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APPLYING ARTIFICIAL INTELLIGENCE TO IMPROVE TRANSPLANT PATIENTS' OUTCOMES: A SCOPING REVIEW

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ABSTRACT

Solid organ transplantation significantly enhances the survival and quality of life for patients with severe organ dysfunction. However, transplanted patients need lifelong Immunosuppressive Therapy (IST) to prevent organ rejection. Adherence to IST is critical, as non-adherence can lead to severe consequences, including organ failure and elevated healthcare costs. Challenges in IST adherence are prevalent globally, impacting patient outcomes and burdening healthcare systems. In this context, this study aims to identify how artificial intelligence (AI) can help transplant patients adhere to ISTs and improve their quality of life. We conducted a scoping review, searching five databases in March 2024. After a critical appraisal of the articles initially retrieved, 23 studies were included in this review. The results indicate that AI and health information technology hold significant promise for supporting transplant patients and improving their quality of life and adherence to IST. However, these results should be analyzed carefully due to the methodological limitations present in the analyzed studies. We identified the major limitations of the analyzed studies. We argued that studies involving more significant, more diverse populations, more extended follow-up periods, and more rigorous designs are essential to understand and fully optimize the AI potential.

Keywords: Artificial intelligence; mHealth; Organ transplantation; Immunosuppressive therapy adherence; Scoping review.

1 INTRODUCTION

Solid organ transplantation can save and improve the quality of life of countless patients with severe functional impairment of one or more vital organs. However, every transplant patient must take medication for the rest of their life – Immunosuppressive Therapy (IST) – to increase the chances of their body accepting the transplanted organ (Almeida, Araujo, Roza, Siqueira, & Rocha, 2021). Thus, adherence to immunosuppressant therapy is crucial for solid-organ transplant recipients, as non-adherence to treatment after transplant surgery is a risk factor that can lead to decreased graft function, increased morbidity, and healthcare costs. It turns out that non-adherence to ISTs is a common and complex problem after solid organ transplantation, burdening healthcare systems in both developed and developing countries and affecting patients' health outcomes and quality of life (Chisholm, 2012; Schäfer-Keller, Steiger, Bock, Denhaerynck, & Geest, 2008; Shih & Tsai, 2014). Adherence to therapy can be defined as the process by which patients take their medication as prescribed. More specifically, medication adherence refers to the degree or extent of conformity to recommendations about day-to-day treatment by the provider concerning timing, dosage, and frequency (Cramer et al., 2008; Vrijens et al., 2012). In turn, quality of life (QOL) can be defined as physical, mental, and social well-being (Testa & Simonson, 1996).

In Brazil, non-adherence to immunosuppressants is prevalent among transplant recipients, negatively impacting these patients' quality of life (Fuzinato, Marin, & Maissiat, 2013; Sanders-Pinheiro et al., 2020; Sanders-Pinheiro, Colugnati, Marsicano, De Geest, & Medina, 2018). The high incidence of non-adherence to immunosuppressive medication among transplant recipients calls for new solutions to enhance patient engagement and education. Mellon et al. (2022) conducted a systematic literature review to examine the benefits and harms of interventions for increasing adherence to immunosuppressant therapies in solid organ transplant recipients, including adults and children with heart, lung, kidney, liver, and pancreas transplants. Their results indicate that interventions to increase immunosuppressant adherence in solid organ transplant recipients show uncertain evidence of improving medication adherence and reducing graft failure. In this regard, the literature has indicated that new technologies, including mobile health applications, intensified care programs, and automated reminder systems, can help patients adhere to medication (Alves, da Silva, Schmitz, & Alencar, 2020; Cossart, Staatz, Campbell, Isbel, & Cottrell, 2018; Joost, Dörje, Schwitulla, Eckardt, & Hugo, 2014; Levine, Torabi, Choinski, Rocca, & Graham, 2019; Reese et al., 2017).

In recent years, artificial intelligence (AI) has gained significant prominence, and its

rapid evolution has impacted various aspects of medicine and healthcare, enhancing diagnostic accuracy, improving patient care, and transforming workflows (F. Jiang et al., 2017; Kaul, Enslin, & Gross, 2020). AI includes diverse techniques aimed at developing systems capable of emulating human intelligence, from basic task execution to complex problem-solving. One prominent subset of AI is Machine Learning (ML), which focuses on identifying patterns within datasets to enable machines to learn and adapt without explicit programming. Deep Learning (DL), a subset of ML, utilizes neural networks to process data hierarchically. DL excels in handling unstructured data like images, audio, and text, enabling image recognition and natural language processing tasks. Generative AI, a subset of DL, specializes in producing text, images, or code based on input data and has gained widespread use with the release of ChatGPT (OpenAI, 2021), further popularizing generative AI applications across various fields. AI applications in medicine and healthcare include improving diagnostics, aiding medical imaging analysis, enabling personalized treatment plans, facilitating remote health monitoring, supporting telemedicine through virtual health assistants and chatbots, streamlining administrative workflows by automating tasks like medical coding and billing, enhancing precision and minimally invasive procedures with surgical robotics (Beam et al., 2023; Hamet & Tremblay, 2017; Montaleão Brum Alves, Ferreira da Silva, Assis Schmitz, & Juarez Alencar, 2022).

Specifically concerning transplants, artificial intelligence can help improve patient's adherence to medications and enhance healthcare professionals' ability to guide patients toward optimal health status (Eggerth, Hayn, & Schreier, 2019). AI can also detect and monitor medication self-administration errors, potentially improving medication safety with minimal overhead for patients and health professionals (Zhao, Hoti, Wang, Raghu, & Katabi, 2021).

Labovitz, Shafner, Reyes Gil, Virmani, and Hanina (2017) evaluated the use of an artificial intelligence platform on mobile devices in measuring and increasing medication adherence in stroke patients on anticoagulation therapy and concluded that these devices can increase medication adherence. Likewise, the study conducted by Bain et al. (2017) revealed that AI platforms on mobile devices can increase medication adherence and predict future nonadherence in schizophrenia patients. However, the literature regarding the application of AI to improve patient's quality of life and adherence to immunosuppressive therapy still needs to be explored. Levine et al. (2019) argue that mHealth apps and smart watches are promising strategies for increasing medication adherence in transplant recipients, but further research is needed to determine their best use. Seyahi and Ozcan (2021) conducted a literature review on

the theme and concluded that AI and, more specifically, machine learning techniques improve kidney transplantation by accelerating evaluation, standardization, and providing personalized patient care.

