

12. Adherence in Solid Organ Transplantation

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12.1 Consensus conference reports and recommendations

Tong A, et al. (2022) Patient-Reported Outcomes as Endpoints in Clinical Trials of Kidney Transplantation Interventions. *Transplant International*, vol. 35. Retrieved from:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9163311/>

- This review highlights the importance of the Standardized Outcomes in Nephrology (SONG)-Tx Initiative in establishing core patient-reported outcome measures (PROMs) and its integration into future clinical trials related to kidney transplantation.
- PROMs aim to facilitate the assessment of a patient's perspective of their health. The patient-reported outcomes (PRO) domains of physical, emotional, and cognitive functioning, mental health, and health-related quality of life are relevant for considerations in trials in kidney transplantation.

Karpen SR, et al. (2021) The Role of Patient-Reported Outcomes and Medication Adherence Assessment in Patient-Focused Drug Development for Solid Organ Transplantation. *Transplantation*, vol. 105, no. 5. Retrieved from:

https://journals.lww.com/transplantjournal/Fulltext/2021/05000/The_Role_of_Patient_reported_Outcomes_and.4.aspx

- Report from a 2-day public workshop between the US Food and Drug Administration and Critical Path Institute addressing the impact of patient reported outcomes (PROs) and medication adherence integration into patient-focused drug development (PFDD) for transplantation.
- An expert panel of transplant recipients provided insight on complexities of posttransplant life, personal methods to maintain medication adherence, and areas of concern.
- The existing PRO, Patient-Reported Outcome-Common Terminology Criteria for Adverse Events (PRO-CTCAE) developed by the National Cancer Institute, may have the ability to be adapted for use in solid organ transplant. Development or modification of an existing PRO measures is an essential component of integrating PFDD in transplantation.

Ettenger R, et al. (2018). Meeting report: FDA public meeting on patient-focused drug development and medication adherence in solid organ transplant patients. *Am J Transplant*, 18(3), 564-573. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/29288623/>

- This report highlights the need to individualize and simplify IST to mitigate short- and long- term adverse side effects, and gain clarity about optimal vs acceptable medication adherence.
- Participants were clear that problems with current nonspecific IST lead not only to adverse physiological health conditions, but myriad emotional health problems. As new approaches to therapy are being developed, it is critical for the drug developers and regulatory agencies to

include the issues articulated by patients, such as those discussed in this conference, if the innovations are to accomplish the goal of better healthcare for solid organ transplant recipients.

Maldonado AQ, et al. (2018). Meeting report: Consensus recommendations for a research agenda to address immunosuppressant nonadherence in organ transplantation. *Clin Transplant*, 32(9):e13362. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/30053319>

- In these consensus recommendations, members of the AST TxPharm COP met to identify unmet research needs related to medication nonadherence in transplant and presented on past, present and future directions of medication nonadherence and unmet research needs in the area. Key next steps for addressing nonadherence that were identified include development of a cost-effective, nonspecialized intervention(s) that does not require high levels of health literacy and can be adapted to multiple organs, as well as the use of tools to detect nonadherence that also address the issue as well. This meeting also resulted in the development of the AST Transplant Pharmacy Adherence Consortium (TPAC), which is dedicated to fostering development of a research agenda and connecting resources/researchers in the areas of adherence.

Myaskovsky L, Jesse MT, Kuntz K. (2018). Report from the American Society of Transplantation Psychosocial Community of Practice Adherence Task Force: Real-world options for promoting adherence in adult recipients. *Clin Transplant*. 2(9). Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/30022527>

- In these consensus recommendations, the AST Psychosocial and Pharmacy CoPs came together to develop a list of strategies using available resources, clinically feasible methods of screening and tracking adherence, and activities that ultimately empower patients to improve their own self management

Neuberger JM, et al. (2017). Practical recommendations for long-term management of modifiable risks in kidney and liver transplant recipients: A guidance report and clinical checklist by the Consensus on Managing Modifiable Risk in Transplantation (COMMIT) Group. *Transplantation*, 101, S1–S56. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/28328734/>

- The COMMIT group was formed in 2015 and is composed of 20 leading kidney and liver transplant specialists from 9 countries across Europe. The objective of this supplement is to provide specific, practical recommendations, through the discussion of current evidence and best practice, for the management of modifiable risks in those kidney and liver transplant patients who have survived the first postoperative year. In addition, the provision of a checklist increases the clinical utility and accessibility of these recommendations, by offering a systematic and efficient way to implement screening and monitoring of modifiable risks in the clinical setting

Fine RN, et al. (2009). Nonadherence consensus conference summary report. *Am J Transplant*, 9(1), 35-41. Retrieved from: <http://www.ncbi.nlm.nih.gov/pubmed/19133930>

- This report aimed to define non-adherence, describe its prevalence, how it can be measured, what the risk factors might be, and what clinical impacts it can have on patients using immunosuppressant medications. Additionally, this report attempted to provide recommendations for future study.

12.2 Review articles

Fan, Z., Han, Y., Sun, G., & Dong, Z. (2025). Immunosuppressant adherence after heart transplantation: a review on detection, prevention, and intervention strategies in a multidisciplinary. *Frontiers in Cardiovascular Medicine*, 12, 1558082. Retrieved from: <https://doi.org/10.3389/fcvm.2025.1558082>

- This systematic review found non-adherence was linked to higher hospitalization, costs, and worse outcomes. More reliable measures include drug levels and electronic monitoring. Multidisciplinary strategies were most effective.

Corr, M., Walker, A., Maxwell, A. P., & McKay, G. J. (2024). Non-adherence to immunosuppressive medications in kidney transplant recipients—a systematic scoping review. *Transplantation Reviews*, 100900. Retrieved from: <https://doi.org/10.1016/j.trre.2024.100900>

- This scoping review found non-adherence rates in kidney transplant ranged from 2%–89% (median 34%). Non-adherence was linked to rejection, donor-specific antibodies, and reduced graft survival especially in adolescents. Of 47 interventions, 38% showed no benefit, with medication regimen simplification (switching immunosuppressant from twice-daily to once-daily) being the most promising.

Melilli, E., Díaz, M. I., Gomis-Pastor, M., González, E., Gutierrez-Dalmau, A., Nuño, E. I., Pérez, A. M., Plasencia, I., Sangrador, A., Lázaro, E., Montero, N., & Soria, C. (2025). Predictors of Treatment Adherence in Kidney Transplant Patients: A Systematic Review of the Literature. *Journal of clinical medicine*, 14(5), 1622. Retrieved from: <https://doi.org/10.3390/jcm14051622>

- This systematic review identified multiple factors influencing immunosuppressive adherence in kidney transplant recipients: socioeconomic (e.g., age, education, social support), patient-related (e.g., mental health, awareness), treatment-related (e.g., regimen complexity, side effects), disease-related (e.g., time post-transplant, dialysis history), and healthcare system–related (e.g., provider relationship, access to care).

Karahan, A., & Akgün Çıtak, E. (2024). Effectiveness of Interventions to Increase Medication Adherence in Pediatric Renal Transplant Patients: Systematic Review. *Experimental and clinical transplantation: official journal of the Middle East Society for Organ Transplantation*, 22(Suppl 5), 71–77. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/39498924/>

- The goal of this review was to determine what interventions were effective in increasing medication adherence for pediatric kidney transplant recipients. The authors concluded that integrating multiple components such as a team-based approach, user-friendly technology, patient involvement, self-management promotion, identifying barriers, and motivational incentives can help with medication adherence.

Zhao, Q., Dong, L., Wang, L., Zhao, H., Zhu, X., Zhang, Z., & Liu, J. (2024). Immunosuppressant medication behaviours in solid organ transplant recipients: a cross-sectional study from south-central China during COVID-19 reopening period. *BMJ open*, 14(3), e080998. Retrieved from: <https://doi.org/10.1136/bmjopen-2023-080998>

- This study aimed to investigate the prevalence of immunosuppressant medication non-adherence and associated factors during the COVID-19 reopening period among Chinese SOT recipients. Some key findings from this study were high intensity physical activity was associated with lower rates of non-adherence while a higher monthly income and depression were associated with higher rates of non-adherence.

Tanaka, T., Kakiuchi, S., Tashiro, M., Fujita, A., Ashizawa, N., Eguchi, S., Kenmochi, T., Egawa, H., & Izumikawa, K. (2023). Adherence to recommended vaccination policies for pre- and post-solid organ transplantation patients: A national questionnaire survey in Japan. *Vaccine*, 41(52), 7682–7688. Retrieved from: <https://doi.org/10.1016/j.vaccine.2023.11.033>

- This was a review of a survey among transplant facilities in Japan to assess discrepancies in adherence to vaccine recommendations and policies pre- and post- solid organ transplantation. They found multiple etiologies for unresponsiveness to vaccinations including inadequate time before transplantation, cost burden, high number of vaccinations, no recognition of the need for vaccination, and the requirement to explain the need for vaccination.

Stefanizzi, P., Bianchi, F. P., Moscara, L., Martinelli, A., Di Lorenzo, A., Gesualdo, L., Simone, S., Rendina, M., & Tafuri, S. (2023). Determinants of compliance to influenza and COVID-19 vaccination in a cohort of solid organ transplant patients in Puglia, Southern Italy (2017-2022). *Human vaccines & immunotherapeutics*, 19(3), 2266932. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/37842986/>

- This study looks at influenza and COVID-19 vaccination compliance in Italy. Conclusions: Vaccination coverage (VC)s were suboptimal, especially for constant yearly influenza vaccination (17.7%) and COVID-19 vaccination's second booster (1.94%). Logistic regression highlighted that influenza VCs are higher for SOT recipients than SOT candidates, as well as for older patients, although when considering both vaccination seasons only age significantly impacts the vaccination uptake. Older age was the only influential variable for COVID-19 VC. VCs for SOT patients seem to be unsatisfying and stronger interventions are required.

