Kidney transplantation: interventions to improve medication adherence

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Learning outcomes

On completion of this continuing professional development activity, participants should be able to:

• Recognise the overwhelming nature of self-care required by the kidney transplant recipient at all time points post-renal transplantation.
• Recognise some of the factors that may lead to non-adherence with medications.
• Articulate specific domains that may be targeted as interventions to promote consistent medication adherence.
• Appreciate the imperative of person-centred care in maintaining an empowered sense of control for the recipient.
• Consider the significance of individualised, patient-specific education.

Keywords evidence-based summaries, best practice, medication non-adherence, renal transplantation


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Introduction

One of the most exciting and stressful times for persons on the transplant waiting list is the actual receipt of a kidney. Kidney transplant recipients frequently report feeling overwhelmed both physically and emotionally, often feeling burdened with an enormous sense of “social responsibility” to care well for their new graft (Jamieson et al., 2016).

The initial, intensive postoperative routine of frequent (daily) pathology assays to monitor graft function, check the wound and assess general health subsides gradually, and is replaced by a need for increasing patient autonomy and control over all self-care responsibilities. Included in this are many expectations of behaviour modification – maintaining adequate fluid intake, restricting risky health practices (smoking, sun exposure),

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being mindful of infection potential – in order for the recipient to remain as healthy as possible. Yet, along with the frequent desire to get back to everyday living, is the reality of the long-term risks inherent with transplantation, including an increased potential for cardiovascular disease, diabetes, weight gain, infection and cancer (Jamieson et al., 2016; Low et al., 2015).

In addition, several conditions post-kidney transplantation may ultimately result in graft loss. Medication adherence remains the most important modifiable factor in preventing transplant rejection; the most obvious and severe consequence of non-adherence is allograft rejection (Belaiche et al., 2017; Mathes et al., 2017). To ensure optimal graft function, strict adherence to all prescribed medications – immunsuppressive medications in particular – is therefore essential.

Collaborative support and individually tailored education and self-management strategies can help transplant recipients maintain optimal medication adherence, and a review of current evidence may assist clinicians to find the most appropriate interventions to improve medication adherence for their patients. Whilst identification of factors for non-adherence are important, and will be briefly considered in the discussion, the main purpose of this paper is to highlight interventions that may promote medication adherence.

**Methods**

This is the fifth continuing professional development (CPD) paper comprising an evidence summary and best practice recommendations from the Joanna Briggs Institute (JBI) renal node. The clinical question addressed by this evidence summary was – What is the best available evidence regarding the effectiveness of interventions in improving adherence to prescribed medicines following kidney transplantation?

A streamlined rapid review approach based on a structured search of selected databases was conducted via the JBI Database of Systematic Reviews and Implementation Reports, Cochrane Library, Medline (PubMed), CINAHL and Google Scholar. A range of keywords and subject headings appropriate for each database were used to identify pivotal studies providing evidence on the efficacy of intervention strategies to improve post-transplantation medication adherence. Key points from the evidence were summarised and specific evidence-based recommendations for practice were developed.

**Characteristics and key points from the evidence**

Three systematic reviews, including randomised controlled trials (RCTs), were identified, all reporting findings at Level 1 in accordance with the JBI levels of evidence for effectiveness (Figure 1). In addition, one qualitative systematic review was located; this was also Level 1 evidence. The key points from these systematic reviews are outlined below.

A systematic review (Low et al., 2015) that included 12 studies (eight RCTs, two retrospective cohort and two quasi-experimental) evaluated the effectiveness of interventions designed to improve adherence to medication in adults following kidney transplantation. All interventions were implemented for at least three months, except for trials that involved a one-off interview or feedback from a nurse. The

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**Figure 1. Joanna Briggs Institute levels of evidence for effectiveness.**

- Level 1.a – Systematic review of randomized controlled trials (RCTs)
- Level 1.b – Systematic review of RCTs and other study designs
- Level 1.c – RCT
- Level 1.d – Pseudo-RCTs

- Level 2.a – Systematic review of quasi-experimental studies
- Level 2.b – Systematic review of quasi-experimental and other lower study designs
- Level 2.c – Quasi-experimental prospectively controlled study
- Level 2.d – Pre-test – post-test or historic/retrospective control group study

- Level 3.a – Systematic review of comparable cohort studies
- Level 3.b – Systematic review of comparable cohort and other lower study designs
- Level 3.c – Cohort study with control group
- Level 3.d – Case-controlled study
- Level 3.e – Observational study without a control group