In this context, the proposed research aims to identify how artificial intelligence (AI) can help transplant patients adhere to immunosuppressive therapy, improving their quality of life. In summary, the general research question is: *how can artificial intelligence help transplant patients adhere to ITs and enhance their quality of life?* To answer this question, this study collects and organizes evidence regarding the theme through a scoping literature review. As a theoretical framework to analyze the studies, we applied the three factors proposed by Dellande, Gilly, and Graham (2004) as necessary for encouraging patients to adhere to prescribed health treatments: *role clarity* - knowledge and understanding of what needs to be done, what activities need to be performed; *ability* - customers' ability to do what they are supposed to do; and *motivation* - incentives that consumers have to play their role. Within our literature review, we also depict, as a secondary objective, the limitations found by these studies.

2 METHODOLOGICAL PROCEDURES

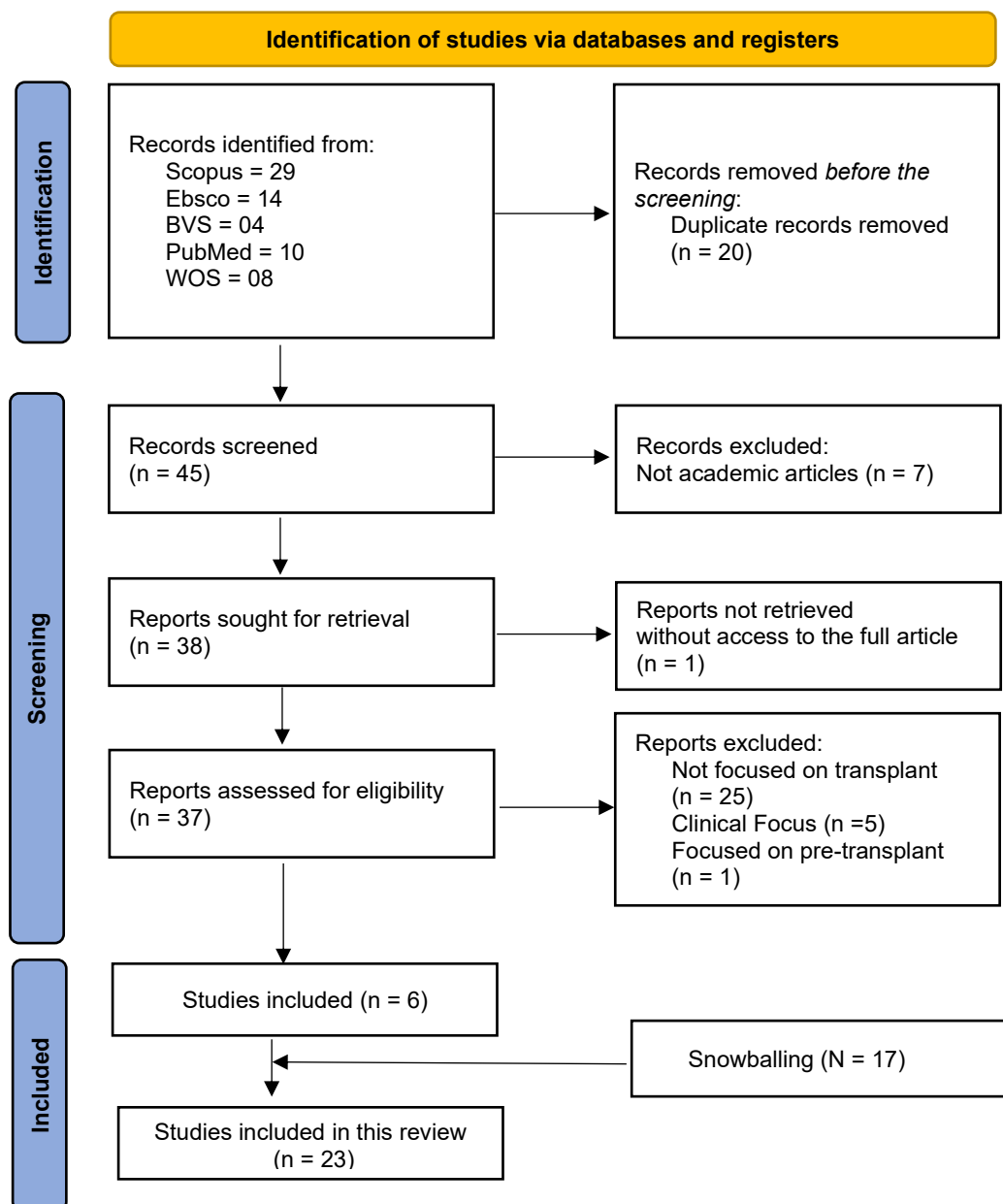
The method chosen was a scoping review, as it allows the identification and understanding of existing literature, providing a broad map of the evidence on the theme investigated (Armstrong, Hall, Doyle, & Waters, 2011; Lockwood, dos Santos, & Pap, 2019).

The search was carried out in March 2024 in the databases EBSCO, Scopus, PUBMED, the Virtual Health Library (VHL), and Web of Science by combining the following terms: "artificial intelligence" AND ("transplant patient*" OR posttransplant* OR post transplantation OR post-transplantation OR transplant*) AND (adherence OR adhesion OR compliance OR non-adherence OR non-compliance) AND (immunosuppressant* OR immunosuppressive* OR treatment OR care OR medication* OR medicine* OR drugs), in Portuguese, Spanish and English. The established inclusion criteria were academic articles published in journals with abstract and full text available. There was no restriction on the year of publication, resulting in articles published from 2008 to 2024.

The eligibility criteria for our study limited the nature of texts to academic articles, with full online texts available, written in either English, Spanish, or Portuguese. We excluded not academic articles (e.g., letters, commentaries, and correspondences), studies focused on clinical aspects and the pre-transplantation stage. Aiming at a broad chronological examination of the

topic, no filters were applied regarding the year of publication and the journal's impact factor. We also decided to include systematic literature reviews in the articles analyzed in this scoping review, as we intend to map the evidence on the theme and identify knowledge gaps, scope a body of literature, clarify concepts, or investigate research conduct (Munn et al., 2018). We conducted the snowballing strategic searching of the references of previous systematic reviews to identify articles adherent to our research. Figure 1 presents the PRISMA protocol applied in this research to identify, assess, and select existing studies (Page et al., 2021).