Corr M, et al. (2023). The educational needs of adolescent and young adult renal transplant recipients – a scoping review. *Healthcare*, 11(4), 566. Retrieved from: <https://www.mdpi.com/2227-9032/11/4/566>

- This review included 29 studies assessing themes of non-adherence for adolescent and young adult renal transplant recipients. Several themes were identified, showing that good family support and help in developing organizational skills, especially with medications, were protective against worse health outcomes. Additionally, those who have high educational and professional attainment have been found to be more adherent to immunosuppression.

Gandolfini I, et al. (2022) Detecting, Preventing and Treating Non-Adherence to Immunosuppression after Kidney Transplantation. *Clinical Kidney Journal*, vol. 15, no. 7. Retrieved from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9217626/>

- This literature reviewed intentional and unintentional risk factors for medication non-adherence (MNA) as well as strategies for its prevention and treatment. The article also discussed the defining and measuring of MNA.

Hammond C, et al. (2021) Medical Adherence and Liver Transplantation: A Brief Review. *Canadian Liver Journal*, vol. 4, no. 1. Retrieved from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9203162/>

- This review discussed potential risk factors and techniques for improving medication non-adherence post liver transplant. The authors focused on the risk factors of socio-demographic and alcohol relapse and emphasized that multiple risk factors create an additive risk for potential medication non-adherence.

Sandal S, Chen T, Cantarovich M. (2021). Evaluation of transplant candidates with a history of nonadherence: an opinion piece. *Canadian Journal of Kidney Health and Disease*, 8, 1-7. Retrieved from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7863559/>

- This opinion piece provides a review of nonadherence in transplant, nonadherence definitions, the need for these assessments, and current practices that may be contributing to disparities in access to transplantation. The authors also review interventions to assist with nonadherence, duration of adherence assessment, and who to assess.

Kuypers DRJ. (2020). From nonadherence to adherence. *Transplantation*, 104,1330-1340. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/31929426/>

- This review provides suggestions on how different types of transplant centers can set up dedicated medication nonadherence programs according to available resource to define and achieve realistic clinical goals in managing medication nonadherence.

Lee H, et al. (2020). Effectiveness of eHealth interventions for improving medication adherence of organ transplant patients: A systematic review and meta-analysis. *PLoS ONE*, 15(11),1-18. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/33152010/>

- This systematic review and meta-analysis aimed to evaluate the effects of eHealth interventions for improving medication adherence in organ transplant patients as compared to usual or conventional care alone. Results of this study suggest that eHealth interventions were similar to standard care or advanced care for improving medication adherence.

Pruette CS & Amaral S. (2020). Empowering patients to adhere to their treatment regimens: a multifaceted approach. *Pediatr Transplant*, 00, e13849. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/33152010/>

- This article reviews recent literature published over the last 5 years on the topic of adherence in transplant recipients. The purpose was to highlight various insights and opportunities to promote adherence at the individual patient level, family level, healthcare system level, and community level.

Chisholm-Burns MA, Spivey C, Pickett L. (2018). Health literacy in solid-organ transplantation: a model to improve understanding. *Patient Prefer Adherence*, 12, 2325–2338. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/30464420>

- This literature review developed a model to better depict factors associated with low health literacy, including adherence. The impact of these factors and their relationships to solid organ transplant recipient outcomes are reviewed.

Duncan S, et al. (2018). A systematic review of immunosuppression interventions in transplant recipients: Decoding the streetlight effect. *Pediatric Transplant*, 22, e13086. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/29218760>

- This systematic review identified 41 studies that evaluated outcomes of various interventions to improve medication adherence in solid organ transplant recipients. The authors conclude that adherence interventions to date have been largely ineffective in improving transplant outcomes. Future interventions may wish to concentrate on non-adherent patients rather than using convenience sampling, use direct measures of adherence to guide the interventions, and employ strategies that are intensive and yet engaging enough to ensure that non-adherent patients are able to participate.

Kilian MO, et. al. (2018). Psychosocial predictors of medication non-adherence in pediatric organ transplantation: A systematic review. *Pediatr Transplant*, 22, e13188. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/29637674/>

- There is limited literature surrounding psychosocial predictors of non-adherence. This article sought to identify studies of the psychosocial predictors of non-adherence.

Zhu Y, et al. (2017). Efficacy of interventions for adherence to the immunosuppressive therapy in kidney transplant recipients: a meta-analysis and systematic review. *J Investig Med*, 65,1049-56. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/28483983/>

- This study investigated whether adherence interventions improve adherence of kidney transplant recipients to immunosuppressive regimens. Primary outcomes included adherence rate and score. Among participants receiving intervention, the adherence rate and score was significantly higher than the control group. Examples of interventions included inclusion of a pharmacist, continuing education, and behavior contract.

Doyle IC, Maldonado AQ, Heldenbrand S, Tichy EM, Trofe-clark J. (2016). Nonadherence to therapy after adult solid organ transplantation: A focus on risks and mitigation strategies. *Am J Health Syst Pharm*, 73(12), 909-920. Retrieved from: <http://www.ncbi.nlm.nih.gov/pubmed/27189855>

- This commentary comprehensively reviews current literature to identify factors that contribute to solid-organ transplant patient non-adherence and to explore potential solutions.

Heldenbrand S, et al. (2016). Assessment of medication adherence app features, functionality, and health literacy level and the creation of a searchable Web-based adherence app resource for health care professionals and patients. *J Am Pharm Assoc*, 56(3),293-302. Retrieved from:

<https://www.ncbi.nlm.nih.gov/pubmed/27067551>

- This study searched for and identified 367 unique evaluable adherence applications. The results of this study included scoring of apps and inclusion of the 100 highest-scoring apps onto a searchable website for healthcare providers and patients to use to identify potential apps that may benefit them (www.medappfinder.com).

Fredericks EM, Dore-Stites D. (2010). Adherence to immunosuppressants: How can it be improved in adolescent organ transplant recipients? *Curr Opin Organ Transplant*, 15(5), 614-20. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/20651598/>

- This review examined recent studies and position statements to determine current issues related to improving medication adherence in adolescent transplant recipients. The authors identify technology, such as internet and cell phones, as a promising mechanism for delivering adherence promoting interventions to this population. The authors conclude that strategies for promoting adherence in adolescent transplant recipients should incorporate health-related education, motivational and behavioral skills.

Denhaerynck K, et al. (2005). Prevalence, consequences, and determinants of nonadherence in adult renal transplant patients: a literature review. *Transplant Int*, 18(10), 1121-1133.

<https://www.ncbi.nlm.nih.gov/pubmed/16162098>

- In this literature review of 38 articles measuring nonadherence, nonadherence was associated with poor clinical outcomes, lower lifetime costs because of shorter survival, and a lower number of quality adjusted life years. Consistent determinants of nonadherence were found to be younger age, social isolation, and cognitions such as low self-efficacy, specific health beliefs. A limitation of this review is that the evidence summarized is based on older immunosuppressive regimens; further research would need to be conducted in order to characterize determinants of nonadherence in newer immunosuppressive regimens.

12.3 Adherence assessment tools

Leino, A. D., Kaiser, T. E., Khalil, K., Mansell, H., & Taber, D. J. (2024). Electronic health record-enabled routine assessment of medication adherence after solid organ transplantation: the time is now. *American journal of transplantation: official journal of the American Society of Transplantation and the American Society of Transplant Surgeons*, 24(5), 711–715. Retrieved from:

<https://pubmed.ncbi.nlm.nih.gov/38266711/>

- Medication nonadherence after solid organ transplantation is recognized as an important impediment to long-term graft survival. Yet, assessment of adherence is often not part of routine care. This Personal Viewpoint calls for the transplant community to consider implementing a systematic process to screen and assess medication adherence.

Kindem, I. A., Åsberg, A., Midtvedt, K., & Bjerre, A. (2023). Optimizing medication adherence with home-monitoring - A feasibility study using capillary microsampling and mHealth in solid organ-transplanted adolescents. *Pediatric transplantation*, 27(7), e14590. Retrieved from:

<https://pubmed.ncbi.nlm.nih.gov/37543722/>

- This study looked at methods for detection of medication nonadherence in adolescent solid organ transplants. Conclusions: Home-monitoring, combining Tac finger-prick microsampling and a medication-manager app, is feasible in adolescent SOT recipients with 70% perceived improvement in medication timing-adherence. There were no significant long-term changes in TacCV% confirming the need for continuous use and individualized interventions.

Denhaerynck K, et al. Psychometric properties of the BAASIS: a meta-analysis of individual participant data. *Transplantation*, Publish Ahead of Print. Retrieved from:

<https://pubmed.ncbi.nlm.nih.gov/36949037/>

- This meta-analysis reviewed 26 studies including 12,109 adult solid organ transplant recipients whose data was reviewed to examine the reliability and validity of BAASIS. Results showed that BAASIS-assessed nonadherence was significantly associated with electronically monitored adherence ($p < 0.03$), other self- and collaterally-reported nonadherence ($p < 0.001$), higher variability in tacrolimus concentrations ($p = 0.02$), higher barriers ($p < 0.001$), lower self-efficacy ($p < 0.001$), lower intention ($p < 0.001$) and higher worries ($p = 0.02$). Overall, the study demonstrated favorable validity and reliability of BAASIS as a nonadherence assessment tool.

