

# **Evidence Based Practice Guidelines for the Nutritional Management of Adult Kidney Transplant Recipients**

**Developed by the  
NEW SOUTH WALES RENAL SERVICES NETWORK  
TRANSPLANT WORKING GROUP  
Greater Metropolitan Clinical Taskforce**

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The guidelines are available to members of the Dietitians Association of Australia from [www.daa.asn.au](http://www.daa.asn.au).



These guidelines have been endorsed by the Dietitians Association of Australia

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# Executive Summary

According to information collated by the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA), in 2006, 2,378 new patients commenced treatment for end-stage renal failure in Australia (a rate of 115 per million population). In New Zealand, 484 new patients commenced treatment (rate of 117 per million of population) in 2006. These are the highest incidence rates ever recorded in either country. (1)

Due to the progressive improvements in both graft and patient survival among kidney transplant recipients in recent decades transplantation has become the treatment of choice for end-stage kidney disease. (2, 3)water

There are 20 transplant units in Australia (three of which are paediatric transplant units) and three in New Zealand. In Australia, 641 transplant operations were performed in 2006 (a 3% increase from the 2005 figure) and at 31st December 2006 there were 6,845 patients with a functioning kidney transplant (332 per million population). There were 1,344 patients receiving dialysis on the transplant waiting list (15% of the 9,182 patients dialysing). In New Zealand, 90 transplant operations performed in 2006 (a decrease of 3% from 2005). At 31<sup>st</sup> December, there were 1253 patients with a functioning kidney transplant (303 per million population) and 327 dialysing patients on the transplant waiting list (17% of the 1,971 patients dialysing). (2)

The metabolic abnormalities and the side effects of immunosuppressive medications significantly impact on the long-term morbidity and quality of life of kidney transplant recipients. With improving patient survival rates, the prevention and management of post-transplant complications, such as obesity, dyslipidaemia, hypertension, diabetes, bone disease and anaemia, have become increasingly important.

The average weight gained after kidney transplantation has been reported at 10 and 35 per cent (4-7) which is a serious health concern with obesity an independent risk factor for poor graft survival (8-11) and associated with hypertension, coronary artery disease, chronic obstructive pulmonary disease and peripheral vascular disease, hyperlipidaemia, stroke, diabetes, coronary artery disease and mortality(8, 12, 13). Dyslipidaemia affects 60% of kidney transplant recipients, with lipoprotein alterations that are particularly atherogenic; in fact cardiovascular mortality rates among organ transplant recipients are up to 10-fold of those in the non-transplant population (11, 14-17). Post-transplant arterial hypertension, another risk factor for cardiovascular disease (18), also appears to be a primary risk factor for carotid lesions in the kidney transplant recipients (19) and is associated with chronic allograft nephropathy and acute rejection (20). New-onset diabetes after renal transplantation (NODAT) affects 20% of this patient group by one year post-transplant and places patients at increased risk of death with function and chronic allograft dysfunction (21). NODAT is an independent predictor of major cardiovascular events after transplantation (22, 23) and is also a likely contributor to chronic allograft dysfunction (24). Bone disease is a problem for kidney transplant recipients with the risk of bone fractures four times that of the general population (25). Hypophosphataemia affects up to 93% of transplant recipients in the first four months (26) and may be a long-term concern related to persistent hyperparathyroidism (27). In severe phosphate depletion, haemolytic anaemia, rhabdomyolysis, decreased myocardial contractility and respiratory failure may occur. Long-term hypophosphataemia is associated with post-transplantation osteodystrophy (28, 29). Anaemia is a long-term problem for many kidney transplant recipients, including those with normal graft function, with the prevalence reported between 30 and 62 per cent (30-33). It is a risk factor for cardiovascular disease and there is a positive correlation between creatinine clearance and haemoglobin level (34).

Nutrition therapy is likely to be of benefit to the kidney transplant population, given the potential for nutrition-related complications following renal transplant, as well as the potential change in nutritional needs. Whilst each of the adult transplant units in Australia and New Zealand has a dietetics service, staffing levels and practices vary from site to site (Fry K et al, 2006, unpublished data). Up until now, there have been no comprehensive evidence based practice guidelines for the nutritional management of kidney transplant recipients.

The development of guidelines for the nutritional management of adult kidney transplant recipients was funded by the Greater Metropolitan Clinical Taskforce (GMCT) of New South Wales (NSW), Australia. GMCT was established in July 2004 by the New South Wales Minister of Health to promote clinician and consumer involvement in planning and health service delivery in NSW. This relatively autonomous organisation works actively with NSW Area Health Services and reports to the NSW Minister for Health and to the NSW Department of Health via the Deputy Director General and the Director General. The Renal Services Network (RSN) is one of the twenty GMCT clinical networks chaired by clinicians and involving doctors, nurses, allied health professionals, scientists, managers, and consumers. The Transplant Working Group of RSN identified the absence of and need for comprehensive, evidence based practice guidelines for this important aspect of patient care. In 2006, GMCT allocated funding to RSN to develop these best practice guidelines.

The guidelines have been developed with a strong emphasis on quality of evidence, using methodology endorsed by the *National Health and Medical Research Council of Australia*. Health professionals with substantial experience in managing kidney transplant recipients have contributed to the guidelines as have adult kidney transplant recipients. This combination of scientific literature and professional and patient experience has resulted in a set of recommendations that will assist health professionals in various clinical settings to provide the best possible nutritional management to adult kidney transplant recipients. They can be used as they stand, or can provide the starting point for local adaptation of the guidelines. They may be useful for those wishing to identify future areas of research.

# Introduction

## Scope and Purpose

These guidelines address the nutritional management of adult kidney transplant recipients from immediately post-transplant and for the lifetime of the transplant. They do not cover the management of paediatric patients or kidney-pancreas transplant recipients.

Specific objective(s) and clinical question(s) are presented for each guideline. The first guideline addresses nutritional assessment and diagnosis. Guidelines 2-10 address nutritional interventions, monitoring and evaluation for specific post-transplant health concerns.

## Target Users

The guidelines have been designed for use by health professionals in various clinical settings who care for adult kidney transplant recipients, particularly dietitians. The first draft of the document was piloted and evaluated by physicians and dietitians based at fourteen kidney transplant units in Australia and New Zealand between July and October 2007.

## Guideline Development Process

The Appraisal of Guidelines for Research and Evaluation (AGREE) instrument (35) was used to ensure that the guidelines were developed according to high standards.

The following steps were identified as central to the process of identifying sources of rigorously objective, peer reviewed information; and reviewing, grading, and synthesising the literature to generate guideline recommendations.

### 1. Guideline Steering Committee and Project Dietitian

A multidisciplinary steering committee was convened with the responsibility for overseeing the project and ensuring that valid, relevant and rigorous guidelines were produced and for agreeing on the final grading of the recommendations. The committee also had a central role in ensuring that recommendations were consistent in terms of the overall wording, presentation and clinical coherence. The committee was made up of three dietitians, two transplant physicians, one service manager from GMCT and one consumer representative, a kidney transplant recipient. A fourth dietitian with experience in renal transplant nutrition was assigned the role of Project Dietitian with the responsibility for undertaking the systematic literature review, consulting with key stakeholders and drafting the guidelines document.

## **Guideline Steering Committee and Project Dietitian**

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## **2. Defining guideline topics and clinical questions**

A survey of 163 transplant recipients and 67 clinicians involved in the care of transplant recipients based at 23 hospitals (including the 20 adult kidney transplant units) in Australia and New Zealand was undertaken between June and October 2006, designed to ascertain which post-transplant nutrition issues are of greatest concern to key stakeholders and to collect information on current nutritional management practices (Fry K, 2006, unpublished data).

The health concerns considered by both health professionals and kidney transplant recipients to be of greatest concern were poor wound healing and protein requirement, diabetes, infection risk, excessive weight gain, diabetes and dyslipidaemia. The survey revealed considerable variation in nutritional management practices (including referral systems and follow-up protocols, as well as nutritional assessment and specific dietary interventions). See Appendix A.

Ten topics were chosen for inclusion in the guidelines, taking into consideration the findings of the survey as well as prevalence data and available evidence on the health impact of particular post-transplant concerns.

The first guideline addresses nutrition assessment and diagnosis. The remaining guidelines address nutrition intervention, monitoring and evaluation with respect to the issues identified to be of most concern among kidney transplant recipients, namely, dietary protein requirements; overweight and obesity; dyslipidaemia; hypertension; diabetes mellitus; bone disease; hypophosphataemia; anaemia; and food safety. Background information for each guideline topic is presented below.