Figure 1. Diagram of selection and evaluation



Source: Based on the PRISMA flow diagram (Page et al., 2021)

The authors performed data extraction using a standardized Microsoft Excel spreadsheet, in which columns represent the categories of analysis. The 23 included publications were classified according to several descriptive and analytical aspects to present a comprehensive analysis of the theme: authors; year and journal of publication; number of citations; country where the research was conducted; research objective; methodological approach; type of platform investigated; main findings; how AI can assist transplant patients in adhering to immunosuppressants and improve their quality of life – role clarity, ability or motivation; and main research limitations.

3 DISCUSSION AND DATA ANALYSIS

3.1 Characteristics of Studies

The 23 selected studies were published between 2008 and 2024 in 19 scholarly journals (Table 1). The most frequent country is the United States (12/23;52%), followed by Spain, with two articles (9%), and China and South Korea with one study each (4%). Different methods were applied to the methodology; the most frequently used were the Randomized Controlled Trial (RCT) (6/23;26%) and Systematic Literature Review (SLR) (7/23;30%). The RCT studies present a sample size ranging from N = 30 to N = 450. Half of the selected papers (50%) investigated a mHealth application, a general term for the use of mobile phones and other wireless technology in medical care. Regarding the outcomes in terms of adherence – role clarity, ability, or motivation, nine articles reported improvement in role clarity (9/23;39%) and nine in patients' ability (9/23;39%), while the focus on motivation was present in only four studies (4/23;17%). Some articles reported more than one outcome. Figure 1 presents outcomes and sample size used in the studies organized by year.

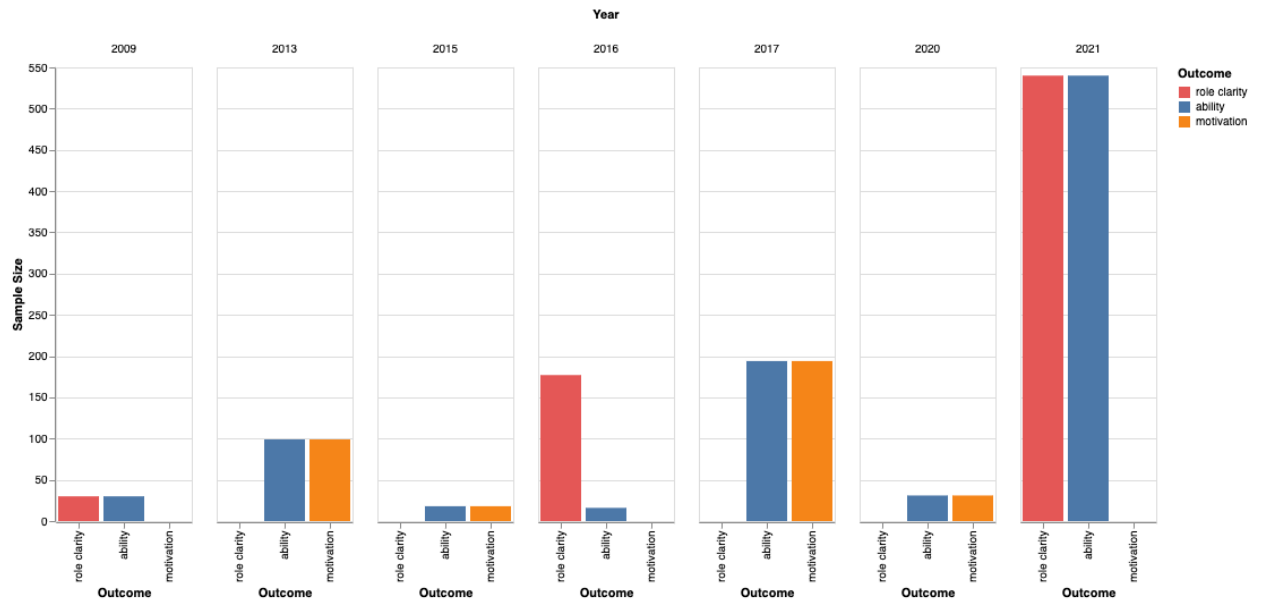


Figure 1. Outcome and Sample Size by Year (Source: Authors own work)

Table 1 – Characteristics of the studies

Authors (Year); Country	Journal; Citation	Research objective (Platform)	Methodological approach (Sample Size)	Main findings	Adherence and QOL outcome	Research limitations
Staes et al. (2008); USA	Journal of the American Medical Informatics Association; 39	Evaluate the impact of computerized alerts on outpatient laboratory monitoring for transplant patients. (medical device)	Observational Study (Not Applicable)	Improved completeness and timeliness of reporting due to computerized alerts.	Improves efficiency and timely management of lab results. (ROLE CLARITY)	Assumptions on routine chemistry results, reliability of alerts, and enrollment delays.
DeVito Dabbs et al. (2009); USA	Clinical Transplantation; 91	Assess the efficacy of a mobile assistant (Pocket PATH) in promoting self-care and quality of life post-lung transplantation (mHealth - Pocket PATH)	Randomized Controlled Pilot Trial (n=30)	Higher self-care agency and behaviors, better quality of life in the Pocket PATH group.	Enhances self-monitoring and adherence and encourages timely healthcare communication. (ROLE CLARITY AND ABILITY)	Small sample size, short follow-up.
Park et al. (2010); USA	Journal of the American Medical Informatics Association; 15	Investigate if an automated clinical management system improves outcomes in transplant recipients' medication management (clinical management system)	Retrospective Cohort Study (Not applicable)	Fewer rejection episodes and toxicity events, cost-effective, improving the quality of life for years.	Efficient management of therapy, reducing complications and response time for adjustments, leading to better patient care and adherence. (ROLE CLARITY)	Observational, not randomized, unmeasured confounders
John William McGillicuddy et al. (2013);	Journal of Medical Internet Research; 178	Assess renal transplant recipients' attitudes towards mobile-based	Survey (n=99)	Positive attitude towards mobile health monitoring.	Provides personalized reminders, tracks medication, and offers	Limited to a single center, interest may not

