evaluate the adherence, was used the BAASIS instrument and to identify the learning style, the VARK questionnaire. Were held four meetings with each patient and, the educational interventions that happened in the first three meetings, which in each one was approach issues about rejections. Except for the first meeting, which had last for 60 minutes, the others had 20 minutes at the most.

The steps of the interventions are presented in figure 1

The educational plan was established with the utilization of specific tools to each learning style, which were created based on the individual characteristics of each style. To the visual, colorful images from urinary system were used, with the transplanted kidney and a colorful clock.

To the aural videos were made three videos of at most 90 seconds duration, which were deal subjects about the rejection. The videos bring the story of a nurse solving doubts about transplant and the immunosuppressive therapy of a sister of a recently kidney transplanted.

To the Read/Write was used an orientation manual with subjects proposed and, in some part of this manual, have a blank space allowing the patient to write with your own words, what was your understanding about the orientation.

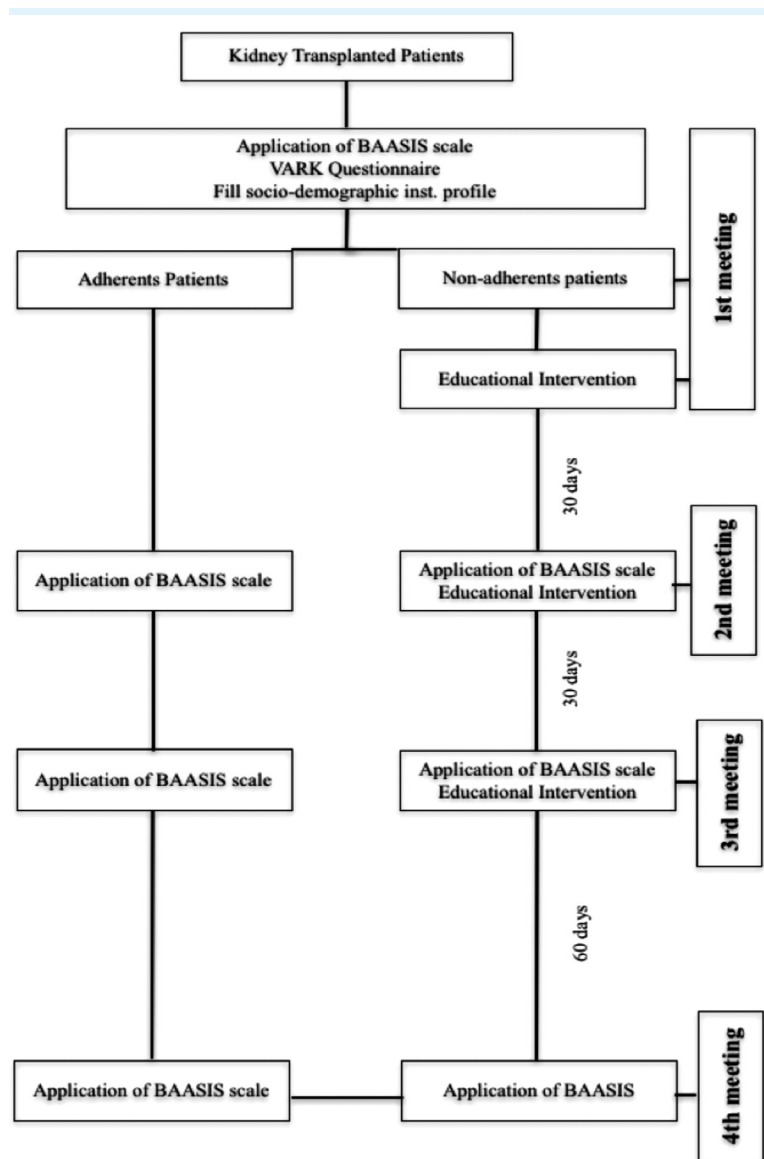


Figure 1: Steps of educational interventions

Source: Authors.

To the Kinesthetic, were used plastic apron which was insert a picture of the urinary system, allowing the patient to handle identifying the graft. Also, was created kidneys with different sizes and textures, which simulates normal and atrophied kidneys.

A descriptive and inferential statistics was used with the Statistical Package for the Social Sciences (SPSS) software, 20 version in the comparisons.

The "Fisher's exact test (Monte Carlo methods or Monte Carlo experiments) was used, the Student's t-tests was used to independents samples and the Wilcoxon rank-sum test was used to non-normality variables. To verify the association between the categorical variables,  $p < 0,05$  to the results need to be considered as significant.