### *Nutritional assessment*

A nutritional assessment usually includes an evaluation of dietary, anthropometric, clinical and biochemical information as well as medical, health and psychosocial data. Due to variations in current practice, noted in the survey of health professionals in Australia and New Zealand conducted in 2006 (Fry K, 2006, unpublished data), guidelines for the following components of nutritional assessment were developed: dietary intake assessment; anthropometric assessment; biochemical and clinical assessment; and medication review.

### *Protein requirements*

Treatment with glucocorticoids causes wasting of proximal skeletal muscles (36, 37), dietary protein requirements are likely to be elevated in the early post-transplant period, when high dose glucocorticoids are necessary, to prevent poor wound healing, muscle mass loss and other morbidities (38-40). In the later post-transplant period, dietary protein restriction may assist in delaying the progression to end-stage kidney disease, as is the case in non-transplant patients with chronic kidney disease (41). Chronic allograft nephropathy is the most frequent cause of long-term kidney allograft loss, potentially affecting over 58 percent of transplant recipients by 10 years (42, 43) Other contributors to graft failure include a recurrence of the original renal disease and chronic cyclosporine toxicity (44).

### *Overweight and obesity*

Weight gain after kidney transplantation is common and the resulting overweight and obesity is associated with serious health complications. The average post-transplant weight gain has been reported to be as high as 35 per cent, with the majority of the weight gain occurring in the first 12 months post-transplant (4-6, 45). Much of the weight gained is abdominal fat (6, 46). Steroids are known to enhance appetite and to have an adverse effect on body fat distribution and lipid metabolism thus contributing to the pattern of weight gain seen after transplantation. However, other factors including an improved sense of wellbeing may play an equally important role (5, 46-50). Obesity is an independent risk factor for poor graft survival (8-11, 51) and obese kidney transplant recipients have a higher prevalence of hypertension, coronary artery disease, chronic obstructive pulmonary disease and peripheral vascular disease, hyperlipidaemia, stroke, diabetes and mortality (8, 12, 13).

### *Dyslipidaemia*

Dyslipidaemia is common after transplantation, present in about 60% of kidney transplant recipients. The typical post-transplant lipid profile includes elevations in both total serum cholesterol and low-density lipoprotein cholesterol (LDL-C), with variable high-density lipoprotein cholesterol (HDL-C) and triglycerides. (52-55). Lipoprotein abnormalities may be a persistent problem even 10 years post-transplant (56, 57). Whilst dyslipidaemia may often be present prior to transplantation, anti-rejection medications, such as calcineurin inhibitors, sirolimus and corticosteroids, as well as lifestyle factors and post-transplant renal function are also implicated in abnormal serum lipid levels post-transplantation (58-64). The correlation between dyslipidaemia and cardiovascular disease (CVD) risk in non-transplant populations has been well established (65) and studies confirm this correlation among kidney transplant recipients (18). Indeed, compared to the general population, transplant recipients tend to develop lipoprotein alterations that are particularly atherogenic with CVD mortality rates among organ transplant recipients up to 10-fold of those in the non-transplant population (11, 14-17).

### *Hypertension*

The development of arterial hypertension is common after kidney transplantation. Whilst the aetiological factors of post-transplant hypertension have not been clearly elucidated, it has been correlated with male sex, age, donor age, the presence of diabetes, weight gain, body mass index and delayed graft function (66). Calcineurin inhibitors are known to contribute to hypertension and prednisone may also play a role (67, 68). Post-transplant arterial hypertension appears to be one of the primary risk factors for carotid lesions in the kidney

transplant recipients (19) and is a risk factor for cardiovascular disease (CVD), a significant cause of morbidity and mortality in kidney transplant recipients (18). Hypertension adversely affects kidney graft survival, associated with chronic allograft nephropathy and acute rejection (20).

### *Diabetes Mellitus*

The incidence of new-onset diabetes after renal transplantation (NODAT) has been reported at around 20% at one year post-transplant (21) and best available data suggest that the disorder is a life-long problem for the majority of those diagnosed, not a temporary aberration driven by high dose steroid exposure in the early post-transplant phase (69). NODAT is caused by the combination of insulin resistance and deficient insulin production (70). Whilst risk factors for the development of NODAT include age, ethnicity, family history of type-2 diabetes and hepatitis C infection, obesity and the choice of immunosuppressive regimen, particularly steroid exposure and use of tacrolimus, are important modifiable risk factors (70-74). Prospective studies have shown a strong correlation between post-transplant weight gain and NODAT (71, 75). A relative risk of 1.4 for post-transplant diabetes has been documented for every 10kg increase in body weight greater than 60kg (76). NODAT places patients at increased risk of the key causes of premature graft failure - death with function and chronic allograft dysfunction (21). Several studies have documented that NODAT is an independent predictor of major cardiovascular events after transplantation (22, 23). NODAT is also a likely contributor to chronic allograft dysfunction (24).

### *Bone disease*

The rapid decline in bone mineral density which occurs in the early post-transplant period is a significant problem for kidney transplant recipients (77, 78). Though the rate of bone loss may decelerate or cease by around 3 years post-transplant, bone mineral density remains below normal (79). The risk of bone fractures among kidney transplant recipients is four times that among the general population (25). At the time of transplantation, there are usually already significant abnormalities of bone remodelling related to chronic kidney disease (80). Reduced calcium absorption due to prednisone (81), hyperparathyroidism (82) and abnormal vitamin D metabolism (83) are among the factors potentially contributing to the further weakening of bones and the risk of bone disease post-transplantation. There is an increased risk of bone loss among females, particularly post-menopausal (84).

### *Hypophosphataemia*

Hypophosphataemia affects up to 93% of transplant recipients in the first four months (26), but may be a long-term concern, related to persistent hyperparathyroidism (27). In the short term, the effects include muscle weakness and osteomalacia. In severe phosphate depletion, haemolytic anaemia, rhabdomyolysis, decreased myocardial contractility and respiratory failure may occur. Long-term hypophosphataemia is associated with post-transplantation osteodystrophy (28, 29).

### *Anaemia*

Anaemia, defined as a haemoglobin concentration of < 11-12 g/dL in women or < 12-13g/dL in men (85, 86) is common in patients with end-stage renal failure. In kidney transplant recipients anaemia is a significant independent risk factor for cardiovascular death and for all-cause mortality (87, 88). There is a positive correlation between haemoglobin and creatinine clearance in renal transplant patients (89, 90), which seems to be a function of endogenous erythropoietin production by the graft (91). Therefore after successful kidney transplantation, with the rise in endogenous erythropoietin production, haemoglobin levels generally rise and normalise within the first two to four months (92). In a large, cross-sectional study, the prevalence of anaemia was found to be 38.6% in long term kidney transplant recipients (ranging from 6 months to 5 years post-transplant), including patients with normal graft function (93) Smaller studies have supported this data (30-33, 94, 95). Whilst post-transplant anaemia is

associated with treatment with azathioprine, sirolimus and mycophenolate mofetil, as well as ACE inhibitors and angiotensin II receptor antagonists (96, 97), nutritional factors appear to be potentially important in the aetiology and management of post-transplant anaemia. In a sample of 438 kidney transplant recipients in whom anaemia had not been diagnosed, 20.1% of subjects were found to be iron-deficient (94). Smaller studies have also found a high prevalence of iron deficiency (94, 98-100). Folate and B12 deficiencies may also contribute to anaemia in stable kidney transplant recipients (101).

#### *Food safety*

Food-borne illness, such as listeriosis, is recognised as a particular risk for a person whose immune system is compromised. Organ transplant recipients are considered to be more susceptible to listeriosis than other at risk subpopulations. (102-104) There are few data on the incidence of listeria infection in the kidney transplant recipient population, however a listeria carriage rate of 5.6% among kidney transplant recipients, without the development of listeria infection, has been reported (105). Reported listeriosis outcomes among kidney transplant recipients include central nervous system involvement, bacteraemia, pneumonia and a mortality rate of 26% (106).

### **3. Literature search strategy**

Relevant reviews and studies were obtained from the databases below. Reference lists of nephrology textbooks, review articles and relevant trials were also used to locate studies.

*Databases searched:* MEDLINE – 1966 to week 1 September 2006; EMBASE – 1980 to week 1 September 2006; the Cochrane Renal Group Specialised Register of Randomised Controlled Trials and Central.

*Search terms:* MeSH terms and text words for kidney transplantation were combined with MeSH and text words for nutrition assessment and nutrition interventions. Searches were limited to studies on humans, *adult* kidney transplant recipients, single organ transplants and to studies published in English. Unpublished studies were not reviewed.