USA		remote monitoring and management. (mHealth)			educational support. (ABILITY AND MOTIVATION)	translate to actual use.
Dabbs et al. (2016); USA	Telemedicine and e-Health; 114	Compare a computer-based Bayesian algorithm with a manual nurse decision process for clinical intervention triage in lung transplant recipients. (mHealth)	Randomized Controlled Trial (n=65)	No significant differences in clinical outcomes between groups.	Aids in early detection and triage of complications (ROLE CLARITY)	Small sample size, broader implementation; needs more data.
John W McGillicuddy et al. (2015); USA	Progress in Transplantation; 59	Evaluate the long-term sustainability of improved blood pressure control via a mobile health pilot program in kidney transplant recipients. (mHealth)	Retrospective Analysis: A Generalized Linear Mixed Model (GLMM) was used to assess clinic-recorded blood pressure post-trial from patient medical records. (n=18)	Significant reduction in systolic blood pressure at 12-month follow-up.	Enhances long-term self-management and clinical outcomes. (ABILITY AND MOTIVATION)	Small sample size, lack of hard adherence data, variable measurement protocols.
Y. Jiang, Sereika, Dabbs, Handler, and Schlenk (2016); USA	International Journal of Medical Informatics; 28	Examine adherence to decision support messages and identify predictors in lung transplant recipients using Pocket PATH. (mHealth -	Cross-Sectional Correlational Study (n=96)	High adherence to decision-support messages.	Facilitates early interventions and improves quality of life and survival rates. (ROLE CLARITY)	Small sample size, limited generalizability.

		Pocket PATH)				
Israni et al. (2016); USA	JMIR Public Health and Surveillance; 29	Explore kidney transplant recipients' adherence perceptions and their willingness to use a mobile app for medication management. (mHealth)	Qualitative Study (n=16)	While all participants were interested in using an app to remind them to take their medication, they reported potential barriers to app usage.	Provides reminders and facilitates pharmacy communication. (ROLE CLARITY AND ABILITY)	Self-reported data, no actual app testing.
Nerini, Bruno, Citterio, and Schena (2016); Not applicable	Journal of Nephrology; 43	Analyze the role of various technologies, particularly mobile-phone-based, in enhancing compliance among kidney transplant recipients (Not Applicable)	Review article (Not applicable)	Low adherence leads to poor outcomes; technology can help through reminders and education.	AI can offer personalized reminders, tracking, and educational content. (NOT APPLICABLE)	Needs more extensive trials.
Niazkhan i, Pirnejad, and Khazaei (2017); Not applicable	International Journal of Medical Informatics; 29	Systematically review the impact of Health Information Technology on organ transplant care. (Not Applicable)	Systematic Literature Review (Not applicable)	Beneficial impact on lab values and cost savings; unclear effects on clinical outcomes like mortality.	Personalized medication reminders, support through virtual assistants (NOT APPLICABLE)	Lack of quantitative studies, high risk of bias.
Zanetti-Yabur et al. (2017); USA	The American Journal of Surgery; 52	Investigate the efficacy of a mobile app in promoting medication adherence among transplant patients. (mHealth)	Questionnaire-Based Study (n=74)	Transplant patients exhibited negative beliefs about medication, which could predict higher rates of nonadherence. Although not statistically significant,	AI can provide timely reminders, educational support, and positive reinforcement for medication adherence. This can decrease nonadherence	Self-reported data; need for longer, larger studies.

				app users demonstrated higher rates of medication recollection.	and improve patient education, enhancing quality of life. (ABILITY AND MOTIVATION)	
Reese et al. (2017); USA	American Journal of Kidney Diseases; 130	Determine if automated reminders improve immunosuppression adherence among kidney transplant recipients with or without physician notification. (mHealth)	Randomized Controlled Trial (RCT) (n=120)	Improved adherence with reminders and physician notification, no significant differences in tacrolimus levels.	Enhances adherence through automated reminders and physician involvement, which is crucial for preventing organ rejection. (ABILITY AND MOTIVATION)	Lack of evaluation of clinical endpoints like graft survival or rejection; study design may influence adherence due to more frequent contact.
Mark, Goldsman, Gurbaxani, Keskinocak, and Sokol (2019); USA	PLOS ONE; 71	Develop a predictive model for kidney transplant survival and identify important variables. (Model proposal)	Predictive Modeling Study (Not applicable)	Improved accuracy in predicting kidney transplant survival, aiding in organ allocation and patient management and outcomes.	AI can assist transplanted patients in adhering to immunosuppressors by predicting individual risks and personalizing patient monitoring and management. (NOT APPLICABLE)	Research limitations are not explicitly mentioned.
Han et al. (2019); South Korea	PLOS ONE; 55	Evaluate if the Adhere4U app improves medication adherence in renal transplant recipients' post-transplantation	Prospective RCT: (n=138)	No significant improvement in adherence rates with the Adhere4U app; high.	Intended to improve adherence through reminders and tracking but showed no significant effect. (NOT APPLICABLE)	The high attrition rate and single-center study potentially overestimate baseline medication.

		n (mHealth - Adhere4U app)				
Cresswell et al. (2020); Not applicable	Health Informatics Journal; 58	Investigate the effectiveness of AI-based computerized decision support systems in health and social care settings (Not Applicable)	Systematic Literature Review (Not applicable)	Mixed evidence on AI effectiveness in improving patient outcomes.	Quantifies risk and aids in medication adherence decision-making. (NOT APPLICABLE)	Limited RCTs, immature field, ethical/legal considerations.
Luo et al. (2020); China	Annals of Translational Medicine; 27	Develop a machine learning model to predict severe pneumonia in recipients of deceased donor transplants during the perioperative period. (Model Proposal)	Predictive Modeling (Not applicable)	Identified high-risk patients for severe pneumonia, Random Forest had the best performance.	Helps in timely interventions to prevent complications (ROLE CLARITY)	Retrospective and monocentric, more extensive multicenter studies are needed.
Gomis-Pastor et al. (2020); Spain	JMIR Mhealth Uhealth; 23	Validate the mHeart mobile app for measuring medication nonadherence among early-stage heart transplant recipients (mHealth - mHeart)	Prospective Validation Study (n=31)	App was as effective as traditional methods and improved adherence by 16-26%.	Increases adherence through personalized interventions (ABILITY AND MOTIVATION)	Limited sample size, excludes chronic-stage recipients, needs long-term evaluation.
Schwantes and Axelrod (2021); Not applicable	Current Transplantation Reports; 27	Discuss the role of AI and machine learning in improving pretransplant, donor selection, and post-operative management in transplant	Review article (Not applicable)	AI tools have been developed to optimize immunosuppression management, track patient adherence, and assess graft survival.	Through predictive modeling for complications, optimization of immunosuppression management, and technology-	Research limitations are not explicitly mentioned.