Krause A, et al. (2021). Use of an electronic medication monitoring device to estimate medication adherence in kidney transplant patients. *Transl Behav Med*, ibaa122. Retrieved from:

<https://pubmed.ncbi.nlm.nih.gov/33710349/>

- This study aimed to assess the effectiveness of a wireless electronic medication monitoring device, SimpleMed+, in 55 kidney transplant patients. Adherence was assessed at 98.3% over an eight week study period for the 41 patients who completed the study. Fourteen patients either stopped using the device or did not use the device >70% of the time. The study authors concluded that further assessment of the practicality of an electronic medication monitoring device is warranted.

Varnell CD, et al. (2021). Predicting acute rejection in children, adolescents, and young adults with a kidney transplant by assessing barriers to taking medication. *Pediatr Nephrol*, ePub ahead of print.

Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/33501558/>

- In this 2-year observational, prospective cohort study, 98 kidney transplant recipients were assessed for barriers to adherence using a barriers assessment tool (a 14-item checklist) to determine the association with acute rejection. Kaplan-Meier analyses identified that patients were more likely to have an episode of acute rejection ($p = 0.02$) than those who did not have an

identified barrier via the assessment tool. Within the pediatric and adolescent kidney transplant recipients, identification of adherence barriers may assist in guiding targeted interventions to reduce risk of acute rejection.

Cushman GK. et. al. (2020). Caregivers' barriers to facilitating medication adherence in adolescents/young adults with solid organ transplants: Measure development and validation. *Pediatr Psychol.* 45, 498-508. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/32374379/>

- This study evaluated the factor structure, validity, and reliability of the Caregiver Medication Barriers to Adherence Scale (CMBAS) to assess caregivers' barriers to facilitating medication adherence in adolescent and young adults with solid organ transplants.

Van Pilsum Rasmussen SE, et. al. (2020). Psychosocial factors and medication adherence among recipients of vascularized composite allografts. *SAGE Open Med*, 8, 2050312120940423. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/32695395/>

- The authors studied various psychosocial factors using validated tools to assess medication adherence among vascularized composite allotransplantation recipients.

Gomis-Pastor M, et. al. (2019). Multimorbidity and medication complexity: New challenges in heart transplantation. *Clin Transplant*, 33, e13682. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/31368585/>

- This study was a single-center, observational study that included heart transplant recipients > 1.5 years from transplant and assessed multimorbidity and therapeutic complexity, which are recognized problems in heart transplant population. The patient-level Medication Regimen Complexity Index Spanish version (pMRCI-S) score was utilized and the impact of the index score on specific variables was assessed.

Gustavsen MT, et al. (2019). Evaluation of tools for annual capture of adherence to immunosuppressive medications after renal transplant. *Transplant International*, 32(6):614-625. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/30770608>

- This study evaluated tools suitable for annual routine capture of adherence data in renal transplant patients. The BAASIS© overall response rate was over 80%. Intensive BAASIS© assessment early after transplantation increased the chance of capturing a nonadherence event, but did not influence the 1year adherence prevalence. The adherence-tools generally captured different populations. Combining these tools is feasible for annual capture of adherence status.

Zhang M, et. al. (2019). Prevalence and risk factors of immunosuppressant nonadherence in heart transplant recipients: A single-center cross-sectional study. *Patient Prefer Adherence.* 13, 2185-2193. Retrieved from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6930119/>

- This study assessed immunosuppressant adherence based on the Basel Assessment of Adherence with Immunosuppressive Medication Scale (BAASIS). Immunosuppressant nonadherence was categorized into five domains of contributing factors which were then compared between adherent and nonadherent patients.

Rich KL, et. al. (2018). Predicting health care utilization and charges using a risk score for poor adherence in pediatric kidney transplant recipients. *Clin Pract Pediatr Psychol*, 6, 107-116. Retrieved from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6910652/>

- The authors developed a novel risk score to identify patients at risk for poor adherence behaviors and evaluated whether it would predict future health utilization and charges. The score consisted

of three metrics of adherence including: immunosuppression drug levels, timely laboratory monitoring, and timely clinic visits.

Williams A, Low JK, Manias E, Dooley M, Crawford K. (2016). Trials and tribulations with electronic medication adherence monitoring in kidney transplantation. *Res Social Adm Pharm*, 12(5), 794-800. Retrieved from: <http://www.ncbi.nlm.nih.gov/pubmed/26616159>

- This paper outlines the challenges in measuring medication adherence using electronic medication monitoring of kidney transplant patients.

Hugon A, et al. (2014). Influence of intention to adhere, beliefs and satisfaction about medicines on adherence in solid organ transplant recipients. *Transplantation*, 98(2):222-228. Retrieved from: <http://www.ncbi.nlm.nih.gov/pubmed/24926826>

- This study aimed to determine whether parameters of a model adapted from the theory of planned behavior (attitudes and beliefs) could predict adherence in transplant patients

Marsicano Ede O, et al. (2013). Transcultural adaptation and initial validation of Brazilian-Portuguese version of the Basel assessment of adherence to immunosuppressive medications scale (BAASIS) in kidney transplants. *BMC Nephrol*. 14(1):108. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/23692889>

- This study aimed to validate an instrument for accurately estimating immunosuppressant nonadherence in Brazilian/Portuguese-speaking transplant patients known as the BAASIS.

Dharancy S, Giral M, Tetaz R, Fatras M, Dubel L, Pageaux GP (2012). Adherence with immunosuppressive treatment after transplantation: results from the French trial PREDICT. *Clin Transplant*, 26(3), E293E299. Retrieved from: <http://www.ncbi.nlm.nih.gov/pubmed/22686953>

- This observational study evaluated patient adherence using the “compliance evaluation test” and through physician a “visual analog scale”. Determinants of adherence were then explored.

Schäfer-Keller P, Steiger J, Bock A, Denhaerynck K, De Geest S. (2008). Diagnostic accuracy of measurement methods to assess non-adherence to immunosuppressive drugs in kidney transplant recipients. *Am J Transplant*, 8(3), 616-626. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/18294158>

- In this cross-sectional study, nonadherence was measured using electronic monitoring, assays, selfreporting and clinician reports. The findings suggested that combining multiple measures resulted in increased accuracy in diagnosing nonadherence.

Chisholm MA, Lance CE, Williamson GM, Mulloy LL. (2005). Development and validation of the immunosuppressant therapy adherence instrument (ITAS). *Patient Educ Couns*. 59(1)13–20. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/16198214>

- This study assessed and validated a five-item scale that measures patients' adherence to immunosuppression therapy. The scale included one item that was deleted due to lack of response variability, and the published results of the four-item scale are the first published and validated instrument for measurement of adherence to immunosuppressive therapy.

12.4 Interventions

Zhong, C., Yao, L., Chen, L., Wang, X., Zhu, X., Wen, Y., Deng, L., Chen, J., Hui, J., Shi, L., & You, L. (2025). The use of virtual reality-assisted interventions on psychological well-being and treatment

adherence among kidney transplant recipients: A randomized controlled study. *Acta psychologica*, 253, 104700. Retrieved from: <https://doi.org/10.1016/j.actpsy.2025.104700>

- This 12-month randomized controlled trial of 372 kidney transplant patients found that virtual reality-assisted psychological and educational interventions significantly improved medication adherence ($p < 0.0001$), reduced depressive symptoms, enhanced functional independence, and shortened hospital stays compared to conventional education.

Bae, E. K., Chandran, M. M., Everitt, M. D., Benz, E., & Bock, M. (2024). LCP-Tacrolimus Extended-Release (Envarsus XR) Use in Adolescent and Young Adult Solid Organ Transplant Recipients. *Clinical transplantation*, 38(8), e15417. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/39087462/>

- Conclusion: Successful conversion from IR-Tac to LCP-Tac was demonstrated in AYA heart, kidney, and liver transplant recipients. These AYA SOT recipients experienced reduced pill burden and improved tacrolimus trough concentration variability. However, the impact on medication adherence warrants further investigation. Future research should explore the targeted use of LCP-Tac to enhance IS tolerability and medication adherence in young SOT populations.

Householder S, et al. (2024). The use of once-daily LCP-Tacrolimus with adolescent and young adult solid organ transplant recipients. *Pediatr Transplant*, 28(4), e14777. Retrieved from <https://pubmed.ncbi.nlm.nih.gov/38702932/>

- This is a retrospective, single-center study including 29 adolescent and young adult heart, liver, and kidney transplant recipients comparing provider assessment of adherence and medication level variability index (MLVI) prior to and after conversion to LCP-Tacrolimus.
- Adherence per provider assessment was 68.4% 12 months after conversion to LCP-Tacrolimus compared to 45% at the time of the LCPT prescription ($p = 0.140$) indicating a numerically greater but not statistically significant difference in adherence. Per MLVI value, nonadherence was defined as an MLVI value ≥ 2 . At 0-6 months before the LCPT prescription, the $MLVI < 2$ was 40% compared to 71.4% at 6-12 months after LCPT prescription ($p = 0.276$).