The research project was approved by the Research Ethics Committees from the Federal University of Health Sciences of Porto Alegre, by the legal advice 1.636.572 and of Pontifical Catholic University of Rio Grande do Sul, approved by the legal advice 1.669.050/2017.

## Results

From 68 kidney transplanted patients that fulfilled the inclusion criteria proposed to the study, 59 agreed to participate and signed an informed consent. The demographic and clinical characteristics of the sample are described in table 1.

In relation to the learning style of the patients of the study, 37 (62,8%) aural, 15 (25,4%) Kinesthetic, 4 (6,8%) visual, and 3 (5,0%) had the Read/Write style.

In the evaluations of the adherence to the immunosuppressant, 10 (16,9%) were adherents in the first evaluation. In the second, 39 (66,1%), in the third 47 (79,7%) and in the fourth 50 (84,7%) were classified as adherents. The evolution of the patient adherence rate is illustrated in figure 2.

**Table 1: Demographic and clinical characteristics of a sample of 59 kidney transplanted patients**

Variables	n (59)	%
<b>Gender</b>		
Male	34	57,6
Female	25	42,4
<b>Age</b>		
Mean±DP	45,8±13,1	
<b>Color</b>		
White	47	79,7
Black	12	20,3
<b>Instruction Level</b>		
Primary school	34	57,6
Secondary school	20	33,9
College education	5	8,5
<b>Religion</b>		
Catholic	43	72,9
Spirit	3	5,1
Evangelical	5	8,5
Others	8	13,6
<b>Dialysis Modality</b>		
Haemodialysis	51	86,4
Peritoneal dialysis	7	11,9
Not done	1	1,7
<b>Previous Transplant</b>		
Yes	2	3,4
No	57	96,6
<b>Hospital days</b>		
Mean±DP (Median)	17,2±10,6 (14,0)	
<b>Responsible for imunossuppressors</b>		
Pacient	53	89,8
Familiar	6	10,2
<b>Time in list*</b>		
Mean±DP (Median)	19,5±24,3 (12,0)	
<b>Transplant time**</b>		
Mean±DP (Median)	207,1±90,5 (191,0)	

\* Months; \*\* Days; DV: standard deviation.

Source: Authors.

Statistically significant differences were not found between demographic and clinical variables that composed the sampling profile. The explanation of this analysis is shown in table 2.

Between the first and the second evaluation, happened a significant increase ( $p < 0,001$ ) from number of adherents patients in the sec-

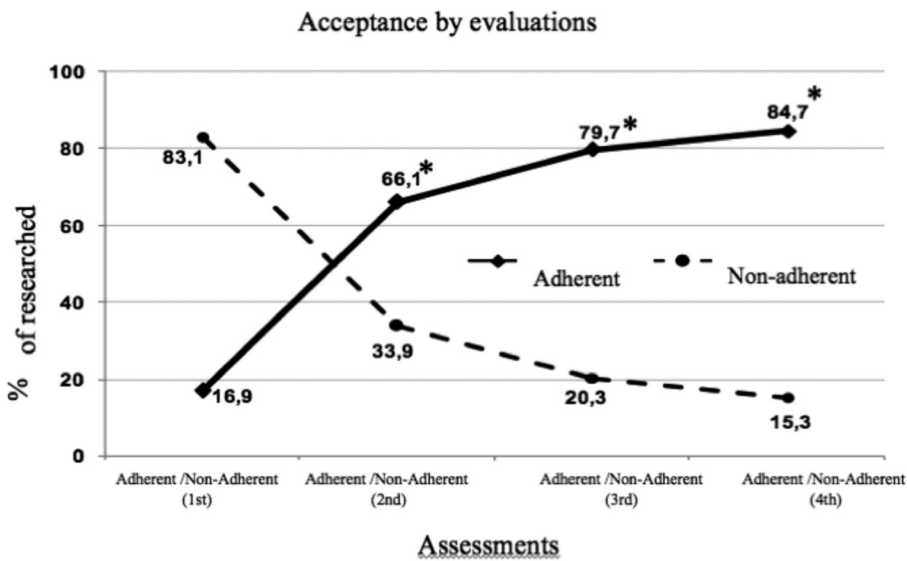


Figure 2: Adherence tax in four evaluations.

\* Statistical difference between first evaluation

Source: Authors.

ond [66,1% (n=39)] in comparison to the number of patients in the first evaluation [16,9% (n=10)].

About the comparison of the adherence between the first and the third evaluation, happened a significant increase again ( $p < 0,001$ ) of the number of adherents patients in the third evaluation, 47 (79,7%) in relation to the first evaluation, 10 (16,9%), representing 68,8% to the third evaluation.