The literature was systematically searched to locate systematic reviews and meta-analyses, randomised trials and other types of studies using a combination of subject heading and free text searches. The search yield was sorted on the basis of scientific rigor and relevance to the topic area, using the criteria in the table below. The literature search was repeated in week 3 June 2008 using the original search terms. No new relevant evidence was found in this search.

The search strategies and yields for each database are presented in Appendix B.

## **Criteria for considering studies**

**Types of studies:** Experimental, comparative and other observational studies were included in the literature review. Letters and editorials were excluded.

**Participants:** Only studies about adult kidney transplant recipients were included. Recipients of any transplant other than a kidney transplant were excluded, including the exclusion of kidney-pancreas transplant recipients.

**Interventions:** Studies about nutrition-related assessment were included. Studies comparing nutrition assessment methods with one another or with a different type of assessment method were included. Studies about nutrition-related assessment were included. Studies comparing nutrition interventions with one another or with no treatment or another type of treatment were included.

**Outcomes:** Any benefit or harm of the assessments or interventions was of interest.

## **4. Critical appraisal**

A systematic review of the literature was conducted, according to standards set by the National Health and Medical Research Council (NHMRC) (107, 108).

The assessment and data abstraction of each retrieved paper were conducted independently by at least two reviewers: Karen Fry, Project Dietitian, and at least one dietitian member of the Steering Committee: Maria Chan, Aditi Patwardhan or Catherine Ryan. The authors assigned a level of evidence to each paper based on their assessment of risk of bias. Disagreements were resolved by discussion. Included studies are presented in Appendix C.

## **5. Development of evidence statements and recommendations**

The process developed by the NHMRC (109) for synthesising and assessing the body of evidence and formulating recommendations was used. The volume, consistency, clinical impact, generalisability and applicability of the evidence was assessed and graded.

Where it was not possible to produce evidence-based recommendations due to gaps in the evidence, consensus amongst current experts in the field was sought to produce expert opinion-based recommendations. An Expert Panel consisting of 36 health professionals at 19 kidney transplant units across Australia and New Zealand was convened. Over a six-month consultation period, consensus-based recommendations were derived using the Delphi technique in which a series of anonymous self-administered questionnaires were used. This technique has been used widely in health research as it enables a large group of experts to be contacted cheaply without geographical limitations (110-117).

## **Consultation Process**

### **Health Professionals in Australia and New Zealand**

As described above, 163 transplant recipients and 67 clinicians involved in the care of transplant recipients based at 23 hospitals (including the 20 adult kidney transplant units) in Australia and New Zealand were consulted between June and October 2006 to identify the

most clinically important topics for inclusion in the guidelines and to allow clinical questions to be formulated.

In January 2007, following the literature review, an Expert Panel consisting of thirty-six health professionals at nineteen kidney transplant units across Australia and New Zealand was convened. The panel was consulted in order to formulate consensus-based recommendations where evidence-based recommendations were not possible.

The first draft of the guidelines was piloted and evaluated by health professionals based at fourteen sites (kidney transplant units and other hospitals) in Australia and New Zealand, between July and October 2007. The Guideline Development Group discussed the feedback received and appropriate modifications were accordingly made to the guideline document.

## **Consumer consultation**

Kidney transplant recipients have been involved in the development of the guidelines from the outset and have greatly shaped the guideline format and content.

Consumer organisations, including Kidney Health Australia and Transplant Australia, have supported the project, assisting in the initial survey of the 167 transplant recipients between June and October 2006 and by updating members on the development of the guidelines.

Consumer representatives with previous experience in reviewing patient publications provided feedback on the first draft of the guidelines. We are particularly grateful to Evan Eggins (NSW Chair, Consumer Participation Committee, Kidney Health Australia) for his assistance.

## **Implementation and Audit**

It is recommended that the nutritional management of adult kidney transplant recipients is reviewed against these guidelines. Evaluation is necessary to determine whether or not the guidelines have an effect on improving clinical practice.

## **Applying the Guidelines**

This document provides a guide to appropriate practice based on the best information available at the date of compilation. It is assumed that health professionals will also bring to bear their clinical knowledge and judgment in making decisions about the care of individual patients. It may not always be appropriate to apply either specific recommendations or the general messages in this document to each individual or in every circumstance. Users of the guidelines should be aware of the strength of the evidence supporting each recommendation.

The information contained in these guidelines should be conveyed to kidney transplant recipients and their families in an understandable manner, possibly with the use of specifically developed educational support materials.

In applying the guidelines organisational and cost barriers need to be considered. Potential resource implications include the need for additional staff or changes to staff roles. The availability of resources, including time and staff, will impact greatly on whether or not recommendations can be adopted. The information and recommendations contained in this document may assist in lobbying healthcare administrators to make adequate resources available to enable the full implementation of the guidelines.

The guidelines have been disseminated with support materials, including a document which summarises the guidelines and hand-outs for dietitians to use when educating kidney transplant recipients. The guideline document may be viewed by members of the Dietitians Association of Australia (DAA) on the DAA website: [www.daa.asn.au](http://www.daa.asn.au).

The gaps in current knowledge are clearly identified in this document. It is anticipated that clinicians and researchers in the field of post-transplant nutrition will find this information of great value for developing research questions and strengthening justification when writing submissions for funding.

## **External Review Process**

The guidelines have been submitted to the Dietitians Association of Australia for external review and endorsement. Reviewers are not members of the Guideline Development Group and include experts in the renal transplantation as well as methodological experts.

## **Guideline Updates**

These guidelines should be reviewed in 2012 or earlier, should pertinent information become available from studies currently underway, for instance, a multicentre, prospective study of the prevalence, management, and repercussions on the quality of life of anaemia in kidney transplant recipients (the ARES study) and the Folic Acid for Vascular Outcome Reduction in Transplantation (FAVORIT) Trial.

## **Responsibility and Support for the Guidelines**

GMCT funded the development of these guidelines and is responsible for the implementation, review and updating of the guidelines.

For further information please contact Karen Fry (Project Dietitian) at GMCT (Renal) PO Box 6314, North Ryde, NSW 2113 or email: [karen.fry@hnehealth.nsw.gov.au](mailto:karen.fry@hnehealth.nsw.gov.au).

## **Editorial Independence**

The views and interests of the Greater Metropolitan Clinical Taskforce did not in any way influence the final recommendations. No member of the Guideline Development Group had any conflict of interest to declare. There was no external funding for any member of the Guideline Development Group to undertake research, draft the guidelines or attend conferences relating to the guidelines.

## Acknowledgements

The time generously contributed by each member of the Expert Panel, listed below, is greatly appreciated.

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# Guidelines and Evidence

## Features of the guidelines

- The presentation of the guidelines reflects the stages in the nutrition care process: nutrition assessment, nutrition diagnosis; nutrition intervention; and nutrition monitoring and evaluation.
- Guideline 1 addresses nutritional assessment and diagnosis. Guidelines 2-10 address nutritional interventions, monitoring and evaluation for specific post-transplant health concerns. It is acknowledged that there is usually more than one health complication that must be addressed.
- For each guideline, objective(s) and clinical question(s) are presented.
- Evidence statements addressing the clinical question(s) are presented.
- Evidence-based practice recommendations are explicitly linked to clinical questions and are graded based on an assessment of the body of available evidence. See below.
- Where no evidence was found to address a clinical question, this is acknowledged and ungraded practice recommendations, based on expert opinion, are provided.
- All practice recommendations should be reviewed as new evidence becomes available.

## Levels of evidence and recommendation grading

The *National Health and Medical Research Council's* designations of levels of evidence according to the type of research question were used and recommendations were graded based on an assessment of the body of evidence (109). The NHMRC designations of levels of evidence are shown in Table 1.

The overall grade of recommendation reflects the strength of the evidence supporting it. It is based on a summation of the grading of individual components of the body of evidence assessment. Applying evidence in real clinical situations is not usually straightforward and thus the body of evidence supporting a recommendation is rarely entirely one grade for all important components. For example, a body of evidence may contain a large number of studies with a low risk of bias that are consistent but may not be directly applicable to the target population or Australian healthcare context or may not be expected to have a very large clinical impact. Alternatively, a body of evidence may only consist of one or two randomised trials with small sample sizes that have a moderate risk of bias but have a very large clinical impact and are directly applicable to the Australian healthcare context and target population. The grading process using the "Body of Evidence Assessment Matrix" (Table 2) allows for this mixture of components while still reflecting the overall strength of the body of evidence supporting a recommendation.