Sayegh CS, et al. (2024). Randomized pilot trial of cell phone support to improve medication adherence among adolescents and young adults with chronic health conditions. *BMC Digit Health*, vol. 2,1 (2024): 13. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/39211575/>

- This single center randomized controlled pilot trial enrolled adolescent and young adult patients with epilepsy, sickle cell disease, a solid organ transplant, or type 2 diabetes and randomized them to receive Cell Phone Support (CPS) through phone calls, CPS through text messages, and automated text message reminders. Ten patients of the 34 were solid organ transplant recipients.
- Participants in both CPS intervention groups self-reported a greater increase in adherence post-treatment from baseline when compared to the automated text message reminders group

Stringer D, et al. (2023). Optimized immunosuppression to prevent graft failure in renal transplant recipients with HLA antibodies (OuTSMART): a randomized controlled trial. *E Clinial Medicine*, 56:101819. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/36684392/>

- This prospective, open-label, randomized trial included adult kidney transplant recipients that received either standard care or unblinded biomarker led care (BLC). HLA Ab+ BLC patients underwent interviewing to emphasize the importance of adherence and all immunosuppression was optimized to maximum tolerated doses of mycophenolate and tacrolimus along with a steroid boost and taper if patients were agreeable.
- DSA development was predictive of graft failure, but hazard ratio for graft failure in the unblinded DSA+ was 1.54 (95% CI 0.72-3.30) compared to 0.97 (95% CI 0.54-1.74) for the non-DSA+ groups, demonstrating no evidence of intervention effect. Non-inferiority for the unblinded group versus the blinded group was not demonstrated.

Wagner-Skacel J, et al. (2023). Improving adherence to immunosuppression after liver or kidney transplantation in individuals with impairments in personality functioning – a randomized controlled single center feasibility study. *Front Psychol*, 14:1150548. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/36968754/>

- This is a prospective, randomized, controlled single-center feasibility study evaluating a step guided multicomponent interprofessional intervention program in 41 kidney or liver transplant recipients to improve adherence to immunosuppression. The program included group therapy and daily training along with individual sessions.
- There was no difference between intervention and control groups in regards to the coefficient of variation (CV%) of tacrolimus as well as adherence assessed by the BAASIS tool. Exploratory analyses found an association between impairments in personality functioning and CV% of tacrolimus in the control group.

Verma, et al. (2023). Improved medication adherence with use of extended-release tacrolimus in liver transplant recipients: a pilot randomized controlled trial. *J Transplant*, 7915781. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/36642992/>

- This randomized, controlled study sought to evaluate medication adherence, clinical efficacy, and safety of extended-release tacrolimus (TAC-ER) compared to immediate-release tacrolimus (TAC-IR) in 31 adult liver transplant recipients.
- Adherence in the TAC-ER group was 100% compared to 63.6% in the TAC-IR group ($p=0.035$). Two patients switched from TAC-ER to TAC-IR due to elevated LFTs after conversion which were both deemed to be acute rejection unrelated to TAC-ER. No differences were noted in eGFR, HbA1c, QOL, TAC trough levels, or liver function tests between groups.

Abtahi H, et al. (2022) Pragmatic Solutions to Enhance Self-Management Skills in Solid Organ Transplant Patients: Systematic Review and Thematic Analysis. *BMC Primary Care*, vol. 23, no. 1. Retrieved from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9247970/>

- This systematic review included 40 studies, 32 that focused on e-health programs for telemonitoring, non-electronic educational programs, non-electronic home-based symptom-monitoring programs, electronic educational plans for self-monitoring, and Telerehabilitation in the post-transplant phase.
- The results demonstrated that successful self-management for patients must utilize various tools and domains with the patient placed in the center of care.

Sambucini D, et al. (2022) Psychosocial Treatment on Psychological Symptoms, Adherence, and Physiological Function on Transplanted Patients: A Systematic Review and Metanalysis. *Journal of Psychosomatic Research*, vol. 154. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/35032913/>

- This systematic review and metanalysis assessed the difference between pre and post-psychosocial intervention assessment on the psychological variables, medical adherence, and organ functioning outcome.
- Supportive therapy produced moderate improvements in depressive and anxious symptoms overall in kidney recipients and in anxiety on heart recipients. This study also found that psychosocial intervention for anxious symptoms was more effective in the pre-transplant phase for kidney and post-transplant phase for heart recipients.

Prom A, et al. (2021) Impact of a Clinical Pharmacist in an Outpatient Heart Transplant Clinic. *JACCP: JOURNAL OF THE AMERICAN COLLEGE OF CLINICAL PHARMACY*, vol. 4, no. 12. Retrieved from: <https://accpjournals.onlinelibrary.wiley.com/doi/10.1002/jac5.1534>

- This study assessed the impact that a clinical pharmacist has on goal blood pressure, goal hemoglobin A1c, aspirin and statin compliance, and outpatient tacrolimus trough level coefficient variability among heart transplant recipients
- Integration of a clinical pharmacist was associated with improved attainment of blood pressure goal, appropriate statin utilization, and fewer total hospital readmissions at 1-year post transplant. No differences were found in diabetes management, aspirin use, and tacrolimus trough level coefficient variability.

Fleming JN, et al. (2021) Impact of a Pharmacist-Led, MHealth-Based Intervention on Tacrolimus Trough Variability in Kidney Transplant Recipients: A Report from the TRANSafe Rx Randomized Controlled Trial. *American Journal of Health-System Pharmacy*, vol. 78, no. 14. Retrieved from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8599187/>

- TRANSafe Rx is a secondary planned 12-month, parallel, 2-arm semiblind, 1:1 randomized control trial involving 136 kidney transplant recipients between 6-26 months after transplantation. The intervention arm demonstrated a statistically significant decrease in tacrolimus intra-patient variability (IPV) over time compared to the control arm (P=0.0133). In conclusion, pharmacist-led mobile health-based intervention demonstrated an association between the active intervention in the trial and improved tacrolimus IPV.

Marco B, et al. (2021). Adherence to, and patient convenience of, prolonged-release tacrolimus in stable kidney and liver transplant recipients after conversion from immediate-release tacrolimus in routine clinical practice in Switzerland. *Swiss Med Wkly*. 151, w20453. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/33638353/>

- This multi-center, observational, 12-month study evaluated medication adherence in liver and kidney transplant recipients converted from immediate-release tacrolimus to prolonged-release tacrolimus. Investigators utilized interview questionnaires and tacrolimus trough levels to assess non-adherence for up to 12 months post-conversion. Of the 75 patients assessed, majority of patients reported decreased pill burden and ease of remembering to take prolonged-release tacrolimus. Overall, 1-year non-adherence rates were similar before and after conversion.

Serper M, et al. (2021). Transplant regimen adherence for kidney recipients by engaging information technologies (TAKE IT): Rationale and methods for randomized controlled trial of a strategy to promote medication adherence among transplant recipients. *Contemp Clin Trials*. 103,106294. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/33515781/>

- This publication dictates the proposed methods and background for the TAKE IT trial, a two-arm, patient randomized controlled trial at two transplant centers. The study plans to recruit 450 kidney transplant recipients within two years of transplant. The intervention arm will implement the TAKE IT strategy, which involves use of an adherence mobile application, self-reported adherence assessments, care alert notifications, adherence reports, and tailored adherence support tools when needed. The primary outcome will assess medication adherence through pill count. The planned follow up period after inclusion is two years.

Fedderson N, et al. (2020). Adherence in pediatric renal recipients and its effect on graft outcome, a single-center, retrospective study. *PETR*, 00, e13922. Retrieved from: <https://onlinelibrary.wiley.com/doi/full/10.1111/petr.13922>

- The aim of the study was to determine the intra-patient immunosuppressant variability as measured by the trough-level CoV% in a single-center study and to correlate this with biopsy-proven rejections within up to 6 years following transplantation. The authors also compared

subjective adherence ratings of patient, families, and healthcare professional and correlated those with both the immunosuppressants' trough level CoV%, as well as formation of dnDSA and rejection episodes. Results of the study showed the CoV% was by-trend higher in those patients with biopsy-proven rejection. Also the psychologist's assessment correlated significantly with both rejection as well as with the formation of dnDSA. The authors concluded that medication adherence is important, but also stresses the role of a multi-disciplinary treatment approach to support pediatric renal transplant patients and their families.

Wadhvani S, et al. (2020). Implementing a process to systematically identify and address poor medication adherence in pediatric liver transplant recipients. *Pediatr Qual Saf.* 5(3), e296.

Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/32656465/>

- This cohort study describes the implementation of a process to appropriately assess and address medication nonadherence in the pediatric liver transplant population. The paper describes a multidisciplinary approach transplant clinic to identify poor adherence through a barriers assessment tool, implement a patient directed intervention bundle, and assess the intervention through variability in tacrolimus trough levels and episodes of late acute cellular rejection. During the 6 month follow up period, >90% of the 85 patients received an intervention bundle. The most common identified adherence barrier was forgetfulness.

Hall CL, et. al. (2019). Improving Transplant Medication Safety Through a Technology and Pharmacist Intervention (ISTEP): Protocol for a Cluster Randomized Controlled Trial. *JMIR Res Protoc.* 8, e13821.

Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/31573933/>

- This study focused on the clinical and economic effectiveness of a pharmacist-led, technology-enabled intervention versus usual care, in veteran organ transplant recipients. This was a 24 month, prospective, parallel-arm, cluster-randomized, controlled multicenter trial. The final results of this study are expected to be submitted for publication August 2021.

Paterson TS, et. al. (2019). Impact of once- versus twice-daily tacrolimus dosing on medication adherence in stable renal transplant recipients: A Canadian single-center randomized controlled trial. *Can J Kidney Health Dis,* 6, 2054358119867993. Retrieved from:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6699008/>

- This was a 4 month controlled medication dosing trial in adult renal transplant patients in a Canadian sample. The authors further described the relationship between tacrolimus dosing schedule and implementation adherence.