The significant increase of the number of cases classified as adherents remained in the fourth evaluation, 50 (84,7%) in relation to the first, 10 (16,9%), which implies in an increase of 67,8% on the number of adherents ( $p = 0,009$ ).

When related the learning style and the adherents and non-adherents patients identified in the first BAASIS's evaluation, didn't happen a statistically significant differences ( $p = 0,602$ ), predominating the aural style [adherence: 60,0% - n=5 vs. non-adherence: 63,3% - n=31], followed by the Kinesthetic [adherence: 30,0% - n=3 vs. Non-adherence: 24,5% - n=12].

About the results of the last evaluation of the adherence, didn't have significant differences ( $p = 0,105$ ).

## Discussion

The results of this study, related to the immunosuppressant adherence didn't have statistically significant differences when related to the demographic and clinical data of the patients. But, a study with 209 kidney transplanted demonstrated significant difference when associated the adherence to the gender and time to transplant, it means that feminine gender and longer time of trans-

planted patients were more likely to adherence to immunosuppressant treatment<sup>13</sup>. Also, there are papers with results showing that variables as age, color, instruction level do not associate with the non-adherence<sup>14,15</sup>.

Generally, the studies that evaluate immunosuppressant adherence in transplanted are characterized by a considerable number of patients of the male gender, White color, and the mean age varying between 45 and 60 years old<sup>16,17</sup>. These results corroborate with the characterized patients in this research, where the mean age is the highest in adherents patients.

Similarly in Brazilian population, 57% of the patients with chronic kidney disease are male, and the age group between 20 to 64 years old, represented by 66% of the patients<sup>18</sup>.

There are authors that confirm that the adherence is related to self-care and self-management of the therapeutic that sustains the transplant<sup>19</sup>.

With regard to self-management of the immunosuppressive treatment, should be uninterrupted and realized by the transplanted, because the autonomy and the empowering are fundamental subsidies to the success of the

**Table 2: Relation of the adherence as BAASIS instrument with demographic and clinical variables**

	Total sample (n=59)				p
	Adherence (n=10)		Non-adherence (n=49)		
	n	%	n	%	
<b>Gender</b>					
Female	3	30,0	22	44,9	0,494‡
Male	7	70,0	27	55,1	
<b>Age</b>					
Mean±DP (Median)	50,1±13,8 (50,5)		44,9±12,9 (47,0)		0,256¥*
<b>Cor</b>					
White	8	80,0	39	79,6	>0,999‡*
Black	2	20,0	10	20,4	
<b>Instruction Level</b>					
Primary school	7	70,0	27	55,1	0,662‡*
Secondary school	3	30,0	17	34,7	
College education			5	10,2	
<b>Religion</b>					
Catholic	9	90,0	34	69,4	0,904‡*
Spirit			3	6,1	
Evangelical			5	10,2	
Others	1	10,0	7	14,3	
<b>Dialysis Modality</b>					
Haemodialysis	8	80,0	43	87,8	0,458‡*
Peritoneal dialysis	2	20,0	5	10,2	
Not done			1	2,0	
<b>Transplante time</b>					
Mean±DP (Median)	199,8±92,1 (190,5)		208,6±91,1 (191,0)		0,781¶*
<b>Hospital days</b>					
Mean±DP (Median)	16,7±8,2 (15,5)		17,3±11, (14,0)		0,866¶*

‡: Fisher's exact test (Monte Carlo methods or Monte Carlo experiments); ¥: Student's t-tests for independent groups assuming homogeneity of variances; ¶: Teste de Mann Whitney; \* There was no significant difference. DP: standard deviation

Source: Authors.

therapeutic. These elements can be generated through educational interventions by professionals that assist the patients, because they feel safer when explained about the risks and benefits to their health when they don't adhere the therapeutic treatment<sup>20,21</sup>.

The educational interventions about the importance of Administration of immunosuppressant are essential to this study. A randomized study with 111 kidney transplant patients

assessed immunosuppressive adherence before and after application of an educational plan on immunosuppressive drugs. In that study, authors concluded that even though there was no difference in rejection rates, patient knowledge and perception of immunosuppressive drugs significantly improved short-term therapy adhesion<sup>22</sup>.

Likewise, a systematic review sought to identify research on educational interventions for patients suffering from chronic kidney disease. It concluded that preparation of frequent interactive educational plans is fundamental for optimizing treatment for kidney disease. Another important factor observed by the review was the effectiveness of individualized and group strategies to promote knowledge on the disease, as well as to improve patients' self-management of their treatment<sup>23</sup>.