**Table 1. Designations of levels of evidence according to type of research question (109)**

Level	Intervention	Diagnosis	Prognosis	Aetiology	Screening
I	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies
II	A randomised controlled trial	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among consecutive patients with a defined clinical presentation	A prospective cohort study	A prospective cohort study	A randomised controlled trial
III-1	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among non-consecutive patients with a defined clinical presentation	All or none	All or none	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)
III-2	A comparative study with concurrent controls: <ul style="list-style-type: none"> <li>• Non-randomised, experimental trial</li> <li>• Cohort study</li> <li>• Case-control study</li> <li>• Interrupted time series with a control group</li> </ul>	A comparison with reference standard that does not meet the criteria required for Level II and III-1 evidence	Analysis of prognostic factors amongst untreated control patients in a randomised controlled trial	A retrospective cohort study	A comparative study with concurrent controls: <ul style="list-style-type: none"> <li>• Non-randomised, experimental trial</li> <li>• Cohort study</li> <li>• Case-control study</li> </ul>
III-3	A comparative study without concurrent controls: <ul style="list-style-type: none"> <li>• Historical control study</li> <li>• Two or more single arm study</li> <li>• Interrupted time series without a parallel control group</li> </ul>	Diagnostic case-control study	A retrospective cohort study	A case-control study	A comparative study without concurrent controls: <ul style="list-style-type: none"> <li>• Historical control study</li> <li>• Two or more single arm study</li> </ul>
IV	Case series with either post-test or pre-test/post-test outcomes	Study of diagnostic yield (no reference standard)	Case series, or cohort study of patients at different stages of disease	A cross-sectional study	Case series

**Table 2. Body of evidence assessment matrix (109)**

Component	A	B	C	D
	Excellent	Good	Satisfactory	Poor
<b>Volume of evidence</b>	Several level I or II studies with low risk of bias	One or two level II studies with low risk of bias or a SR/multiple level III studies with low risk of bias	Level III studies with low risk of bias, or level I or II studies with moderate risk of bias	Level IV studies, or level I to III studies with high risk of bias
<b>Consistency</b>	All studies consistent	Most studies consistent and inconsistency may be explained	Some inconsistency reflecting genuine uncertainty around clinical question	Evidence is inconsistent
<b>Clinical impact</b>	Very large	Substantial	Moderate	Slight or restricted
<b>Generalisability</b>	Population/s studied in body of evidence are the same as the target population for the guideline	Population/s studied in the body of evidence are similar to the target population for the guideline	Population/s studied in body of evidence different to target population for guideline but it is clinically sensible to apply this evidence to target population	Population/s studied in body of evidence different to target population and hard to judge whether it is sensible to generalise to target population
<b>Applicability</b>	Directly applicable to Australian/New Zealand healthcare context	Applicable to Australian/New Zealand healthcare context with few caveats	Probably applicable to Australian/New Zealand healthcare context with some caveats	Not applicable to Australian/New Zealand healthcare context

NHMRC grades of recommendation are provided to assist users of these guideline in making clinical judgements and to indicate the strength of the recommendation. While Grade A and B recommendations are generally based on a body of evidence which can be trusted to guide clinical practice, Grade C and D recommendations must be applied carefully to individual clinical and organisational circumstances and should be followed with care. See Table 3.

The grade allocated to a recommendation is based on an assessment of the body of evidence, according to NHMRC guidelines (109).

The five components that were considered in judging the body of evidence were:

- The volume of evidence
- The consistency of the study results
- The potential clinical impact of the proposed recommendation (including the balance of risks and benefits, the relevance of the evidence to the clinical question, the size of the patient population and resource issues)
- The generalisability of the body of evidence to the target population
- The applicability of the body of evidence to the healthcare context in Australia and New Zealand

**A recommendation cannot be graded A or B unless the volume and consistency of evidence components are both graded either A or B.** A standardised form was used to assess the body of evidence for each clinical question requiring a recommendation in this guideline.

**Table 3. Grades of recommendation (109)**

Grade	Description
<b>A</b>	Body of evidence can be trusted to guide practice
<b>B</b>	Body of evidence can be trusted to guide practice in most situations
<b>C</b>	Body of evidence provides some support for recommendation(s) but care should be taken in its application
<b>D</b>	Body of evidence is weak and recommendation must be applied with caution

## General Practice Recommendations

The following practice recommendations are based on current expert opinion in Australia and New Zealand. They are designed to be used in conjunction with the recommendations and practice tips contained in the guidelines which follow.

- All kidney transplant recipients should be referred to a dietitian as soon as practicable after transplantation to ensure that any potential nutritional concerns are identified and managed appropriately.
- A complete nutrition assessment should take place at least monthly for the first 3 months post-transplant, ideally in conjunction with transplant clinic appointments, and annually thereafter, unless more regular consultations are deemed necessary.

The nutrition assessment comprises:

- a. Dietary intake assessment
  - b. Anthropometric assessment
  - c. Biochemical and clinical assessment
  - d. Medication review
- A dietitian should provide all kidney transplant recipients with individualised verbal and written advice for preventing and/or managing potential post-transplant health complications, including excessive weight gain, dyslipidaemia, hypertension, diabetes, and bone disease.
  - An individual's weight, biochemistry, co-morbidities, medications and lifestyle should be taken into consideration in planning dietary advice.
  - Dietary advice should be realistic and practical to ensure compliance.
  - Fluid requirement in the early post-transplant period should be determined by the transplant physician, however, low kilojoule choices should be encouraged.
  - Kidney transplant recipients should be encouraged to do at least 30 minutes of moderate intensity physical activity, such as brisk walking, swimming, cycling or gentle aerobics) on at least five days of the week, in line with general population guidelines.
  - The advice provided by other members of the health care team should be consistent with and supportive of the advice provided by the dietitian.
  - Continued dietetic support should be available to all kidney transplant recipients and arranged by the dietitian as appropriate.

## Guideline 1a – Dietary Intake Assessment

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### Guideline objective:

To ensure that an assessment of the dietary intake of an adult kidney transplant recipient allows their nutritional status to be accurately evaluated.

---

### Clinical questions:

1. When should the dietary intake of adult kidney transplant recipients be assessed?
  2. What specific tools for assessing dietary intake best reflect nutritional status or change in nutritional status in adult kidney transplant recipients?
  3. What are the defining characteristics of dietary intake that describe nutritional status in adult kidney transplant recipients?
- 

### Evidence statements:

1. There are no published studies examining when the dietary intake of adult kidney transplant recipients should be assessed.
  2. There are no published studies examining the accuracy or predictive value of tools used for assessing the dietary intake of adult kidney transplant recipients.
  3. With respect to the defining characteristics of dietary intake that describe nutritional status see the evidence statements for Guidelines 2-10.
- 

### Evidence-based recommendations

**No evidence-based recommendations possible**

## Practice recommendations

- **Dietary intake should be assessed at the time of transplantation.**
- **Dietary intake should be assessed by means of dietary interviews, 3-day food diary or 24-hour recall, as appropriate.**
- **Dietary intake should be assessed as part of a nutritional assessment with access to anthropometric, biochemical and clinical and medication information.**

## Practice tips

### 1. Evaluating dietary intake

The interventions summarised in the *Nutrition Intervention and Monitoring Summary* section (pages 51-52), along with the considerations presented in Guidelines 2-10, should be used in evaluating the nutritional adequacy of the diet and diagnosing potential nutritional problems.

### 2. Lifestyle considerations

As part of the nutritional assessment, it is prudent to determine the current level of physical activity with the goal of maintaining current level or reaching physical activity goals appropriate to the individual.

# Guideline 1b – Anthropometric Assessment

## Guideline objective:

To ensure that the anthropometric measures used in a nutritional assessment accurately reflect nutritional status or change in nutritional status of adult kidney transplant recipients.

## Clinical questions:

1. What specific anthropometric measures best reflect nutritional status or change in nutritional status in adult kidney transplant recipients?
2. What are the defining anthropometric characteristics that describe nutritional status?