Triplett KN, et. al. (2019). Digital medicine program with pediatric solid organ transplant patients: Perceived benefits and challenges. *Pediatr Transplant.* 23, e13555. Retrieved from:

<https://onlinelibrary.wiley.com/doi/10.1111/petr.13555>

- This paper describes the implementation of a digital medicine program (DMP) where transplant patients' medications were co-encapsulated with ingestible sensors. Adherence was monitored via a patient mobile application and a provider portal.

Tsapepas DS, et al. (2018). Using technology to enhance medication regimen education after solid organ transplantation. *Am J Health Syst Pharm,* 75(23),1930-1937. Retrieved from:

<https://www.ncbi.nlm.nih.gov/pubmed/30463868>

- In this retrospective cohort study, a digital education intervention was introduced to 282 kidney transplant recipients. Patients were able to correctly answer questions related to medication indications, dosing, and administration considerations (90%), but many (61%) had issues properly

identifying adverse effects. This study does not directly address an intervention for improving adherence, but instead focuses on optimizing medication education in solid organ transplant recipients.

Abedini S, et al. (2018). Immunosuppression adherence in stable kidney transplant patients converted from immediate-to prolonged-release tacrolimus in clinical practice: A Norwegian study. *Transplantation direct*. 4(2). Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/29464199>

- This was a non-interventional, observational, multicenter study involving over 90 Norwegian kidney transplant recipients who were converted from immediate to prolonged-release tacrolimus formulations. Immediately in the first month following conversion, patients were more adherent as compared to baseline; however, the increased adherence was not sustained through 12-months post conversion.

Sayegh CS, et. al. (2018). Cell phone support to improve medication adherence among solid organ transplant recipients. *Pediatr Transplant*, e13235. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/29920879/>

- This study investigated the potential efficacy of a 12-week cell phone support intervention to improve immunosuppressant medication adherence.

Cukor D, Ver Halen N, Pencille M, Tedla F, Salifu M. (2017). A pilot randomized controlled trial to promote immunosuppressant adherence in adult kidney transplant recipients. *Nephron*. 135(1), 6-14. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28049201/>

- The aim of this pilot study was to test whether a culturally sensitive cognitive-behavioral adherence promotion program could significantly improve medication adherence to tacrolimus prescription as measured by telephone pill counts among kidney transplant recipients.

Dobbels F, et al. (2017). Efficacy of a medication adherence enhancing intervention in transplantation: The MAESTRO-Tx trial. *J Heart Lung Transplant*, 36(5), 499-508. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28162931>

- In this randomized controlled trial, half of a cohort of heart, liver, and lung transplant recipients on twice daily tacrolimus-based immunosuppression regimens received patient tailored behavioral interventions over a 6-month period. Post-intervention, this group was noted to have higher-dosing adherence in comparison to the control (no intervention) group. The intervention group also trended to have better event-free survival at 5 years, with regards to mortality and retransplantation.

Mellon L, et al. (2017). Intervention for improving medication adherence in solid organ transplant recipients. *Cochrane Database of Systematic Reviews*, 12, 1-15. Retrieved from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6486115/>

- This review aimed to look at benefits and harms of using interventions for improving adherence to immunosuppressant therapies in solid organ transplant recipients, including pediatric and adult heart, lung, kidney, liver, and pancreas transplant recipients.

Reese PP, et al. (2017). Automated reminders and physician notification to promote immunosuppression adherence among kidney transplant recipients: a randomized trial. *Am J Kidney Dis*. 69(3), 400-409. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27940063>

- The aim of this randomized single center trial was to evaluate the impact of varying forms of custom reminders on tacrolimus adherence. Patients were provided wireless pill bottles containing tacrolimus which allowed for pill bottle opening recordings.

Low JK, Crawford K, Manias E, Williams A. (2016). A compilation of consumers' stories: the development of a video to enhance medication adherence in newly transplanted kidney recipients. *J Adv Nurs*, 72(4), 813-824. Retrieved from: <http://www.ncbi.nlm.nih.gov/pubmed/26709034>

- This paper describes the design and development of a video created to educate new kidney transplant recipients about the importance of medication adherence.

Low JK, Williams A, Manias E, Crawford K. (2015). Interventions to improve medication adherence in adult kidney transplant recipients: a systematic review. *Nephrol Dial Transplant*. 2015, 30(5),752-761. Retrieved from: <http://www.ncbi.nlm.nih.gov/pubmed/24950938>

- This systematic review aimed to assess the effectiveness of interventions to improve medication adherence to immunosuppressive medications in adult kidney transplant patients

Williams A, et al. (2015). Examining the preparation and ongoing support of adults to take their medications as prescribed in kidney transplantation. *J Eval Clin Pract*. 21(2), 180-186. Retrieved from: <http://www.ncbi.nlm.nih.gov/pubmed/25318842>

- This paper examines how adult transplant recipients are prepared and supported by transplant coordinators and pharmacists to take their medications as prescribed.

Joost R, Dörje F, Schwitulla J, Eckardt K, Hugo C. (2014). Intensified pharmaceutical care is improving immunosuppressive medication adherence in kidney transplant recipients during the first posttransplant year: a quasi-experimental study. *Nephrol Dial Transplant*, 29(8), 1597-1607. Retrieved from: <http://www.ncbi.nlm.nih.gov/pubmed/24914089>

- This prospective trial utilized a pharmaceutical intensified care program led by clinical pharmacists to see if patient adherence would improve compared to patients who only received standard care

Muduma G, Odeyemi I, Smith-palmer J, Pollock R. (2014). Budget impact of switching from an immediate release to a prolonged-release formulation of tacrolimus in renal transplant recipients in the UK based on differences in adherence. *Patient Prefer Adherence*, 8, 391-399. Retrieved from: <http://www.ncbi.nlm.nih.gov/pubmed/24729687>

- This study assessed the cost differential between using a long-acting formulation of tacrolimus versus standard tacrolimus when considering the cost of non-adherence

Srivastava K, Arora A, Kataria A, Cappelleri JC, Sadosky A, Peterson AM. (2013). Impact of reducing dosing frequency on adherence to oral therapies: a literature review and meta-analysis. *Patient Prefer Adherence*,7,419-434. Retrieved from: <http://www.ncbi.nlm.nih.gov/pubmed/23737662>

- This meta-analysis assessed the impact of reduced frequency dosing on adherence, compliance, persistence, and associated economic impact.

Beckebaum S, et al. (2011). Efficacy, safety, and immunosuppressant adherence in stable liver transplant patients converted from a twice-daily tacrolimus-based regimen to once-daily tacrolimus extended-release formulation. *Transpl Int*. 24(7), 666-675. Retrieved from: <http://www.ncbi.nlm.nih.gov/pubmed/21466596>

- This study set out to determine the efficacy, safety, and adherence implications of switching patients from twice daily to once daily tacrolimus dosing.

Miloh T, et al. (2009). Improved adherence and outcomes for pediatric liver transplant recipients by using text messaging. *Pediatrics*, 124, e844–e850. Retrieved from:

<https://www.ncbi.nlm.nih.gov/pubmed/19822583>

- The aims of this prospective study were to pilot-test the effects of medication reminders via text message on patients' adherence and outcomes

12.5 Tacrolimus inpatient variability

Gavcovich, T. et al. (2025). Inpatient tacrolimus variability is associated with medical nonadherence among pediatric kidney transplant recipients. *Frontiers in transplantation*, 4, 1572928. Retrieved from:

<https://doi.org/10.3389/frtra.2025.1572928>

- In this prospective study of 75 pediatric kidney transplant recipients, higher tacrolimus inpatient variability (IPV) strongly correlated with nonadherence ($p < 0.001$); IPV $\geq 30\%$ indicated nonadherence and was associated with increased T cell mediated rejection (46% vs. 10%) and a history of dnDSA Class II (68% vs. 42%).

Lloberas, N. et al. (2025) Customizing Tacrolimus Dosing in Kidney Transplantation: Focus on Pharmacogenetics. *Therapeutic Drug Monitoring* 47(1):p 141-151. Retrieved from:

<https://doi.org/10.1097/FTD.0000000000001289>

- The aim of this review is to provide an overview of the current studies regarding the different population pharmacokinetic including pharmacogenetics and those translated to the clinical practice for individualizing tacrolimus dose adjustment in kidney transplantation. This review highlights that tacrolimus inpatient variability (IPV) in kidney transplant recipients is influenced by pharmacogenetics with fast metabolizers (CYP3A5*1 carriers) showing higher IPV and increased rejection risk.

Marquet P. (2025). Getting Tacrolimus Dosing Right. *Therapeutic drug monitoring*, 47(1), 41–48.

Retrieved from: <https://doi.org/10.1097/FTD.0000000000001266>

- This review highlights that high inpatient variability (IPV) in tacrolimus exposure—reflected by fluctuations in AUC and trough levels—is associated with increased risk of rejection. Individualized dosing using Bayesian-guided AUC/C₀ monitoring significantly reduced IPV, improved target attainment, and demonstrated superior stability over time compared to raw or dose-standardized AUC or C₀, even up to 15 years post-transplant. This finding holds true across various tacrolimus formulations (Prograf and Advagraf) and patient populations, including both adult and pediatric kidney transplant recipients.

Lee, S. K. et al. (2025). Optimal tacrolimus levels for reducing CKD risk and the impact of inpatient variability on CKD and ESRD development following liver transplantation. *Clinical and molecular hepatology*, 31(1), 131–146. Retrieved from:

<https://doi.org/10.3350/cmh.2024.0451>

- In this retrospective study of 952 liver transplant recipients, tacrolimus doses and levels were recorded every 3 months for a mean follow-up of 97.3 month. Higher tacrolimus inpatient variability (IPV) $\geq 35\%$ was significantly associated with increased risk of CKD. IPV was also a strong predictor of ESRD, with ESRD patients exhibiting the highest IPV.