Also, researches that analyzed the relationship of adherence to medicines with educational interventions, concluded that early and continuous interventions contribute positively to the promotion of the adhere of the kidney transplanted patients<sup>24,25</sup>.

In identifying the learning style of the participants of this study, the aural style was the pre-

dominant, followed by kinesthetic.

In relation to the learning style of the patients of the study, 37 (62,8%) aural, 15 (25,4%) Kinesthetic, 4 (6,8%) visual, and 3 (5,0%) had the Read/Write style.

The learning styles and the application of educational interventions through the tools according to each style had no relationship with the membership of the immunosuppressive therapy.

In this context, were not found in the literature studies that evaluate the learning style with immunosuppressive therapy.

In the same perspective, get information about the importance of immunosuppressants in video form, was favorable in view of 33 newly transplanted kidney from a study that evaluated the opinion that evaluated the opinion of this population to receive the information by means of patients already transplanted<sup>26</sup>. A study conducted with 354 students, in which it was applied the VARK questionnaire to identify their learning styles, the kinesthetic was prevalent in more than half of the sample.

In this same study, the authors concluded that consider learning styles is an important factor for planning of activities intended to develop<sup>27</sup>.

Another study randomized two groups of diabetic patients, totaling 160 subjects. Researchers applied educational strategies aimed at promoting knowledge on diabetes to the intervention group. Strategies were based on patients' learning styles. This study showed a significant improvement on patient knowledge about the disease<sup>28</sup>.

The results presented in this study could be justified by the fact that the small number of patients between the groups after the characterization of learning style, considering this the greatest limitation of the study.

## Conclusion

Finally, most of the patients were non-adherence in the first evaluation, however there was improvement of this behavior in the course of operations, making the results statistically mean.

This research showed that immunosuppressive treatment adherence of renal transplant patients is not associated with specific educational interventions to learning styles.

To promote educational strategies that aim the understanding of aspects covering the transplantation, with emphasis on the importance of

immunosuppressants, can contribute to an improvement of adherence of renal transplanted patients and, consequently, increased survival of the graft and improvement in quality of life.

## References

1. Prihodova L, Nagyova I, Rosenberger J, Majernikova M, Roland R, Groothoff JW, et al. Adherence in patients in the first year after kidney transplantation and its impact in graft loss and mortality: a cross-sectional and prospective study. *J Adv Nurs*. 2014;70(12):2871-83.
2. Tielen M, van Exel J, Laging M, Beck DK, Khemai R, van Gelder T, et al. Attitudes to medication after kidney transplantation and their association with medication adherence and graft survival: a 2-year follow-up study. *J Transpl*. 2014;2014:1-9.
3. Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med*. 2005;353:487-97.
4. Dobbels F, Berden L, De Geest S, Drent G, Lennerling A, Whittaker C, et al. The psychometric properties and practicability of self-report instruments to identify medication nonadherence in adult transplant patients: a systematic review. *Transplantation*. 2010;90(2):205-19.
5. Marsicano E de O, Fernandes N da S, Colugnati F, Grincenkov FR dos S, Fernandes NM da S, De Geest S, et al. Transcultural adaptation and initial validation of Brazilian-Portuguese version of the Basel assessment of adherence to immunosuppressive medications scale (BAASIS) in kidney transplants. *BMC Nephrology*. 2013;14:108.
6. Skelton SL, Waterman AD, Davis LA, Peipert JD, Fish AF. Applying best practices to designing patient education for patients with end-stage renal disease pursuing kidney transplant. *Prog Transplant*. 2015;25(1):77-84.
7. Ladin K, Daniels A, Osani M, Bannuru RR. Is social support associated with post-transplant medication adherence and outcomes? A systematic review and meta-analysis. *Transplant Rev*. 2018;32(1):16-28.
8. Waterman AD, McSorley A-MM, Peipert JD, Goalby CJ, Peace LJ, Lutz PA, et al. Explore Transplant at Home: a randomized control trial of an educational intervention to increase transplant knowledge for Black and White socioeconomically disadvantaged dialysis patients. *BMC Nephrology*. 2015;16(1):150.