## Evidence statements

## Level of Evidence

### 1. Body mass index (BMI) is predictive of health outcomes:

- |        |   |                |
|--------|---|----------------|
| (i)    | Delayed graft function is significantly more likely in kidney transplant recipients with a BMI $\geq 30$ kg/m <sup>2</sup> .  | III-2 (8, 118) |
| (ii)   | A BMI $\geq 30$ kg/m <sup>2</sup> is associated with a higher prevalence of diabetes, hypertension, coronary artery disease and peripheral vascular disease.  | III-2 (8)      |
| (iii)  | Prolonged hospitalisation (>14 days), acute rejection episodes and graft failure are more likely in kidney transplant recipients with a BMI $\geq 35$ kg/m <sup>2</sup> .   | III-2 (118)    |
| (iv)   | Higher cardiovascular death risk in kidney transplant recipients with a BMI < 20kg/m <sup>2</sup> or > 30 kg/m <sup>2</sup> .   | III-2 (118)    |
| (v)    | Higher infectious disease death risk in kidney transplant recipients with a BMI < 22kg/m <sup>2</sup> or > 30 kg/m <sup>2</sup> .   | III-2 (118)    |
| (vi)   | Death with a functioning graft more likely in kidney transplant recipients with a BMI <20 or >34.   | III-2 (118)    |
| (vii)  | Graft loss more likely in kidney transplant recipients with a BMI of < 20kg/m <sup>2</sup> or > 30 kg/m <sup>2</sup> with the most elevated risk observed in the most patients with a BMI>36 kg/m <sup>2</sup> .  | III-2 (118)    |
| (viii) | The risk of chronic allograft nephropathy is significantly increased in patients with a 10% increase in BMI sustained throughout at least 2 years post-transplantation.   | III-2 (10)     |
| (ix)   | Kidney transplant recipients with a BMI <21 kg/m <sup>2</sup> are more likely to have lower serum protein, albumin and haemoglobin, higher serum creatinine levels and experience more frequent and severe co-morbidity conditions compared with those with a BMI 21-25 kg/m <sup>2</sup> . | IV (119)       |

**2. Good method agreement exists between dual energy x-ray absorptiometry (DEXA) and anthropometry (multiple skin-fold measurements) for the estimation of body fat and fat-free mass in kidney transplant recipients.**

IV (120)

**3. Multi-frequency bioelectrical impedance analysis (MF-BIA) is an accurate method of estimating total body water in kidney transplant recipients (compared to the isotope dilution method, considered to be the gold standard). However, in kidney transplant recipients MF-BIA may overestimate percentage body fat.**

IV (120)

## Evidence-based recommendations

- **Body mass index (BMI) should be used to monitor weight changes and the efficacy of nutrition interventions. (*Grade C recommendation*)**

## Practice recommendations

- **As truncal adiposity is correlated to disease risk in the general population, waist circumference should be used in the anthropometric assessment, if possible. (*Expert Opinion*)**

## Practice tips

### 1. Body mass index

According to the World Health Organization classifications, a BMI of 18.5-24.9 kg/m<sup>2</sup> represents normal weight; a BMI of 25-29.9 kg/m<sup>2</sup> represents overweight; and a BMI of >30 kg/m<sup>2</sup> represents obesity (121, 122). Whilst the classification must be viewed as a broad generalisation, it is designed to relate to risk of disease, based on observational and prospective epidemiological studies in various population groups [29-37]. The available evidence suggests that in the kidney transplant population a BMI 21-25 kg/m<sup>2</sup> is associated with the best health outcomes (8-10, 119).

Clinical judgment must be used in interpreting BMI in situations in which it may not be an accurate indicator of total body fat. Examples are the presence of oedema, high muscularity, muscle wasting, or for very short people. The relationship between BMI and body fat content varies somewhat with age, sex, and possibly ethnicity because of differences in factors such as composition of lean tissue and hydration state (121). It is suggested that the healthy weight range for older adults be set at 22.0-27.0 kg/m<sup>2</sup> (123).

### 2. Waist circumference

Waist circumference provides an independent prediction of disease risk over and above that of BMI. In the general population, a high waist circumference with a BMI 25-34.9 kg/m<sup>2</sup> is associated with an increased risk of type 2 diabetes, dyslipidaemia, hypertension and cardiovascular disease. At BMI  $\geq$  35 kg/m<sup>2</sup>, waist circumference has little added predictive power. [41-44]

The National Health and Medical Research Council suggest the following cut-offs: < 90cm for men and < 80cm for women. These are based mainly on evidence of increased risk of death in European populations and it is acknowledged that they may not be appropriate for all age and ethnic groups. [16]

Whilst there was no evidence for the use of waist circumference in the adult kidney population, it was the consensus opinion among experts across Australia and New Zealand that this assessment measure should be used. Monitoring changes in waist circumference over time may be helpful, in addition to measuring BMI, since it can provide an estimate of increased abdominal fat even in the absence of change in BMI.

### **3. Body fat estimations by skin-fold and DEXA**

Whilst there may be a role for DEXA and skin-fold measurements in an anthropometric assessment, neither DEXA nor anthropometry can be considered a gold standard. Furthermore current consensus expert opinion is that these methods are not as simple and useful in a clinical setting as BMI and waist circumference.

If they are to be used, practitioners should be aware that body fat estimations by these methods are based on certain assumptions: that the overall conductivity of the human body is closely related to lean tissue; that fat is anhydrous; and that lean body mass contains a constant proportion of water (73.2%). Since body hydration can vary considerably, estimations of body fat by these methods can be inaccurate. [28] If these methods are employed, care should be taken to ensure that the patient is at their dry weight.

### **4. Multi-frequency bioelectrical impedance analysis (MF-BIA)**

MF-BIA derives fat-free mass from the measured volume of total body water. When compared to the isotope dilution method (considered to be the gold standard) MF-BIA accurately estimated TBW, However, a disturbed water status can significantly reduce the accuracy of predictions of fat free mass and fat mass by MF-BIA. In renal transplant patients, a constant hydration status cannot be assumed. Therefore, MF-BIA may not accurately estimate the actual percentage of body fat. [28]

### **5. Total body nitrogen.**

It is acknowledged that total body nitrogen (TBN), which quantifies body protein content, is the gold standard in assessing the nutritional status of individuals, including those with end-stage kidney disease. [45]. However, because TBN is not widely available and is not easily applied in clinical practice, this nutritional assessment tool has not been included in the practice recommendations above.

# Guideline1c - Biochemical and Clinical Assessment

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## Guideline objective:

To ensure that the biochemical and clinical measures used in a nutritional assessment accurately reflect nutritional status or change in nutritional status of adult kidney transplant recipients.

---

## Clinical questions:

1. What specific biochemical and clinical measures best reflect nutritional status or change in nutritional status in adult kidney transplant recipients?
  2. What are the defining biochemical and clinical characteristics that describe nutritional status?
- 

## Evidence statement

## Level of Evidence

Subjective global assessment (SGA) is useful for identifying malnutrition in kidney transplant recipients.

IV (124)

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## Evidence-based recommendations

- **Subjective Global Assessment (SGA) should be used to assess nutritional status. (Grade D recommendation)**

## Practice recommendations

- The following parameters should be reviewed if possible (*Expert Opinion*):

Parameter	Suggested target
Blood pressure	<130/85 mmHg <125/75 mmHg (with proteinuria >1 g/day) [17]
Fasting glucose HbA1c	4.4-6.7 mmol/L (with diabetes) [18] <7% (with diabetes) [18]
Total cholesterol Low-density lipoprotein-cholesterol Triglycerides High-density lipoprotein-cholesterol	<4.0 mmol/L [19] <2.5 mmol/L [19] <1.5 mmol/L [19] >1.0 mmol/L [19]
Serum potassium Serum phosphate Serum magnesium	Within normal range
Serum creatinine	Monitor change
Haemoglobin Albumin Inflammatory markers	≥12g/dL (females); ≥13g/dL (males) (85) Within normal range Within normal range – note effect of inflammation on albumin, ferritin
Urinary electrolytes Urinary protein	Within normal range
Fluid balance	Check input/output, particularly in early post-transplant period

† Figures and ranges for optimal biochemical and clinical outcomes have been derived from evidence from studies on the general population and/or expert opinion.

## Practice tips

### 1. Screening for diabetes

It is recommended that fasting plasma glucose be used as the screening test in people at risk of developing type 2 diabetes. However a random measurement may be used. The physician will usually perform an oral glucose tolerance test to confirm diabetes if fasting glucose is 5.5-6.9 mmol/l or random glucose is 5.5-11.0 mmol/l. Diabetes is likely if fasting glucose  $\geq 7.0$  mmol/l or random glucose is  $\geq 11.1$  mmol/l. [46]

### 2. Serum lipids

The Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines for managing dyslipidaemias in kidney transplant recipients [47] recommend treatment goals according to type of dyslipidaemia:

Dyslipidaemia	Goal
Total cholesterol $\geq 5.6$ mmol/L	< 5.6 mmol/L
Low density cholesterol $\geq 2.5$ mmol/L	< 2.5 mmol/L

In high risk kidney transplant recipients, with existing CHD, it may be beneficial to lower LDL-C to levels substantially below the current recommended target of <2.5 mmol/L. A target LDL-C of <2.0 mmol/L for these patients is recommended. [19]

### 3. Albumin and inflammatory markers

The presence of acute or chronic inflammation will limit the specificity of serum albumin as a nutritional marker. [48]

### 4. Blood pressure

Guidelines for the general population suggest the following blood pressure treatment goals for the prevention of cardiovascular events in at-risk individuals. [17]

At risk individuals	Goal (mmHg)
Adults $\geq 65$ years (unless there is diabetes and/or renal insufficiency and/or proteinuria $\geq 0.25$ g/day)	< 140/90
Adults < 65 years and/or Adults with diabetes and/or Adults with renal insufficiency and/or Adults with proteinuria 0.25 – 1.0 g/day	< 130/85
Adults with proteinuria >1 g/day (in people with and without diabetes)	< 125/75

### 5. SGA

See Appendix D for an example of an SGA scoring sheet.