Cossart, A. R. et al. (2025). Examining Whole Blood, Total and Free Plasma Tacrolimus in Elderly Kidney Transplant Recipients. *Therapeutic drug monitoring*, 47(1), 161–168. Retrieved from: <https://doi.org/10.1097/FTD.0000000000001274>

- In this prospective single-center cohort study, the whole-blood tacrolimus (Prograf) concentration was measured in fifteen elderly kidney transplant recipients using ultra-high performance liquid chromatography (UHPLC) and mass spectrometry (UHPLC-MS/MS). Free tacrolimus exposure varied widely despite stable whole-blood levels. Hematocrit significantly affected whole-blood concentrations but not free levels, suggesting free tacrolimus monitoring may better reflect true exposure and guide dosing.

Kopfman, M., et al. (2024). High Inpatient Tacrolimus Variability and Increased Cell-Free DNA in Kidney Transplant Recipients. *Progress in transplantation (Aliso Viejo, Calif.)*, 34(4), 204–210. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/39376164/>

- This single center retrospective study of 99 kidney transplant recipients was designed to assess the relationship between high tacrolimus inpatient variability and elevated donor derived cell-free DNA (dd-cfDNA). The median level of dd-cfDNA was significantly greater in the group with a tacrolimus coefficient of variation $\geq 30\%$ compared to $< 30\%$ (0.22% vs. 0.17%, $P = .031$) and the higher median dd-cfDNA was associated with the formation of de novo DSAs.

Soares, M. E., et al. (2024). Influence of Tacrolimus Inpatient Variability on Allograft Rejection Frequency and Survival Following Liver Transplantation. *Therapeutic drug monitoring*, 46(4), 456–459. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/38648652/>

- This single center retrospective study in 234 liver transplant recipients was designed to assess the effect of inpatient variability on allograft rejection frequency and post-liver transplant survival. Based on the mean and standard deviation tacrolimus trough level, mean absolute deviation (MAD), coefficients of variation (CV), and therapeutic range (TTR), tacrolimus inpatient variability was not a key factor when comparing acute rejection to no acute rejection and survival or no survival in this study.

Xie, W., et al. (2024). Tacrolimus intra-patient variability measures and its associations with allograft clinical outcomes in kidney transplantation. *Transplantation reviews (Orlando, Fla.)*, 38(3), 100842. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/38537484/>

- This review included 33 studies of kidney transplant recipients and aimed to evaluate correlations between measures of tacrolimus inpatient variability and the resultant graft outcomes. They concluded that while many studies point to a positive correlation between high tacrolimus inpatient variability and rejection occurrence, there remain some divergent findings which could be related to differences in tacrolimus inpatient variability threshold, calculation methods, or metabolic status.

Kim, H., et al. (2023). Association of high intra-patient variability in tacrolimus exposure with calcineurin inhibitor nephrotoxicity in kidney transplantation. *Scientific reports*, 13(1), 16502. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/37783764/>

- This single center study of 80 kidney transplant recipients aimed to evaluate the association between tacrolimus inpatient variability and CNI nephrotoxicity as well as the effects of pharmacogenetics on CNI nephrotoxicity and intra-patient variability. Using a coefficient of variation cutoff point of 26.5%, the high inpatient variability group was associated with an increased risk of CNI nephrotoxicity (HR 4.55; 95% CI 0.05–0.95; $p=0.043$) in a multivariate analysis.

Schagen, M. R., et al. (2023). Individualized dosing algorithms for tacrolimus in kidney transplant recipients: current status and unmet needs. *Expert opinion on drug metabolism & toxicology*, 19(7), 429–445. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/37642358/>

- This review included 25 studies in both adults and pediatric kidney transplant recipients with tacrolimus starting dose algorithms. Overall, this review concluded patients using a starting dose algorithm were able to reach tacrolimus target concentrations faster than those using conventional body weight dosing although there was no difference between algorithm based dosing and conventional body weight dosing when considering toxicity and allograft rejection.

Lai E, et al. (2023). Tacrolimus formulation, exposure variability, and outcomes in kidney transplant recipients. *Prog Transplant*, 33(1), 34-42. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/36562176/>

- This was an observational cohort study assess within-patient variability of tacrolimus trough levels pre- and post-conversion from twice-daily to once-daily tacrolimus in 463 kidney transplant recipients. After conversion to once-daily tacrolimus, every 1 unit increase in within-patient variability standard deviation and inpatient variability percent was associated with higher risk of total graft failure [HR 1.19 (p=0.004), 1.02 (p=0.030), respectively]. Additionally, every 0.1 unit increase in coefficient of variation was associated with increased risk of total graft failure [HR 1.13 (p=0.001)].

Kim HJ, et al. (2022) Clinical Association between Tacrolimus Intra-Patient Variability and Liver Transplantation Outcomes in Patients with and without Hepatocellular Carcinoma. *Scientific Reports*, vol. 12, no. 1. Retrieved from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9519914/>

- This single-center retrospective study evaluated intra-patient variability (IPV) in 636 liver transplant recipients, 349 had HCC and 287 had no HCC. The study found that patients in patients with HCC, high tacrolimus IPV was significantly associated with an increased risk of overall mortality and HCC recurrence. However, optimal tacrolimus trough concentrations in liver transplant patients with and without HCC has not been established.

Leino AD, et al. (2019). Assessment of tacrolimus intra-patient variability in stable adherent transplant recipients: Establishing baseline values. *Am J Transplant*, 19(5):1410-1420. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/30506623>

- This study evaluated a cohort of adherent liver and kidney transplant recipients and sought to determine the intra-patient variability of tacrolimus. In this retrospective analysis of 96 patients, results suggested that monitoring standard deviations of routine tacrolimus blood levels can be of utility in detecting non-adherence to immunosuppressant medications prior to clinical rejection and allow for earlier intervention.

Van Der Veer MAA, et al. (2019). High intra-patient variability in tacrolimus exposure is not associated with immune-mediated graft injury after liver transplantation. *Transplantation*, 103(11):2329-2337. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/30801539>

- This study evaluated the impact of inpatient variability on immune-mediated graft injury after month six in 326 liver transplant recipients. Secondary outcomes were the association between tacrolimus IPV on loss of renal function per year follow up and CMV after month 6. They concluded that high IPV in tacrolimus exposure beyond month 6 post-liver transplantation was not associated with immune-mediated graft injury.

Shuker N, et al. (2018). Inpatient variability in tacrolimus exposure does not predict the development of cardiac allograft vasculopathy after heart transplant. *Exp Clin Transplant*, 16(3), 326-332. Retrieved from:

[https://www.ncbi.nlm.nih.gov/pubmed/?term=Experimental+and+Clinical+Transplantation+\(2018\)+3%3A+326-332](https://www.ncbi.nlm.nih.gov/pubmed/?term=Experimental+and+Clinical+Transplantation+(2018)+3%3A+326-332)

- This retrospective study evaluated the impact of tacrolimus IPV on CAV and acute cellular rejection after heart transplant in 86 patients. Results suggest a high inpatient variability in tacrolimus exposure does not appear to influence heart transplant outcomes, unlike its influence on kidney transplant function. A higher immunosuppression exposure after heart transplant, including the use of prednisone often in a combination of 3 immunosuppressive drugs, may protect against the effects of high inpatient tacrolimus variability.

Shemesh E, et al. (2017). The Medication Level Variability Index (MLVI) predicts poor liver transplant outcomes: a prospective multi-site study. *Am J Transplant*, 17(10), 2668-2678. Retrieved from:

<https://www.ncbi.nlm.nih.gov/pubmed/28321975>

- In this prospective, multicenter study that studied the Medication Level Variability Index (MLVI) as a means for detecting nonadherence, results demonstrated that a higher MLVI pre-rejection predicted rejection as well as had significant association with other secondary outcomes. The results of this larger study suggest that MLVI is a marker that can use clinically-derived information in order to predict rejection.

Supelana C, et al. (2014). The Medication Level Variability Index (MLVI) predicts rejection, possibility due to nonadherence, in adult liver transplant recipients. *Liver Transpl*. 20(10), 1168-1177. Retrieved from:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4177441/>

- In this study, a retrospective chart review sought to validate previous findings that a higher MLVI may predict rejection and found that the MLVI was both associated with rejection as well as may predict its occurrence in adult liver transplant recipients.

Stuber ML, Shemesh E, Seacord D, Washington J 3rd, Hellemann G, McDiarmid S. (2008).

Evaluating nonadherence to immunosuppressant medications in pediatric liver transplant recipients. *Pediatr Transplant*, 12(3), 284–288. Retrieved from:

<https://www.ncbi.nlm.nih.gov/pubmed/18331387>

- In this retrospective analysis of 96 patients, results suggested that monitoring standard deviations of routine tacrolimus blood levels can be of utility in detecting non-adherence to immunosuppressant medications prior to clinical rejection and allow for earlier intervention.

12.6 Non-adherence and clinical outcomes

Ho, T. W. et al. (2025). Long-Term Clinical Outcomes of Paediatric Kidney Transplantation in Hong Kong—A Territory-Wide Study. *Nephrology*, 30(3), e70009. Retrieved from:

<https://doi.org/10.1111/nep.70009>

- In this retrospective study of 61 pediatric kidney transplant recipients (median follow-up 6.4 years), 19.7% were non-adherent by self-report
- Patients with rejection had significantly more medication non-adherence compared to those without rejection (47.3% vs. 7.1%, RR 3.68, $p < 0.001$) and poor adherence was also associated with marginally worse graft survival ($p = 0.056$).