9. Haspeslagh A, Bondt DK, Kuypers D, Naesens M, Dobbels FCB. Completeness and satisfaction with the education and information received by patients immediately after kidney transplant: a mixed-models study. *Prog Transplant*. 2013;23(1):12–22.
10. Waterman A, Robbins M, Paiva A, Peipert J, Kynard-Amerson C, Goalby C, et al. Your Path to Transplant: a randomized controlled trial of a tailored computer education intervention to increase living donor kidney transplant. *BMC Nephrology*. 2014;15:166.
11. Sethares KA, Westlake C. Gender and occupational differences in learning styles of older adult heart failure patients. *Hear Lung*. 2015;21;44(6):551.
12. Fleming ND, Mills C. Not Another Inventory, Rather a Catalyst for Reflection. *To Improv Acad*. 1992;11:137–55.
13. Liu J, Liu S, Yan J, Yi Q, Huang H. Adherence to Immunosuppressive Medication in Renal Transplant Recipients From Follow-up Outpatient in China: Association of 2 Different Measurement Methods. *Clin Ther*. 2015;37(11):2572–80.
14. Massey EK, Meys K, Kemer R, Weimar W, Roodnat J, Cransberg K. Young Adult Kidney Transplant Recipients: Nonadherent and Happy. *Transplantation*. 2015;99(8):89–96.
15. Tielen M, van Exel J, Laging M, Beck DK, Khemai R, van Gelder T, et al. Attitudes to medication after kidney transplantation and their association with medication adherence and graft survival: a 2-year follow-up study. *J Transpl*. 2014;2014:1-9.
16. Reese PP, Bloom RD, Trofe-Clark J, Mussell A, Leidy D, Levisky S, et al. Automated Reminders and Physician Notification to Promote Immunosuppression Adherence Among Kidney Transplant Recipients: A Randomized Trial. *Am J Kidney Dis*. 2017;69(3):400–9.
17. Scheel J, Reber S, Stoessel L, Waldmann E, Jank S, Eckardt K-U, et al. Patient-reported non-adherence and immunosuppressant trough levels are associated with rejection after renal transplantation. *BMC Nephrology*; 2017;18(1):1-7.
18. Sesso RC, Lopes AA, Thomé FS, Lugon JR, Martins CT. Inquérito Brasileiro de Diálise Crônica 2016. *J Bras Nefrol*. 2017;39(3):261–6.
19. Jamieson NJ, Hanson CS, Josephson MA, Gordon EJ, Craig JC, Halleck F, et al. Motivations, challenges, and attitudes to self-management in kidney transplant recipients: A systematic review of qualitative studies. *Am J Kidney Dis*. 2016;67(3):461–78.
20. Jamieson NJ, Hanson CS, Josephson MA, Gordon EJ, Craig JC, Halleck F, et al. Motivations, challenges, and attitudes to self-management in kidney transplant recipients: A systematic review of qualitative studies. *Am J Kidney Dis*. 2016;67(3):461–78.
21. Robinson JK, Guevara Y, Gaber R, Clayman ML, Kwasny MJ, Friedewald JJ, et al. Efficacy of a sun protection workbook for kidney transplant recipients: A randomized controlled trial of a culturally sensitive educational intervention. *Am J Transplant*. 2014;14(12):2821–9.
22. Garcia MFFM, Bravin AM, Garcia PD, Contti MM, Nga HS, Takase HM, et al. Behavioral measures to reduce non-adherence in renal transplant recipients: a prospective randomized controlled trial. *Int Urol Nephrol*. 2015;47(11):1899–905.
23. Lopez-Vargas PA, Tong A, Howell M, Craig JC. Educational Interventions for Patients With CKD: A Systematic Review. *Am J Kidney Dis*. 2016;68(3):353–70.
24. Massey EK, Tielen M, Laging M, Beck DK, Khemai R, van Gelder T, et al. The role of goal cognitions, illness perceptions and treatment beliefs in self-report adherence after kidney transplantation: A cohort study. *J Psychosom Res*. 2013;229–34.
25. Low JK, Williams A, Manias E, Crawford K. Interventions to improve medication adherence in adult kidney transplant recipients: A systematic review. *Nephrol Dial Transplant*. 2015;30(5):752–61.
26. Low JK, Crawford K, Manias E, Williams A. The potential of a patient-centred video to support medication adherence in kidney transplantation: A three-phase sequential intervention research. *Transpl J Australasia*. 2017;26(1):12–7.
27. Klement M. How do my students study? An analysis of students of educational disciplines favorite learning styles according to VARK classification. *Soc Behav Sci*. 2014;132:384–90.
28. Koonce TY, Giuse NB, Kusnoor S V., Hurley S, Ye F. A personalized approach to deliver health care information to diabetic patients in community care clinics. *J Med Libr Assoc*. 2015;103(3):123–30.