## Guideline 1d - Medication Review

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### Guideline objective:

To ensure that a medication review assists in the evaluation of the nutritional status or change in nutritional status of adult kidney transplant recipients.

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### Clinical questions:

How do commonly prescribed medications impact on the nutritional status of adult kidney transplant recipients?

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### Evidence statements:

There have been no studies on the effect of the medications commonly-prescribed to kidney transplant recipients on nutritional status.

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### Evidence-based recommendations

**No evidence-based recommendations possible.**

### Practice recommendations

- **There are a number of known side effects of the commonly-prescribed anti-rejection medications which may impact on a transplant recipient's nutritional status, such as nausea, diarrhoea, gastrointestinal discomfort and anorexia. (See tables below)**
- **If it is suspected that nutrient intake and absorption are being adversely affected by side effects such as nausea, diarrhoea and/or vomiting, a symptom diary may help to identify appropriate action. (*Expert Opinion*)**
- **The types of strategies employed in nutritional management will be affected by the types of side-effects experienced, for instance, hyperglycaemia, hypertension and dyslipidaemia.**
- **The potential nutritional side effects and interactions of any prescription or non-prescription medications, including alternative health products and supplements, should be considered in a medication review. (*Expert Opinion*)**

## Practice tips

1. Grapefruit, possibly due to its furanocoumarin content (125), alters the activity of cytochrome P450 3A4 (CYP3A4), the key enzyme involved in the metabolism of many of the medications prescribed to kidney transplant recipients, including cyclosporine, tacrolimus, calcium channel blockers and statins (126). Kidney transplant recipients should be advised against consuming grapefruit in any form.

### 2. Therapeutic Advice and Information Service (TAIS) (Australia)

The National Prescribing Service (TAIS) is a national telephone service for health professionals in Australia, which provides immediate access to independent drug and therapeutics information including interactions with food. It is available Monday to Friday (except national public holidays) (9am-7pm Australian Eastern Standard Time)

Telephone: 1300 138 677 (local call charge)

Email: [tais@nps.org.au](mailto:tais@nps.org.au)

Mail: Austin Health Drug Information, Pharmacy Department, Austin Hospital,  
145 Studley Road, Heidelberg VIC 3084

### 3. Medsafe (New Zealand)

Medsafe is the New Zealand Medicines and Medical Devices Safety Authority, responsible for the regulation of therapeutic products in New Zealand. Through the Medsafe website, health professionals may access data sheets for all prescription and restriction (pharmacist only) medicines, which the pharmaceutical companies are required by law to prepare.

Website: [www.medsafe.govt.nz](http://www.medsafe.govt.nz)

### 4. Recommended reference texts

Aaronson JK, Dukes MNG. Meyler's side effects of drugs: the international encyclopedia of adverse drug reactions and interactions. Oxford: Elsevier; 2006.

Cervelli, MJ. The Renal Drug Reference Guide. Adelaide: MJC Pharma Pty Ltd; 2007.

**Summary of potential side effects of immunosuppressive medications with implications for nutritional status and nutrition therapy**

<b>Medication</b> <i>Generic name (Product name)</i>	<b>Side effects</b>
Azathioprine (Imuran®)	Nausea, vomiting, gastrointestinal discomfort, anorexia (127), Anaemia (96, 97)
Cyclosporin	Hyperkalaemia (128) Hypomagnesemia (129) Gastrointestinal side-effects (130) Hypertension (131) Hyperlipidaemia (132) Hyperuricaemia (133, 134) Anaemia (135, 136)
Mycophenolate mofetil (Cellcept®)	Nausea, vomiting, diarrhoea, gastrointestinal discomfort (137, 138), Anaemia (96, 97)
Prednisone	Increased catabolism (36) Hyperlipidaemia (139, 140) Hyperglycaemia (141-143) Hyperphagia (144) Increased protein requirements (38, 40)
Sirolimus (Rapamune®)	Hyperlipidaemia (145) Anaemia (96, 97)
Tacrolimus (Prograf®)	Hyperkalaemia (135, 136) Gastrointestinal side-effects (diarrhoea, nausea) (135, 136) Hyperglycaemia (135, 136, 146) Hypertension (135, 136) Hyperlipidaemia (147) Anaemia (135, 136)

## Guideline 2 - Dietary Protein Requirements

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### Guideline objectives:

To ensure that appropriate nutrition interventions are used to prevent the loss of lean body mass and achieve neutral or positive nitrogen balance in kidney transplant recipients; and to reduce the risk of chronic kidney failure in stable kidney transplant recipients.

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### Clinical questions:

1. How much dietary protein is required to maintain lean body mass and achieve neutral or positive nitrogen balance in kidney transplant recipients?
  2. What level of protein intake will lower the risk of chronic kidney failure in stable kidney transplant recipients?
- 

### Evidence statements

### Level of Evidence

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1. A diet providing ~30% kJ as protein and at least 1.4g protein/kg body weight in the first four weeks after transplant may reverse negative nitrogen balance and lead to increased muscle mass in kidney transplant recipients. **III-1 (148)**

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2. An intake of 1.3 +/- 0.06g protein/kg body weight and 138+/-12kJ/kg body weight may achieve neutral nitrogen balance in kidney transplant recipients requiring haemodialysis immediately after their transplant due to acute tubular necrosis. **IV (38)**

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3. A low protein intake (0.55g/kg) appears to improve glomerular permselectivity in the short-term, but may be associated with negative nitrogen balance. **III-1 (149)**

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4. In kidney transplant recipients with chronic rejection, a moderated dietary protein intake of 0.73 +/- 0.11g/kg body weight may safely stabilise glomerular filtration rate and slow the progression to kidney failure in kidney transplant recipients with chronic rejection. **IV (150)**

---

5. There is no evidence regarding the long-term protein requirements of stable kidney transplant recipients.

---

## Evidence-based recommendations

- **In the first four weeks after transplantation, kidney transplant recipients should be advised to eat a diet providing 1.3g protein/kg body weight to reverse negative nitrogen balance and maintain lean body mass. (*Grade D recommendation*)**
- **Kidney transplant recipients with chronic rejection should restrict dietary protein to 0.73 +/-0.11g/kg body weight. (*Grade D recommendation*)**

## Practice recommendations

- **Stable kidney transplant recipients on a maintenance immunosuppression regimen, irrespective of renal function, should not exceed the recommended daily intake of protein for the general population of 0.75g protein/kg body weight for females and 0.84g protein/kg body weight for males. (*Expert Opinion*)**
- **During periods when treatment with high dose prednisone is required, for example during acute rejection, protein requirement may be elevated to a level similar to that of the early post-transplant period. (*Expert Opinion*)**
- **Regular review by a dietitian is desirable in the long term to ensure that protein requirements are neither exceeded (particularly in the presence of chronic allograft nephropathy) nor inadequate (particularly in periods of acute rejection when prednisone dose may be increased). (*Expert Opinion*)**

## Practice tips

- There has been very little research investigating the protein requirements post-kidney transplantation. However, the study by Cogan et al (38) which examining nitrogen balance in kidney transplant recipients requiring dialysis immediately after transplant confirms that prednisone increases protein requirements. To correct negative nitrogen balance, patients required 1.3+/-0.06g protein/kg/day.
- The recommendation that 1.4g protein/kg body weight be consumed in the early post-transplant period is based on a single study by Whittier et al (148), in which patients achieved positive nitrogen balance (gaining lean body mass) when they consumed at least 1.4g protein/kg/day. However, it should be noted that patients in this study received 1mg prednisone/kg/day for the first two weeks post-transplant, followed by a progressive reduction of prednisone to 0.5 to 0.7mg/kg/day over the second two-week period. The prednisone dosing regimen used in this study may differ from current practice at transplant units in Australia and New Zealand.
- If the kidney transplant recipient is eating well, protein requirements are usually easily met by the diet. Protein supplements are not generally required.

## Guideline 3 - Management of Overweight and Obesity

### Guideline objectives:

To ensure that appropriate nutrition interventions are used to prevent the excessive weight gain after kidney transplantation; to treat overweight and obesity in adult kidney transplant recipients; and to prevent the adverse health outcomes associated with overweight and obesity.