		patients. (Not Applicable)			enabled remote monitoring to improve adherence. (NOT APPLICABLE)	
Duettmann et al. (2021); Not applicable	Transplant International; 36	Analyze the status of eHealth in transplantation, focusing on clinical post-transplant care studies. (Not Applicable)	Systematic Literature Review (Not applicable)	Identified 52 manuscripts on eHealth in post-transplant care covering various aspects, from mobile apps to remote monitoring.	AI assists with personalized reminders, medication monitoring, educational tools, and proactive interventions. (NOT APPLICABLE)	The limitations of the research were not explicitly mentioned
Serper et al. (2021); USA	Contemporary Clinical Trials; 21	Evaluate TAKE IT, a multifaceted strategy for early identification and prevention of medication nonadherence issues in kidney transplant recipients (Strategy validation)	Randomized Controlled Trial (RCT) (n=450)	Innovative approach to optimizing medication adherence using technology.	Enhances technologies with personalized reminders and predictions, tailored interventions (ROLE CLARITY AND ABILITY)	Exclusion of non-English speakers, recruitment challenges, not suitable for all due to varying tech comfort levels.
Melilli et al. (2021); Spain	Clinical Transplantation; 9	Assess the usage and effectiveness of the TrackYourMed® app in engaging transplant patients and promoting immunosuppression adherence (mHealth - TrackYourMed)	Prospective, observational, multicenter, 2-phase trial. (n=90)	App showed potential benefits in monitoring medication adherence and could improve clinical outcomes.	AI provides reminders, self-awareness, and adherence tracking, leading to improved medication adherence (ROLE CLARITY AND ABILITY)	Limited sample size, single-country focus, did not track long-term adherence.

Naruka et al. (2022); Not applicable	Artificial Organs; 15	Systematically review evidence on the use of AI and machine learning in cardiac transplantation (Not Applicable)	Systematic Literature Review (Not applicable)	AI and ML predict graft failure and mortality more accurately than conventional methods, especially for 1-year outcomes.	AI assists with predicting transplant benefits, graft failures, and supports patient adherence to minimize risk (NOT APPLICABLE)	Requires more granular data for accurate long-term predictions, limited applicability to older adults.
Wingfield et al. (2024); Not applicable	Transplant Journal; 0	Review the utilization and impact of clinical decision support systems on patient outcomes in transplantation (Not Applicable)	Systematic Literature Review (Not applicable)	85% of reviewed studies showed clinical benefits from CDSS in immunosuppressant management.	Suggests implementing CDSS, including AI, to improve patient outcomes (NOT APPLICABLE)	Lack of rigorous testing and perceived lack of usefulness of some tools.

3.2 How can AI assist transplant patients in adhering to immunosuppressants and improve their quality of life?

Artificial Intelligence (AI) offers tools and functionalities to enhance treatment adherence, overall patient health, and quality of life (Duettmann et al., 2021; Wingfield et al., 2024). One of the AI's contributions is the implementation of computerized alerts within electronic health records. These alerts serve as crucial reminders for timely laboratory tests, ensuring that patients maintain optimal levels of immunosuppression critical for the success of their transplant. This system helps prevent organ rejection and promotes a seamless communication channel between healthcare providers and patients (Staes et al., 2008).

Further enhancing patient engagement and adherence, AI facilitates self-monitoring by developing sophisticated apps. These applications are tailored to track medication adherence and foster direct communication with healthcare providers and pharmacies. Such features give patients a sense of control over their health journey, offering them immediate feedback and a structured overview of their treatment regimen (Finkelstein et al., 2013; Israni et al., 2016; Y. Jiang et al., 2016).

The studies also revealed that AI revolutionized how immunosuppressive therapies are

administered. Through automated clinical systems, AI significantly reduces the response time for dosage adjustments and handling potential medication complications. This simplifies the management process and ensures that patients receive the most effective care promptly, mitigating the risk of adverse outcomes (Finkelstein et al., 2013; John William McGillicuddy et al., 2013).

Moreover, AI extends its support through personalized mobile applications. These apps are designed to offer customized reminders, track medication intake, and provide educational support tailored to each patient's needs. This level of personalization ensures that patients are consistently reminded of their medication schedules and are well-informed about their treatment, enhancing adherence and knowledge (Gomis-Pastor et al., 2020; Mark et al., 2019; John William McGillicuddy et al., 2013; Niazkhani et al., 2017).

AI also pioneers the use of home monitoring programs. These programs are instrumental in the early detection of potential complications, a critical factor in maintaining overall health and adherence. By monitoring vital health indicators, these programs can alert healthcare providers and patients about deviations from the norm, allowing for prompt interventions (Marin-Garcia, Vidal-Carreras, & Garcia-Sabater, 2021).

Lastly, AI's deployment of predictive modeling stands out as a forward-thinking approach to patient care. By identifying patients at risk of non-adherence, AI enables healthcare providers to initiate timely interventions. This proactive measure ensures continuous adherence to the treatment plan and significantly improves the patient's quality of life post-transplant (Mark et al., 2019). AI can also identify patients at high risk for severe pneumonia or other complications, which can help in timely interventions, possibly including adjustments to immunosuppressive therapy to prevent infection (Luo et al., 2020; Schwantes & Axelrod, 2021). Finally, AI can predict the potential benefits of transplantation, ascertaining graft failure and mortality (Naruka et al., 2022).

In essence, through a combination of technological innovations, AI has the potential to significantly support transplant patients in adhering to their immunosuppressive therapy and improving their quality of life, addressing the three dimensions proposed by Dellande, Gilly, and Graham (2004):

Role Clarity: (1) AI-powered mobile apps and electronic health records provide clear instructions and information about medication schedules and dosages, ensuring patients understand what activities must be performed. (2) Personalized educational content delivered by AI can help clarify the importance of adherence and its role in transplant success.

Ability: (1) AI systems can track medication intake and alert patients about doses, enhancing their ability to follow the prescribed treatment accurately. (2) Home monitoring programs powered by AI algorithms allow for early detection and management of complications, helping patients maintain their health regimen.

Motivation: (1) By offering interactive and user-friendly platforms, AI encourages patients to engage actively with their treatment plans. (2) AI can also provide positive reinforcement through progress tracking and gamification elements, incentivizing adherence behavior.