Haubrich, K., Broad, K., Hind, T., & Blydt-Hansen, T. (2025). HELP-KIDNEY: Health Literacy and Patient Outcomes in Pediatric Kidney Transplant. *Pediatric Transplantation*, 29(1), e70012. Retrieved from:

<https://doi.org/10.1111/ptr.70012>

- In this retrospective study of 40 pediatric kidney transplant recipients, limited caregiver or patient health literacy was associated with higher healthcare utilization at 3 months ($r_s = -0.36$, $p = 0.024$) and 12 months ($r_s = -0.35$, $p = 0.029$) but showed no significant association with tacrolimus adherence at any time point or allograft function at 2 years posttransplant ($r_s = -0.13$, $p = 0.43$).

Shafiekhani M, et al. (2023). Quality of life associated with immunosuppressant treatment adherence in liver transplant recipients: a cross-sectional study. *Front Pharmacol*, 14:1051350. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/36909168/>

- This cross-sectional study assessed the relationship between quality of life (QOL) and adherence in 122 adult liver transplant recipients utilizing SF-36 and BAASIS tools, respectively. Overall QOL scores were found to be higher in adherent patients compared to non-adherent patients; however, the only QOL dimension in which this difference was significant was mental health ($p=0.01$). Mean Mental Composite Scores were also found to be significantly higher in adherent patients compared to non-adherent patients ($p=0.02$).
- A multivariate linear regression showed that the only influential factor on occurrence of non-adherence was rejection (OR 8.226, 95% CI 1.404-48.196)

Lorenz EC, et al. (2018). Long-term immunosuppression adherence after kidney transplant and relationship to allograft histology. *Transplant Direct*. 4(10). Retrieved from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6233670/>

- This retrospective analysis of over 500 renal allograft recipients at a single-center evaluated the influence of non-adherence on long-term allograft histology and survival.

Malheiro J, et al. (2018). Correlations between donor-specific antibodies and non-adherence with chronic active antibody-mediated rejection phenotypes and their impact on kidney graft survival. *Human Immunology*. 79(6), 413-423. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/29577962>

- A secondary objective in this study was to evaluate chronic-active antibody-mediated rejection (CAABMR) phenotypes between adherent and non-adherent renal transplant recipients found to have CAABMR.

Wiebe C, Nevins TE, Robiner WN, Thomas W, Matas AJ, Nickerson PW. (2015). The synergistic effect of class II HLA epitope-mismatch and nonadherence on acute rejection and graft survival. *Am J Transplant*, 15(8), 2197-2202. Retrieved from: <http://www.ncbi.nlm.nih.gov/pubmed/26095765>

- This study explored the relationship between class II HLA epitope-mismatch and patient medication non-adherence and how it relates to graft survival.

Nevins TE, Robiner WN, Thomas W. (2014). Predictive patterns of early medication adherence in renal transplantation. *Transplantation*, 98(8):878-884. Retrieved from: <http://www.ncbi.nlm.nih.gov/pubmed/24831921>

- This study quantified individual medication adherence patterns in kidney transplant recipients through electronic medication monitoring.

Lieber SR, Volk ML. (2013). Non-adherence and graft failure in adult liver transplant recipients. *Dig Dis Sci*. 58(3), 824–834. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/23053889>

- A sample of 444 patients were reviewed to determine pre-transplant predictors of non-adherence and clinician report of non-adherence. Nonadherence was found in nearly a quarter of the patient population, with factors such as a history of substance abuse and a past history of nonadherence found to be significant independent predictors of nonadherence. The study also found significant

predictors of higher deviation of tacrolimus levels as well as an independent association between SD of tacrolimus levels and graft failure over time.

Sellarés J, et al. (2012). Understanding the causes of kidney transplant failure: the dominant role of antibody-mediated rejection and nonadherence. *Am J Transplant*, 12(2), 388-399. Retrieved from: <http://www.ncbi.nlm.nih.gov/pubmed/22081892>

- This prospective multicenter cohort study reviewed 315 renal transplant recipients that underwent biopsies for clinical indications. The authors aimed to understand the causes of kidney transplant failure, including nonadherence.

Pinsky BW, Takemoto SK, Lentine KL, Burroughs TE, Schnitzler MA, Salvalaggio PR. (2009). Transplant outcomes and economic costs associated with patient noncompliance to immunosuppression. *Am J Transplant*, 9(11), 2597-2606. Retrieved from: <http://www.ncbi.nlm.nih.gov/pubmed/19843035>

- This paper describes factors associated with compliance to immunosuppressive medications and examines relationships between compliance with allograft outcomes and costs.

Fredericks EM, Lopez MJ, Magee JC, Shiek V, Opiari-Arrigan L. (2007). Psychological functioning, nonadherence and health outcomes after pediatric liver transplantation. *Am J Transplant*, 7(8), 1974-1983. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/17617862>

- This study assessed relationships between adherence, HRQOL, psychological function, and family function in pediatric liver transplant recipients and parents in order to characterize the relationship between adherence and health outcomes in children who were within 5 years of their liver transplantation. The results not only related nonadherence to frequency/duration of hospitalizations, liver biopsies, and rejection episodes, but also suggested that empirically based assessment of HRQOL, parenting stress, and family functioning may help identify patients at risk for nonadherence.

Vlaminck H., et al. (2004). Prospective study on late consequences of subclinical noncompliance with immunosuppressive therapy in renal transplant patients. *Am J Transplant*, 4(9), 1509-1513. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/15307839>

- In this study, patients were categorized as either compliant or non-compliant based on self-reported adherence interviews. Investigators sought to compare rates of late acute rejections between these two groups.

12.7 Risk factors for non-adherence

Kankaya, E. et al. (2025). Evaluating the Relationship Between Medication Adherence, Dietary Practices, and Physical Activity in Heart Transplant Recipients. *Clinical Transplantation*, 39(3), e70125. Retrieved from: <https://doi.org/10.1111/ctr.70125>

- In this cross-sectional study of 70 adult heart transplant recipients, 42.85% were nonadherent to immunosuppressive medications after assessment via the BAASIS questionnaire; nonadherence was significantly associated with younger age ($p=0.003$), shorter time since transplant ($p=0.003$), being employed ($p=0.01$), and lower physical activity levels ($p=0.03$).

Ortiz, F., Salonsalmi, A., & Helanterä, I. (2025). Associations between dialysis modality and adherence to immunosuppression after kidney transplantation—A single-center study. *PloS one*, 20(1), e0317435. Retrieved from: <https://doi.org/10.1371/journal.pone.0317435>

- In this cross-sectional study of 201 kidney transplant recipients, patients previously on in-center hemodialysis had significantly higher CNI level variability (mean COV-CNI: 32.2%) compared to those on home dialysis (26.4%, $p=0.011$). However, there was no significant association with dialysis type and non-adherence as assessed with the BAASIS questionnaire.

Celikturk Doruker, N. et al. (2025). Investigation of the Relationship Between Health Literacy and Adherence to Immunosuppressive Therapy in Heart Transplant Patients: A Cross-Sectional Study. Transplantation proceedings, S0041-1345(25)00147-2. Advance online publication. Retrieved from: <https://doi.org/10.1016/j.transproceed.2025.01.008>

- This cross-sectional study assessed the relationship between health literacy and adherence to immunosuppressive therapy in 57 heart transplant patients. Median Immunosuppression Therapy Adherence Scale (ITAS) scores were significantly higher in married patients ($p=0.036$) and in those with a secondary school education compared to those with primary education ($p=0.031$). However, no statistically significant relationship was found between health literacy scores and adherence scores.

Colmenero J, et al. (2024). Risk Factors for Non-Adherence to Medication for Liver Transplant Patients: An Umbrella Review. J Clin Med, vol. 13,8 2348. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/38673620/>

- This review included 11 studies with the goal to identify risk factors for medication non-adherence in liver transplant recipients. Non-adherence factors were sorted according to the WHO classification of factors for non-adherence. Identified factors included not having insurance or having Medicare insurance, males, younger age (<40 years old), being divorced, prior history of alcohol abuse, missing clinical appointments, ongoing psychiatric illness, side effects, high cost, difficulty understanding medication regimen, hospital readmissions after transplant, and a longer time from transplant.

Bae SH, et al. (2023). A cross-sectional analysis of health literacy and compliance to treatment in organ transplant recipients. J Clin Med, 12(3), 977. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/36769625/>

- This cross-sectional study aimed to determine the effects of health literacy and emotional transplant effects (worry, guilt, disclosure, and responsibility) on adherence after kidney and liver transplant. Nearly all variables in the health literacy questionnaire showed a significant positive correlation with adherence to treatment ($p<0.05$). In addition, sense of responsibility towards family, the donor, and the transplant team had a significant positive correlation with adherence ($p=0.001$).

Vaisbourd, et al. (2023). Differences in medication adherence by sex and organ type among adolescent and young adult solid organ transplant recipients. Pediatric Transplantation, 27:e14446. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/36478059/>

- This is a secondary analysis of the Personalizing Immunosuppression to Improve Efficacy (POSITIVE) Adherence study. Adherence between adolescent and young adult kidney, liver, and heart transplant recipients was compared using both self-report and tacrolimus trough levels. Males had lower odds of self-reported adherence than females ($p=0.012$), but were found to have higher odds of adherence based on measured tacrolimus levels ($p=0.006$). There were no significant differences in adherence by organ type.