- Level 4.a – Systematic review of descriptive studies
- Level 4.b – Cross-sectional study
- Level 4.c – Case series
- Level 4.d – Case study

- Level 5.a – Systematic review of expert opinion
- Level 5.b – Expert consensus
- Level 5.c – Bench research/ single expert opinion
Authors report that interventions targeting a combination of behavioural, educational and emotional risk factors are most effective in improving medication adherence. In addition, the review highlights that when patients are encouraged to participate in the development process of interventions, their effectiveness may be further enhanced. Specifically, the authors report that this evidence shows that:

- Multidimensional interventions – for example a combination of a behavioural contract, a self-improvement plan and medication counselling – significantly improve medication adherence, whereas one-off feedback from a nurse or financial programs only result in minimal improvements.
- Behaviour modification, which involves providing patients with specific instructions about the time to take medications and scheduling this to coincide with the patient’s regular routine, is vital. Patients are also encouraged to contact their pharmacist or nurse for more information if in doubt.
- The education of patients, covering the benefits of adherence and consequences of non-adherence, is important. Further, it is noted that individualised interventions are more effective than universal approaches.
- The involvement of significant others – for example family members engaging with the patient's therapy – is also encouraged.
- The encouragement of self-monitoring increases patient awareness of the potential for non-adherence, especially in conjunction with healthcare support. For example, a 6-month patient-tailored, self-improvement intervention is considered to be effective in improving medication adherence scores.
- The identification of barriers to medication adherence and the implementation of strategies to overcome these barriers is therefore seen to be an effective approach.

A systematic review (Zhu et al., 2017) that included eight studies (six RCTs, two quasi-experimental) with a total of 546 participants evaluated the effectiveness of interventions designed to improve adherence to immunosuppressive medication in people who had undergone kidney transplantation. The authors report that medication adherence can be increased with interventions that target education, decision aids, recording, reminders and compliance. In people receiving interventions, the adherence rate was significantly higher than the control group.

A systematic review (Mathes et al., 2017) including 12 studies (eight RCTs, one non-RCT and three cohort), with participant numbers in individual studies ranging from 24–1830, evaluated the effectiveness of interventions on adherence to immunosuppressive drugs after kidney transplantation. Studies that evaluated educational and/or behavioural components generally showed a moderate but statistically significant effect in favour of the intervention. Studies that combined educational and behavioural components, or included an individualised component – for example discussion of individual adherence barriers and feedback on individual adherence behaviour – or more intensive interventions – for example more sessions or longer intervention period – showed larger effects on adherence.

A qualitative systematic review (Jamieson et al., 2016) that included 50 studies with a total of 1238 participants summarised the factors that could influence medication adherence following kidney transplantation. The authors identify some key themes which impact on the ability to adhere to medication schedules – social efficacy, individual empowerment (for example problem-solving skills), managing fear of consequences (for example anxiety, aversion to dialysis), over-medicalisation, and motivation (for example self-efficacy, literacy). They subsequently contrive some “suggestions for clinical practice” which recommend:

- Promoting autonomy and self-efficacy through:
  - providing educational programs about the value of self-management;
  - providing written medication and laboratory results, with explanations after each outpatient visit;
  - accessing peer support groups;
  - accessing mobile phone apps; and
  - considering collaborative ‘behaviour contracts’.
- Providing clear recommendations and to address ambiguities by:
  - giving specific, practical advice; and
  - offering personalised care planning.
- Addressing anxieties by:
  - validating concerns in a context of self-management;
  - facilitating access to psychological services; and
  - addressing guilt and indebtedness to donors.
- Minimising treatment fatigue by:
  - providing clear written appointment times and schedules;
  - developing personalised strategies to minimise treatment burden;
  - suggesting ways to integrate strategies into daily routine; and
  - developing individualised exercise programs.
- Supporting decision-making through:
  - utilising decision aids, taking patient priorities into account.

**Discussion**

In addressing the question regarding the effectiveness of interventions to improve medication adherence following kidney transplantation, this evidence summary identified several systematic reviews providing high-level evidence on the topic.
This allowed the development of specific recommendations for practice – see best practice recommendations below. Systematic reviews are the preferred form of evidence to include in an evidence summary as they provide synthesised results from primary research that has been systematically located and critically appraised for methodological quality/risk of bias. The reported systematic reviews provide solid evidence to address the clinical question, hence it was not necessary to include any individual primary research studies in the evidence summary.