3.3 Studies Limitations

One critical research limitation that needs to be addressed is the small sample size, a common issue across many studies (Finkelstein et al., 2013; John W McGillicuddy et al., 2015). This limitation directly affects the statistical power to unveil true relationships between predictors and outcomes and raises questions about the broader applicability of the findings to diverse transplant recipient populations. Addressing this concern is crucial to ensure the results reflect the broader transplant community, underscoring the need for more comprehensive studies.

Another significant challenge in research is the design of some studies. Observational studies lack randomization and are inclined to introduce confounding variables that could bias outcomes (Melilli et al., 2021; Staes et al., 2008). This, coupled with supporting self-reported data, can lead to inaccuracies in representing actual participant compliance rates. The call for more quantitative studies to evaluate the impact of health information technology systems on transplant care was clear. Rigorous research is needed to build a solid evidence base for implementing these technologies in transplant patient care. Thus, there is a need for more controlled experimental designs to improve the findings' accuracy and for more homogeneous data to tailor AI interventions effectively to diverse patient needs (Israni et al., 2016; Zanetti-Yabur et al., 2017). These limitations reinforce the findings of the systematic literature review conducted by Niazhani et al. (2017) and Cresswell et al. (2020).

The duration of follow-up in several studies was also identified as a limitation (DeVito Dabbs et al., 2009). Short follow-up periods restricted the assessment of the long-term efficacy of AI interventions on medication adherence and overall patient well-being. This shortcoming underscores the necessity for extended study durations, which can provide a more comprehensive understanding of the enduring impacts of these technological aids on patient

health outcomes.

Technological and systemic limitations further constrained the effectiveness of AI tools - the reliability of the electronic health record to deliver computerized alerts, safety, and potential enrollment delays (Finkelstein et al., 2013; Staes et al., 2008). These technological hurdles suggest an area for improvement in making AI tools more user-friendly and integrated within existing healthcare infrastructures.

Moreover, potential enrollment delays and a high waste rate among study participants were highlighted, potentially compromising the findings and their relevance (Han et al., 2019). This limitation points to strategies to enhance participant retention and timely enrollment in such studies.

Clinical decision support systems were significantly concerned about the lack of rigorous testing and perceived usefulness by end-users (Gomis-Pastor et al., 2020; Serper et al., 2021). This limitation indicates that the active involvement of healthcare professionals and policymakers in more comprehensive evaluations and user-centric designs is crucial to effectively integrating these systems into clinical practice.

Ethical and legal considerations around data access and privacy were also mentioned, suggesting a gap in the comprehensive evaluation of AI tools in healthcare settings (Cresswell et al., 2020). This area warrants further exploration to ensure patient data is handled securely and ethically.

4 CONCLUSIONS

Through a scoping review, this study aimed to identify how artificial intelligence can help transplant patients adhere to ITSs and improve their quality of life. Our results indicate that AI and health information technology hold significant promise for supporting transplant patients and improving their quality of life and adherence to IST. AI can improve patients' knowledge and understanding of what needs to be done after organ transplantation (role clarity) and can increase their ability to do what needs to be done through reminders, personalized applications, and closer contact with providers (ability). It can also improve patients' motivation to follow the prescription through motivational messages and feedback on medication adherence and health parameters (motivation). However, these results should be analyzed carefully due to the methodological limitations present in the analyzed studies, as pointed out previously. The potential of these technologies to revolutionize medication adherence and

patient outcomes is enormous. Studies involving larger, more diverse populations, more extended follow-up periods, and more rigorous designs are essential to understand and fully optimize this potential.

Our scoping review has some limitations, such as the risk of overlooking some key literature and the fact that the selected studies comprised distinct research contexts and methods, thus hindering a statistical meta-analysis. Finally, heterogeneity and methodological shortcomings of studies constrain the generalizability of this review's findings. Despite these limitations, this review provides an up-to-date overview of the theme, highlighting the potential of AI to assist transplant patients and the methodological flaws of the studies analyzed. These findings help academics identify research gaps and the various AI applications and methodologies applied. For private and public managers, this review highlights best practices in using AI to support transplant patients, helping them make informed decisions about investments in technology that can improve patient outcomes. Lastly, for society, this study demonstrates how AI can personalize patient care treatment, improve medication adherence, and, thus, potentially decrease complications related to transplant surgeries, benefiting the broader community by enhancing patient outcomes. In this sense, this study reveals how AI can reduce the overall healthcare burden, decreasing hospital readmissions and long-term healthcare costs.

Future studies may benefit from expert panels with transplant physicians to better understand their perspectives on the theme. It is also important to conduct qualitative research on the theme of listening to transplant patients in developing countries, as most of the studies were conducted in the USA.

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REFERÊNCIAS

- Almeida, J., Araujo, C. A., Roza, B. D. A., Siqueira, M. M., & Rocha, E. (2021). *Risk analysis of the organ donation-transplantation process in Brazil*. Paper presented at the Transplantation Proceedings.
- Alves, R. M. B., da Silva, M. F., Schmitz, E. A., & Alencar, A. J. (2020). *Mobile Devices and*