Sakhuja S, et al. (2022). Impact of psychosocial factors on medication level variability index outcomes in pediatric liver transplant recipients. *Pediatric Transplantation*. 27:e14425. Retrieved from: <https://onlinelibrary.wiley.com/doi/full/10.1111/ptr.14425>

- This single center, retrospective study of 136 pediatric liver transplant recipients assessed various psychosocial factors contributing to medication adherence and transplant outcomes. Factors associated with non-adherence were lower maternal and paternal age ($p=0.048$ and 0.015 , respectively), lower parental education level ($p=0.016$ and 0.047 , respectively), lower household income ($p=0.001$), and public insurance ($p=0.007$). There was higher incidence of acute cellular rejection in patients with non-adherence in the first 3 years post-transplant.

Russell CL, et al. (2022) Health Facts Medication Adherence in Transplantation (H-MAT) Study: A Secondary Analysis of Determinants and Outcomes of Medication Nonadherence in Adult Kidney Transplant Recipients. *International Journal of Nephrology*, edited by Tej Mattoo, vol. 2022. Retrieved from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9205738/>

- This secondary analysis of data from Cerner Health Facts data warehouse aims to examine the relationship between the World Health Organization (WHO) model of medication adherence and post-transplant medication nonadherence (MNA) and the association with MNA and clinical outcomes
- There were 16,671 kidney transplant recipients evaluated and 12% with MNA. Socio/economic factors from the WHO model of younger age, Caucasian versus Hispanic race, and being single were independent predictors of MNA. A more rigorous study is required to determine the effect of substance use and mental health disorders on transplant outcomes including MNA.

Ko H, et al. (2021). Association between medication adherence and inpatient variability in tacrolimus concentration among stable kidney transplant recipients. *Nature*, 11:5397. <https://www.nature.com/articles/s41598-021-84868-5>

- In this post-hoc analysis, the variability of tacrolimus trough levels were calculated using coefficient variation and mean absolute deviation in 92 kidney transplant recipients. Patients were required to have more than 5 months of medication event monitoring system (MEMS) use and more than 4 tacrolimus troughs for analysis. Between the nonadherent and adherent groups, no statistically significant differences were identified in the coefficient variation or the adherence detected by MEMS. Self-reports of adherence did not significantly affect the interpatient variability of tacrolimus.

Quast LF, et al. (2020). Adherence barriers for adolescent and young adult transplant recipients: Relations to personality. *Pediatr Psychol*, 45:540-549. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/32291448/>

- The current study examines associations between personality (i.e., agreeableness, conscientiousness, neuroticism) and adherence barriers in a group of adolescent and young adult solid organ transplant recipients.

Cossart AR, Staats CE, Campbell SB, Isbel NM, Cottrell WN. (2019). Investigating barriers to immunosuppressant medication adherence in renal transplant patients. *Nephrology*, 24(1), 102-110. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/29278439>

- This was an analysis of 161 kidney transplant recipients who completed surveys consisting of 5 validated questionnaires. The survey helped identify barriers leading to non-adherence - with forgetfulness and skipped doses being the most prominent reasons.

Danziger-Isakov L, et al. (2019). Perceived barriers to medication adherence remain stable following solid organ transplantation. *Pediatr Transplant*, 23, e13361. Retrieved from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6652201/>

- This study evaluated the perceived barriers to adherence reported by pediatric and adolescent patients and their guardians and whether these would increase in severity as time from transplant increased.

Denhaerynck K, et al. (2018). Multilevel factors are associated with immunosuppressant nonadherence in heart transplant recipients: The international BRIGHT study. *Am J Transplant*, 18:1447–1460. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/29205855>

- This cross-sectional study identified multilevel factors associated with implementation phase immunosuppressant nonadherence in adult heart transplant recipients across 4 continents, 11 countries, and 36 centers.

Ladin K, Daniels A, Osani M, Bannuru RR. (2018). Is social support associated with post-transplant medication adherence and outcomes? A systematic review and meta-analysis. *Transplant Rev*, 32(1):16-28. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28495070>

- This meta-analysis reviewed 32 studies to identify the influence of social factors (e.g. marital status and social support) on post-transplant medication adherence and other post-transplant clinical outcomes.

Lehner LJ, et al. (2018). Evaluation of adherence and tolerability of prolonged-release tacrolimus (Advagraf™) in kidney transplant patients in Germany: A multicenter, non-interventional study. *Clin Transplant*, 32(1), e13142. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/29052906>

- This study reports rates of adherence over an 18-month period among patients receiving a prolonged-release tacrolimus formulation.

Shemesh E, et al. (2018). Trajectory of adherence behavior in pediatric and adolescent liver transplant recipients: The medication adherence in children who had a liver transplant cohort. *Liver Transplant*, 24(1), 80-88. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28779546>

- This publication takes the results from the original MALT study that validated MLVI and evaluated variance in adherence behavior. Results of the study identified potential risk factors for worsening adherence, suggested good baseline adherence does not guarantee adherence, and that monitoring of MLVI be computed frequently in order to characterize nature of nonadherence with MLVI as it may fluctuate over time.

Mehta P, Steinberg EA, Kelly SL, Buchanan C, Rawlinson AR. (2017). Medication adherence among adolescent solid-organ transplant recipients: A survey of healthcare providers. *Pediatr Transplant*, 21(7), e13018. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28670855>

- A cohort of pediatric solid organ transplant providers were administered an anonymous online survey to capture provider perspectives on barriers to medication adherence and recommendations for interventions.

Nevins TE, Nickerson PW, Dew MA. (2017). Understanding medication nonadherence after kidney transplant. *J Am Soc Nephrol*, 28, 2290-2301. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/28630231/>

- The goal of this review was to provide summary of risk factors associated with medication non-adherence (MNA), the strategies to overcome MNA and the effectiveness of these approaches. Risk factors for MNA identified in this review include condition related factors, health

system/healthcare provider factors, sociodemographic factors, patient-related psychosocial factors, treatment related factors.

Belaiche S, Décaudin B, Dharancy S, Noel C, Odou P, Hazzan M. (2017). Factors relevant to medication nonadherence in kidney transplant: a systematic review. *Int J Clin Pharm*, 39(3), 582-593. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28374343>

- This systematic review of 37 studies aimed to identify factors associated with non-adherence.

Brito DC, et al. (2016). Stress, coping and adherence to immunosuppressive medications in kidney transplantation: a comparative study. *Sao Paulo Med J*. 134(4), 292-299. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/26648278>

- This single-center, cross-sectional study compared stress and coping mechanisms between fifty Brazilian renal transplant recipients classified as either adherent and non-adherent using the Basel Assessment of Adherence to Immunosuppressive Medication Scale (BAASIS).

De Geest S, et al. (2014). Describing the evolution of medication nonadherence from pretransplant until 3 years post-transplant and determining pretransplant medication nonadherence as risk factor for post-transplant nonadherence to immunosuppressives: The Swiss Transplant Cohort Study. *Transplant Int*, 27(7), 657-666. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/24628915>

- This prospective nationwide cohort study described the evolution of medication non-adherence from pre-transplant through 3 years post-transplant among more than 1500 Swiss kidney, liver, heart, and lung transplant recipients.

Chun-Wei Su G, et al. (2013). Assessing medication adherence in solid-organ transplant recipients. *Exp Clin Transplant* 2013;6:475-481. Retrieved from: <https://pubmed.ncbi.nlm.nih.gov/24344939/>

- This was a single center, retrospective, cross-sectional cohort study that evaluated 225 outpatient lung, kidney, and liver transplant recipient's adherence to immunosuppressant medications. Surrogate markers were used to measure medication adherence. Markers included medication possession ratio (days of medication supplied/actual days) and gap in prescription refills (> 30-day lapse between expected depletion of supply and next refill). Patients were adherence to their immunosuppressant medication regimens if their medication possession ratio was > 80%. Overall, medication possession ratios were approximately 95% for kidney and lung transplant recipients and 92% for liver recipients.

Gorevski E, et al. (2013). Is there an association between immunosuppressant therapy medication adherence and depression, quality of life, and personality traits in the kidney and liver transplant population? *Patient Prefer Adherence*, 7, 301-307. Retrieved from: <http://www.ncbi.nlm.nih.gov/pubmed/23620661>

- This cross-sectional study aimed to determine the relationship between patient characteristics (e.g. depression, personality, and quality of life) and immunosuppressant medication adherence in kidney and liver transplant patients.

Rodrigue JR, Nelson DR, Hanto DW, Reed AI, Curry MP.(2013). Patient-reported immunosuppression nonadherence 6 to 24 months after liver transplant: association with pretransplant psychosocial factors and perceptions of health status change. *Prog Transplant*, 23(4), 319-328. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/24311395>

- Investigators retrospectively reviewed the influence of pretransplant sociodemographic and psychosocial variables on nonadherence rates post-transplant in a cohort of over 200 liver transplant recipients at two different transplant sites.

Scholz U, et al. (2012). Predicting intentions and adherence behavior in the context of organ transplantation: gender differences of provided social support. *J Psychosom Res*, 72(3), 214-219.

Retrieved from: <http://www.ncbi.nlm.nih.gov/pubmed/22325701>

- This study examined the determinants of intention formation and adherence behavior in transplant patients. Further, this study attempted to characterize the role of a patient's support system (gender dependent) and how it impacts adherence.

Russell CL, Kilburn E, Conn VS, Libbus MK, Ashbaugh C. (2003). Medication-taking beliefs of adult renal transplant recipients. *Clin Nurse Spec*, 17(4), 200-208. Retrieved from:

<http://www.ncbi.nlm.nih.gov/pubmed/12869867>

- This paper aimed to describe medication taking beliefs of renal transplant recipients through comprehensive interviews