### Clinical questions:

1. What are the appropriate nutrition interventions to prevent excessive weight gain after kidney transplantation?
2. What are the appropriate nutrition interventions to reduce body weight in overweight or obese adult kidney transplant recipients?
3. What are the appropriate nutrition interventions to reduce the adverse health outcomes associated with overweight and obesity in adult kidney transplant recipients?

### Evidence statements

### Level of Evidence

- | Evidence statements   | Level of Evidence |
|---|-------------------|
| 1. Early intervention with regular follow-up is effective in preventing excessive weight gain in kidney transplant recipients.                    | III-3 (151)       |
| 2. Regular dietetic intervention among overweight and obese kidney transplant recipients can lead to significant dietary changes and weight loss. | IV (152)          |

### Evidence-based recommendations

#### *To prevent excessive weight gain:*

- **Kidney transplant recipients should be referred to a dietitian for written and verbal advice for preventing weight gain, as soon as practicable after transplantation. (Grade C recommendation)**
- **Regular follow-up should be arranged to prevent excessive weight gain. (Grade C recommendation)**

#### *To reduce body weight in overweight or obese kidney transplant recipients:*

- **A diet that is individually planned with a moderate energy restriction of about 30% of energy expenditure should be applied. (Grade D recommendation)**
- **Overweight and obese kidney transplant recipients are more likely to make dietary changes and lose weight with monthly follow-up with a dietitian. (Grade D recommendation)**

## Practice recommendations

### ***To prevent excessive weight gain:***

- **Advice should be individualised and include meal plans, exercise plans and specific goals. *(Expert Opinion)***
- **All members of the health care team should monitor the weight of individual transplant recipients and arrange review by a dietitian if weight gain is a problem. *(Expert Opinion)***

### ***To reduce body weight in overweight or obese kidney transplant recipients:***

- **The initial goal of weight loss therapy should be to reduce body weight by approximately 10% from baseline, with weight loss of 1-2 kg per month. With success, further weight loss can be attempted if indicated through further assessment. *(Expert Opinion)***
- **The dietitian should arrange regular follow-up for the overweight kidney transplant recipient as appropriate until desired weight loss is achieved. *(Expert Opinion)***
- **Referral to community-based weight management programmes may be appropriate for some individuals – clinical judgement should be used. *(Expert Opinion)***

## Practice tips

- In the general population, weight loss of 10% from baseline has significant favourable effects on health in overweight individuals (121, 153).
- In the general population, a program of combined diet and exercise is more effective in maintaining weight loss than either diet alone or exercise alone. (121, 153)
- Self-monitoring tools may be beneficial, for example, pedometers and exercise diaries.

## Guideline 4 –Management of Dyslipidaemia

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### Guideline objective:

To ensure that appropriate nutrition interventions are used to prevent and manage dyslipidaemia in adult kidney transplant recipients.

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### Clinical question:

What are the appropriate nutrition interventions to prevent or manage dyslipidaemia in adult kidney transplant recipients?

---

### Evidence statements

### Level of Evidence

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- |  |             |
|--|-------------|
| 1. A “modified Mediterranean diet’ which includes low glycaemic index, high fibre carbohydrates and sources rich in vitamin E and monounsaturated fat (providing 47% energy from carbohydrates, 38% from fat and 15% from protein) lowers serum total cholesterol and triglycerides in adult kidney transplant recipients. | III-1 (154) |
| 2. A diet containing a high proportion of wholegrain carbohydrates and monounsaturated fats lowers total cholesterol, LDL-cholesterol, triglycerides and the LDL-C: HDL-C ratio in adult kidney transplant recipients.   | IV (155)    |
| 3. A diet providing less than 35% total kilojoules from fat, with a polyunsaturated to saturated fat ratio > 1, may normalise total cholesterol, triglycerides and high-density lipoprotein-cholesterol in kidney transplant recipients.   | IV (156)    |
| 4. Weight loss is associated with a fall in total cholesterol in kidney transplant recipients.   | IV (152)    |
-

## Evidence-based recommendations

- **A diet rich in wholegrains, low glycaemic index and high fibre carbohydrates as well as rich sources of vitamin E and monounsaturated fat should be recommended to adult kidney transplant recipients with elevated serum total cholesterol, LDL-cholesterol and triglycerides. (*Grade D recommendation*)**
- **Weight reduction in overweight or obese kidney transplant recipients should be encouraged and supported. (*Grade D recommendation*)**

## Practice recommendations

- **Kidney transplant recipients with dyslipidaemia should be advised to eat a diet which is in line with the latest lipid management guidelines for the general population (*Expert Opinion*):**

### **a) Carbohydrate**

Carbohydrate should be consumed predominantly in the form of wholegrains and foods with a low energy density and/or low glycaemic index, aiming for a daily fibre intake of 25g for females and 30g for males. The inclusion of the soluble fibre beta-glucan should be encouraged as it has been shown to lower LDL-cholesterol in non-transplant populations. (157-160)

### **b) Fat**

Total fat should contribute 30-35% of total energy intake.

Saturated and *trans* fatty acids together should contribute no more than 8% of total energy intake.

n-6 polyunsaturated fat should contribute 8-10% of total energy

Monounsaturated fat may contribute up to 20% of total energy intake.

n-3 polyunsaturated fat should be included in the diet as both plant and marine sources. (159, 161, 162)

### **c) Plant sterols and stanols**

Include plant foods which are naturally rich in phytosterols as well as 2-3g phytosterol-enriched food products (such as margarine, breakfast cereal, low fat yoghurt or milk enriched with phytosterols. (163, 164)

- **Alcohol should be limited to two standard drinks (males) or one standard drink (females) per day, with one to two alcohol-free days per week. (*Expert Opinion*)**

## Practice tips

- The Kidney Disease Outcomes Quality Initiative (K/DOQI) has produced clinical practice guidelines for the management of dyslipidaemia in kidney transplant recipients (165). The key guideline statements are supported mainly by data from studies in the general population: when evidence for treatment efficacy was found to be strong in the general population (65, 159, 162, 166, 167), it was extrapolated to kidney transplant patients.
- Other lifestyle interventions that are recommended for improving lipid profiles include at least 30 min of moderate-intensity physical activity on most, and preferably all, days of the week, reducing weight and avoidance of smoking. Lifestyle management may require ongoing support to be sustainable. (159)
- The recommendation to limit alcohol consumption is based on guidelines for the general population for reducing the risk of cancer and cardiovascular disease. (168-170)
- Australian regulations allow a minimum of 0.8 g and a maximum of 1.0 g phytosterols per serve of food, thus 2 or 3 serves of phytosterol-fortified foods should be recommended. (163, 164)

# Guideline 5 - Management of Hypertension

## Guideline objective:

To ensure that appropriate nutrition interventions are used to prevent and manage hypertension in adult kidney transplant recipients.

## Clinical question:

What are the appropriate nutrition interventions to prevent or manage hypertension in adult kidney transplant recipients?

## Evidence statements

## Level of Evidence

- |  |             |
|--|-------------|
| 1. A dietary sodium restriction of 80-100 mmol/day, in combination with antihypertensive medication may be an efficient means of lowering blood pressure in hypertensive kidney transplant recipients. | III-1 (171) |
| 2. A sodium restriction may be more likely to lower blood pressure in hypertensive kidney transplant recipients treated with cyclosporin than in those treated with azathioprine.                      | III-2 (172) |

## Evidence-based recommendations

- **Hypertensive kidney transplant recipients should be advised to restrict sodium intake to 80-100mmol/day. (*Grade C recommendation*)**

## Practice recommendations

- **Encourage and support weight reduction in overweight or obese kidney transplant recipients. (*Expert Opinion*)**
- **Alcohol should be limited to two standard drinks (males) or one standard drink (females) per day, with one to two alcohol-free days per week. (*Expert Opinion*)**
- **Kidney transplant recipients should be encouraged to do at least 30 minutes of moderate intensity physical activity on at least five days per week. (*Expert Opinion*)**
- **Lowering sodium intake to 65-70 mmol per day may cause a greater lowering of blood pressure. (*Expert opinion*)**

## Practice tips

- The recommendation to limit sodium to 80-100 mmol/day is in line with current guidelines for the general population (157). However, clinicians should emphasise adequate fluid intake over sodium restriction in the immediate post-transplant period.
- The practice recommendations above are in line with guidelines for hypertension management in the general population. In the general population, regular aerobic activity and weight reduction by as little as 5 kg reduces blood pressure in most people who are greater than 10% above their ideal body weight. (173)
- The recommendation to limit alcohol consumption is based on guidelines for the general population for reducing the risk of cancer and cardiovascular disease. (168-170)
- The recommendation to lower sodium intake further to 65-70 mmol/day is in line with the Suggested Dietary Target for chronic disease prevention set by the National Health and Medical Research Council and the New Zealand Ministry for Health (174), and recently adopted by the National Heart Foundation of Australia (175).