- Systems in ADHD Treatment*. Paper presented at the WEBIST.
- Armstrong, R., Hall, B. J., Doyle, J., & Waters, E. (2011). Cochrane Update. 'Scoping the scope' of a Cochrane review. *Journal of Public Health, 33* 1, 147-150.
- Bain, E. E., Shafner, L., Walling, D. P., Othman, A. A., Chuang-Stein, C., Hinkle, J., & Hanina, A. (2017). Use of a Novel Artificial Intelligence Platform on Mobile Devices to Assess Dosing Compliance in a Phase 2 Clinical Trial in Subjects With Schizophrenia. *JMIR mHealth and uHealth, 5*.
- Beam, A. L., Drazen, J. M., Kohane, I. S., Leong, T.-Y., Manrai, A. K., & Rubin, E. J. (2023). Artificial intelligence in medicine. In (Vol. 388, pp. 1220-1221): Mass Medical Soc.
- Chisholm, M. A. (2012). Issues of Adherence to Immunosuppressant Therapy After Solid-Organ Transplantation. *Drugs, 62*, 567-575.
- Cossart, A. R., Staatz, C. E., Campbell, S. B., Isbel, N. M., & Cottrell, W. N. (2018). Investigating barriers to immunosuppressant medication adherence in renal transplant patients. *Nephrology, 24*.
- Cramer, J. A., Roy, A. N., Burrell, A., Fairchild, C. J., Fuldeore, M. J., Ollendorf, D. A., & Wong, P. K. (2008). Medication compliance and persistence: terminology and definitions. *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research, 11* 1, 44-47.
- Cresswell, K., Callaghan, M., Khan, S., Sheikh, Z., Mozaffar, H., & Sheikh, A. (2020). Investigating the use of data-driven artificial intelligence in computerised decision support systems for health and social care: a systematic review. *Health Informatics Journal, 26*(3), 2138-2147.
- Dabbs, A. D., Song, M., Myers, B., Li, R., Hawkins, R., Pilewski, J., . . . Connolly, M. (2016). A randomized controlled trial of a mobile health intervention to promote self - management after lung transplantation. *American Journal of Transplantation, 16*(7), 2172-2180.
- Dellande, S., Gilly, M. C., & Graham, J. L. (2004). Gaining compliance and losing weight: The role of the service provider in health care services. *Journal of Marketing, 68*(3), 78-91.
- DeVito Dabbs, A., Dew, M. A., Myers, B., Begey, A., Hawkins, R., Ren, D., . . . McCurry, K. R. (2009). Evaluation of a hand - held, computer - based intervention to promote early self - care behaviors after lung transplant. *Clinical transplantation, 23*(4), 537-545.
- Duettmann, W., Naik, M. G., Zukunft, B., Osmonodja, B., Bachmann, F., Choi, M., . . . Schmidt, D. (2021). eHealth in transplantation. *Transplant International, 34*(1), 16-26.
- Eggerth, A., Hayn, D., & Schreier, G. (2019). Medication management needs information and communications technology - based approaches, including telehealth and artificial intelligence. *British journal of clinical pharmacology, 86*, 2000 - 2007.
- Finkelstein, S. M., Lindgren, B. R., Robiner, W., Lindquist, R., Hertz, M., Carlin, B. P., & VanWormer, A. (2013). A randomized controlled trial comparing health and quality of life of lung transplant recipients following nurse and computer-based triage utilizing home spirometry monitoring. *Telemedicine and e-Health, 19*(12), 897-903.
- Fuzinato, C. R., Marin, S. M., & Maissiat, G. d. S. (2013). Adherence to immunosuppressive treatment in post-renal transplant patients: a descriptive-exploratory study. *Online Brazilian Journal of Nursing, 12*, 269-282.
- Gomis-Pastor, M., Roig, E., Mirabet, S., De Pourcq, J. T., Conejo, I., Feliu, A., . . . Barata, A. (2020). A mobile app (mHeart) to detect medication nonadherence in the heart transplant population: validation study. *JMIR mHealth and uHealth, 8*(2), e15957.

- Hamet, P., & Tremblay, J. (2017). Artificial intelligence in medicine. *Metabolism*, 69, S36-S40.
- Han, A., Min, S.-i., Ahn, S., Min, S.-K., Hong, H.-j., Han, N., . . . Ha, J. (2019). Mobile medication manager application to improve adherence with immunosuppressive therapy in renal transplant recipients: a randomized controlled trial. *PloS one*, 14(11), e0224595.
- Israni, A., Dean, C., Kasel, B., Berndt, L., Wildebush, W., & Wang, C. J. (2016). Why do patients forget to take immunosuppression medications and miss appointments: can a mobile phone app help? *JMIR public health and surveillance*, 2(1), e5285.
- Jiang, F., Jiang, Y., Zhi, H., Dong, Y., Li, H., Ma, S., . . . Wang, Y. (2017). Artificial intelligence in healthcare: past, present and future. *Stroke and vascular neurology*, 2(4).
- Jiang, Y., Sereika, S. M., Dabbs, A. D., Handler, S. M., & Schlenk, E. A. (2016). Using mobile health technology to deliver decision support for self-monitoring after lung transplantation. *International Journal of Medical Informatics*, 94, 164-171.
- Joost, R. H., Dörje, F., Schwitulla, J., Eckardt, K.-U., & Hugo, C. (2014). Intensified pharmaceutical care is improving immunosuppressive medication adherence in kidney transplant recipients during the first post-transplant year: a quasi-experimental study. *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association*, 29 8, 1597-1607.
- Kaul, V., Enslin, S., & Gross, S. A. (2020). History of artificial intelligence in medicine. *Gastrointestinal endoscopy*, 92(4), 807-812.
- Labovitz, D. L., Shafner, L., Reyes Gil, M., Virmani, D., & Hanina, A. (2017). Using Artificial Intelligence to Reduce the Risk of Nonadherence in Patients on Anticoagulation Therapy. *Stroke*, 48, 1416-1419.
- Levine, D. R., Torabi, J., Choinski, K. N., Rocca, J. P., & Graham, J. A. (2019). Transplant surgery enters a new era: Increasing immunosuppressive medication adherence through mobile apps and smartwatches. *American journal of surgery*, 218 1, 18-20.
- Lockwood, C. S., dos Santos, K. B., & Pap, R. (2019). Practical guidance for knowledge synthesis: Scoping Review Methods. *Asian nursing research*.
- Luo, Y., Tang, Z., Hu, X., Lu, S., Miao, B., Hong, S., . . . Liang, H. (2020). Machine learning for the prediction of severe pneumonia during posttransplant hospitalization in recipients of a deceased-donor kidney transplant. *Annals of translational medicine*, 8(4).
- Marin-Garcia, J. A., Vidal-Carreras, P. I., & Garcia-Sabater, J. J. (2021). The Role of Value Stream Mapping in Healthcare Services: A Scoping Review. *International journal of environmental research and public health*, 18(3). doi:10.3390/ijerph18030951
- Mark, E., Goldsman, D., Gurbaxani, B., Keskinocak, P., & Sokol, J. (2019). Using machine learning and an ensemble of methods to predict kidney transplant survival. *PloS one*, 14(1), e0209068.
- McGillicuddy, J. W., Taber, D. J., Mueller, M., Patel, S., Baliga, P. K., Chavin, K. D., . . . Treiber, F. A. (2015). Sustainability of improvements in medication adherence through a mobile health intervention. *Progress in Transplantation*, 25(3), 217-223.
- McGillicuddy, J. W., Weiland, A. K., Frenzel, R. M., Mueller, M., Brunner-Jackson, B. M., Taber, D. J., . . . Treiber, F. A. (2013). Patient attitudes toward mobile phone-based health monitoring: questionnaire study among kidney transplant recipients. *Journal of medical Internet research*, 15(1), e2284.
- Melilli, E., Cestone, G., Revuelta, I., Meneghini, M., Lladó, L., Montero, N., . . . Torregrosa, V. (2021). Adoption of a novel smart mobile - health application technology to track