**Definition and measurements of non-adherence**

Transplant recipients need to consistently take at least 97% of immunosuppressive medication to prevent rejection, with recognition that hospitalisation rates are doubled when the adherence rate drops to 80% as compared to 90% (Low et al., 2015). With the rate of medication non-adherence in recipients frequently estimated to exceed 30% (Jamieson et al., 2016), strategies to improve, or ensure adherence from the outset, are clearly necessary.

Medication adherence may be defined as “the extent to which the patient’s behaviour matches the agreed upon prescriber’s recommendations” (Belaiche et al., 2017, p. 583). Non-adherence of medications may be difficult to monitor without direct indication, as clinicians may not routinely ask patients if they are taking all their medications, and patients may not readily volunteer this information (Low et al., 2015).

The measures for adherence within the quantitative studies of these reviews include electronic monitoring of pharmacy medications and script refills, medical record documentation, medical/nurse discernment, blood assays, and patient self-reporting. Confirmatory and secondary analyses were made through a combination of healthcare questionnaires, and by the measurement of serum medication concentration. The qualitative studies within the systematic review used a range of exploratory analyses according to the conceptual methodological framework utilised.

**Factors relevant to non-adherence**

A brief examination of factors related to non-adherence may be helpful. Belaiche et al. (2017) remind that timely taking of all post-transplant medications is essential – this may include anti-viral, anti-fungal and anti-bacterial agents, antihypertensives, statins, and cardiac medication as well as immunosuppressive therapy. Their systematic review investigating relevant factors for non-adherence reports on 37 studies, two of which were randomised, the remainder being prospective and observational. Five significant domains likely to impinge on medication adherence are presented, with further explanatory comment. These include socio-demographic issues (particularly low social support, poor education, male gender, youth (<50 years), unemployment), disease-related concerns (especially from 3 months after transplant, with more than one transplant and more than six comorbidities), drug-related (with more than five drugs and more than two intakes per day), patient-related (considering individual and negative beliefs, behaviour and satisfaction), and psychological issues (in particular depression and anxiety). They differentiate between intentional and accidental non-adherence, suggesting that “forgetfulness” is more likely when the patient is in non-routine situations, and they make succinct comment on the significance of social isolation, as “with greater social support (patients) are more than twice as likely to be adherent” (Belaiche et al., 2017, p. 590).

All reviews comment on the importance of self-management, both in maintaining consistency of long-term care, and in encouraging responsibility and confidence which enables a sense of empowerment. As such, the on-going collaboration of nurses, physicians, pharmacists and support groups in the setting of continuing education is important. Self-management works best when tailored to individualised patient needs, and when offered alongside family and social support; the flexibility to consider a variety of proven interventions is also seen as important (Zhu et al., 2017). In assessing for non-adherence, and in line with a person-centred framework, comment is made that “self-reports should remain the cornerstone of adherence assessment” (Belaiche et al., 2017, p. 582) as they may be facilitated with open and accessible support.

Ultimately, kidney transplant grafts may remain functional for many years, yet studies consistently indicate a decrease with immunosuppression regimen adherence over time (Jamieson et al., 2016). This highlights the significance of good patient–care-team relationships, and the necessity for education to be ongoing.

**Conclusion**

Within these systematic reviews, the consequences of non-adherence of post-transplant medications are acknowledged as obvious and dire. Author recommendations are succinct and in agreement. The imperatives lie with clinicians encouraging self-monitoring, increasing patient awareness of the importance of all post-transplant medications, along with highlighting any likelihood of, and correction for, their non-adherence. Pivotal, all reviews highlight that individually tailored patient education works best, and that a variety of components are suggested. Additionally, good care–collaborative relationships allow patients to recognise issues and barriers as they may arise, enabling timely implementation of corrective strategies.

**Best practice recommendations**

All of these relate to Grade A in the JBI grades of recommendation scale (see Table 1).

- Health professionals should be aware of effective strategies to promote medication adherence.
Multidimensional interventions, including educational and behavioural components, should be implemented to improve medication adherence.

Patients should receive education regarding the benefits of adherence and consequences of non-adherence.

Patients should be provided with specific instructions about the time to take medications, and this should be scheduled to coincide with the patient’s regular routine.

Patients should be actively involved in determining strategies for improving medication adherence.

Interventions should be individualised to patients and may include discussion of individual adherence barriers and feedback on individual adherence behaviour.

Family members should be encouraged to engage with and support the patient’s therapy.

Patients should be encouraged to contact their pharmacist or nurse if in doubt about their medication regimen.

References