- chronic immunosuppression adherence in solid organ transplantation: Results of a prospective, observational, multicentre, pilot study. *Clinical transplantation*, 35(5), e14278.
- Mellon, L., Doyle, F., Hickey, A., Ward, K. D., de Freitas, D. G., McCormick, P. A., . . . Conlon, P. J. (2022). Interventions for increasing immunosuppressant medication adherence in solid organ transplant recipients. *The Cochrane database of systematic reviews*, 9, CD012854.
- Montaleão Brum Alves, R., Ferreira da Silva, M., Assis Schmitz, E., & Juarez Alencar, A. (2022). Trends, limits, and challenges of computer technologies in attention deficit hyperactivity disorder diagnosis and treatment. *Cyberpsychology, Behavior, and Social Networking*, 25(1), 14-26.
- Munn, Z., Peters, M. D. J., Stern, C., Tufanaru, C., McArthur, A., & Aromataris, E. (2018). Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. *BMC Medical Research Methodology*, 18.
- Naruka, V., Arjomandi Rad, A., Subbiah Ponniah, H., Francis, J., Vardanyan, R., Tasoudis, P., . . . Athanasiou, T. (2022). Machine learning and artificial intelligence in cardiac transplantation: a systematic review. *Artificial Organs*, 46(9), 1741-1753.
- Nerini, E., Bruno, F., Citterio, F., & Schena, F. P. (2016). Nonadherence to immunosuppressive therapy in kidney transplant recipients: can technology help? *Journal of Nephrology*, 29, 627-636.
- Niazkhani, Z., Pirnejad, H., & Khazaei, P. R. (2017). The impact of health information technology on organ transplant care: a systematic review. *International Journal of Medical Informatics*, 100, 95-107.
- Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., . . . Brennan, S. E. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Bmj*, 372.
- Park, E. S., Peccoud, M. R., Wicks, K. A., Halldorson, J. B., Carithers, R. L., Jr, Reyes, J. D., & Perkins, J. D. (2010). Use of an automated clinical management system improves outpatient immunosuppressive care following liver transplantation. *Journal of the American Medical Informatics Association*, 17(4), 396-402.
doi:10.1136/jamia.2009.000992
- Reese, P. P., Bloom, R. D., Trofe - Clark, J., Mussell, A. S., Leidy, D., Levsky, S., . . . Volpp, K. G. M. (2017). Automated Reminders and Physician Notification to Promote Immunosuppression Adherence Among Kidney Transplant Recipients: A Randomized Trial. *American journal of kidney diseases : the official journal of the National Kidney Foundation*, 69 3, 400-409.
- Sanders-Pinheiro, H., Colugnati, F. A. B., Denhaerynck, K., Marsicano, E. d. O., Medina, J., & De Geest, S. M. (2020). Multilevel Correlates of Immunosuppressive Nonadherence in Kidney Transplant Patients the Multicenter ADHERE BRAZIL Study. *Transplantation*.
- Sanders-Pinheiro, H., Colugnati, F. A. B., Marsicano, E. d. O., De Geest, S. M., & Medina, J. (2018). Prevalence and correlates of non-adherence to immunosuppressants and to health behaviours in patients after kidney transplantation in Brazil – the ADHERE BRAZIL multicentre study: a cross-sectional study protocol. *BMC nephrology*, 19.
- Schäfer-Keller, P., Steiger, J. U., Bock, A. H., Denhaerynck, K., & Geest, S. D. (2008). Diagnostic Accuracy of Measurement Methods to Assess Non - Adherence to Immunosuppressive Drugs in Kidney Transplant Recipients. *American Journal of Transplantation*, 8.
- Schwantes, I. R., & Axelrod, D. A. (2021). Technology-enabled care and artificial intelligence

- in kidney transplantation. *Current transplantation reports*, 8, 235-240.
- Serper, M., Ladner, D. P., Curtis, L. M., Nair, S. S., Hur, S. I., Kwasny, M. J., . . . Abecassis, M. M. (2021). Transplant regimen adherence for kidney recipients by engaging information technologies (TAKE IT): rationale and methods for a randomized controlled trial of a strategy to promote medication adherence among transplant recipients. *Contemporary clinical trials*, 103, 106294.
- Seyahi, N., & Ozcan, S. G. (2021). Artificial intelligence and kidney transplantation. *World Journal of Transplantation*, 11, 277 - 289.
- Shih, M.-H., & Tsai, C.-h. (2014). [Factors associated with adherence to immunosuppressive therapy among transplant recipients]. *Hu li za zhi The journal of nursing*, 61 4, 21-25.
- Staes, C. J., Evans, R. S., Rocha, B. H. S. C., Sorensen, J. B., Huff, S. M., Arata, J., & Narus, S. P. (2008). Computerized Alerts Improve Outpatient Laboratory Monitoring of Transplant Patients. *Journal of the American Medical Informatics Association*, 15(3), 324-332. doi:<https://doi.org/10.1197/jamia.M2608>
- Testa, M. A., & Simonson, D. C. (1996). Assessment of quality-of-life outcomes. *The New England journal of medicine*, 334 13, 835-840.
- Vrijens, B., Geest, S. D., Geest, S. D., Hughes, D. A., Przemyslaw, K., Demonceau, J., . . . Urquhart, J. (2012). A new taxonomy for describing and defining adherence to medications. *British journal of clinical pharmacology*, 73 5, 691-705.
- Wingfield, L. R., Salaun, A., Khan, A., Webb, H., Zhu, T., & Knight, S. (2024). Clinical Decision Support Systems Used in Transplantation: Are They Tools for Success or an Unnecessary Gadget? A Systematic Review. *Transplantation*, 108(1), 72-99.
- Zanetti-Yabur, A., Rizzo, A., Hayde, N., Watkins, A. C., Rocca, J. P., & Graham, J. A. (2017). Exploring the usage of a mobile phone application in transplanted patients to encourage medication compliance and education. *The American Journal of Surgery*, 214(4), 743-747.
- Zhao, M., Hoti, K., Wang, H., Raghu, A., & Katabi, D. (2021). Assessment of medication self-administration using artificial intelligence. *Nature Medicine*, 27, 727 - 735.