## Guideline 6 - Management of Diabetes Mellitus

### Guideline objective:

To ensure that appropriate nutrition interventions are used to prevent and manage diabetes mellitus in adult kidney transplant recipients.

### Clinical questions:

1. What are the appropriate nutrition interventions to prevent diabetes mellitus post-kidney transplantation?
2. What are the appropriate nutrition interventions to improve blood glucose control, lower serum lipids and reduce the requirement for hypoglycaemic agents in adult kidney transplantation with diabetes?

### Evidence statements

### Level of Evidence

1. Diabetes is strongly associated with increased body weight post-transplantation.

II (71)

2. There are no published studies examining the efficacy of nutritional interventions for the prevention and management of diabetes mellitus in adult kidney transplant recipients.

### Evidence-based recommendations

- **Minimise post-transplant weight gain (*Grade C recommendation*)**

### Practice recommendations

- **Dietary advice to all adult kidney transplant recipients should reflect current recommendations to reduce the risk of and manage type 2 diabetes in the general population. (*Expert Opinion*)**

## Practice tips

- To reduce the risk of type 2 diabetes, in line with guidelines for the general population (176), a diet with the following characteristics should be recommended:
  - <30% total energy as fat and <10% energy as total saturated fat.
  - Low energy density, containing a wide range of carbohydrate foods rich in dietary fibre and of low glycaemic index (cereals, vegetables, legumes and fruits).
- In the general population, weight loss improves lipid levels in individuals with diabetes and body weight is readily lost during active supervised treatment. (Level II evidence) (176)
- To manage type 2 diabetes, in line with guidelines for the general population, the focus of diet therapy should be the prevention of macrovascular disease by controlling blood pressure and managing dyslipidaemia. (176)
- Weight loss in overweight and obese individuals should be encouraged to both prevent and manage type 2 diabetes. (176)

# Guideline 7 - Management of Bone Disease

---

## Guideline objective:

To ensure that appropriate nutrition interventions are used to minimise bone mineral density loss and reduce the risk of fractures among adult kidney transplant recipients.

---

## Clinical question:

What are the appropriate nutrition interventions to minimise bone mineral density loss and the risk of fractures in adult kidney transplant recipients?

---

## Evidence statements

## Level of Evidence

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<b>1. Treatment with vitamin D (or analogue) compared to placebo has a favourable effect on bone mineral density (BMD) at the lumbar spine and femoral neck.<sup>∞</sup></b>	<b>I (177)</b>
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<b>2. Treatment with vitamin D (or analogue) compared to placebo is <i>not</i> associated with hypercalcaemia or increased plasma creatinine level.</b>	<b>II (178)</b>
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<b>3. Treatment with vitamin D (or analogue) <i>and</i> calcium may have a favourable effect on percentage change in bone mineral density at the lumbar spine and femoral neck.<sup>†</sup></b>	<b>I (177)</b>
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<b>4. Treatment with vitamin D (0.5ug calcitriol alternate days) <i>and</i> calcium (1.5g/d calcium lactogluconate) does <i>not</i> increase the risk of hypercalcaemia nor increase plasma creatinine level compared with treatment with calcium alone.</b>	<b>II (179)</b>
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<b>5. Treatment with vitamin D or analogue <i>and</i> calcium compared to placebo is <i>not</i> associated with a statistically significant difference in risk of fracture at any site, acute graft rejection, presence of low bone turnover on bone histomorphometry, gastro-oesophageal disorder or graft loss or increased plasma creatinine level.<sup>‡</sup></b>	<b>I (177)</b>
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<sup>∞</sup> This is based on a meta-analysis of two randomised controlled trials, 46 patients. Both trials compared treatment with oral calcitriol (0.5ug/d) with no treatment. (180, 181)

<sup>†</sup> This is based on a meta-analysis of two randomised controlled trials, one comparing treatment with 1000mg calcium lactogluconate and 0.25ug 1-alpha-hydroxyvitamin D with no treatment, over a six month period (83), the other comparing treatment with 3000mg calcium carbonate and 40ug 25-hydroxyvitamin D3 with no treatment, over a 12 month period (182). There was a significant difference between treatment and placebo groups favouring active treatment.

<sup>‡</sup> Note: The applicability of these findings is reduced because the reporting of each outcome was limited to one or two trials in the meta-analysis. (177)

## Evidence-based recommendations

- **Kidney transplant recipients should be advised to take a vitamin D (or analogue) supplement at a dose of at least 0.25ug daily. (*Grade B recommendation*)**

## Practice recommendations

- **The treating physician should determine the dose of vitamin D and the necessity of any other treatments for minimising bone mineral density loss, on the basis of available evidence. (*Expert Opinion*)**
- **A diet containing adequate calcium-rich foods to meet the recommended dietary intake for calcium of 1000mg/day (1300mg/day post-menopause) should be encouraged. (*Expert Opinion*)**
- **If the diet does not provide adequate calcium, a calcium supplement should be recommended. (*Expert Opinion*)**

## Practice tips

- Whilst randomised controlled trials have shown that no individual intervention (bisphosphonate, vitamin D sterol or calcitonin) reduces fracture risk after kidney transplantation, the meta-analysis of all available such trials (24 trials, 1299 patients) combined shows that any intervention (bisphosphonate, vitamin D sterol, or calcitonin) for bone disease in kidney transplant recipients does reduce the risk of fracture in this population. Furthermore, these agents also provide a significant improvement in bone mineral density when given after transplantation, although the clinical significance of this is uncertain due to the lack of validation in bone densitometry in chronic kidney disease. (177)
- Two randomised controlled trials (46 patients) have shown that bisphosphonates have greater efficacy to preserve BMD at the lumbar spine and femoral neck than vitamin D sterols. One trial compared treatment with either oral alendronate 10mg/d or treatment with calcitriol 0.5 ug/d with no treatment over 12 months. All groups were treated with elemental calcium 1,000mg/d. (180) The other trial compared treatment with parenteral pamidronate (30 mg every 4 weeks) or treatment with oral calcitriol 0.5ug/d compared with no treatment. All groups took 500mg/d elemental calcium daily. (181)
- Compared with no treatment, treatment with bisphosphonate improves BMD at the femoral neck (meta-analysis of four trials, 149 patients) and at the lumbar spine

favouring treatment with bisphosphonates (meta-analysis outcome of two trials, 131 patients). (177)

- Based on osteoporosis-related research papers and position papers produced by their Medical and Scientific Advisory Committee, *Osteoporosis Australia (OA)* (183) recommend the following lifestyle measures to reduce the risk of fractures:
  - Having a balanced diet rich in calcium and vitamin D.
    - For most people, three serves of dairy foods daily will provide enough calcium
    - Vitamin D to help the body absorb calcium. Vitamin D is in small amounts in foods such as dairy products fortified with vitamin D, egg yolks, saltwater fish and margarine. The best source of vitamin D is from safe sunlight exposure.
  - Weight-bearing, high impact and strengthening exercises (such as walking, tennis, dancing and weight training)
  - Having a bone density test, if appropriate
  - Not smoking
  - Drinking less alcohol

For more information and fact sheets, see [www.osteoporosis.org.au](http://www.osteoporosis.org.au).

- The *Royal College of Physicians of London* (184) recommends the following lifestyle measures to reduce bone loss and fracture risk in glucocorticoid-induced osteoporosis:
  - Adequate levels of dietary calcium intake
  - Good nutrition and normal body weight
  - Avoidance of smoking and alcohol abuse
  - Physical activity, within the limits imposed by the underlying disease

# Guideline 8 - Management of Hypophosphataemia

## Guideline objective:

To ensure that appropriate nutrition interventions are used to correct hypophosphataemia in adult kidney transplant recipients.

## Clinical question:

What are the appropriate nutritional interventions to correct hypophosphataemia in adult kidney transplant recipients?

## Evidence statements

## Level of Evidence

- |   |            |
|---|------------|
| 1. Oral phosphate supplementation in the first 5 weeks post-transplant with 100mg neutral phosphate salt may correct hypophosphataemia and appears to have no adverse effect on serum calcium or parathyroid hormone concentrations.                                | III-1 (26) |
| 2. When administered in the late post-transplant period (over 7 months) to kidney transplant recipients with stable graft function, oral phosphate supplementation may exacerbate hyperparathyroidism and may lead to a decrease in 1,25(OH) <sub>2</sub> D levels. | IV (185)   |

## Evidence-based recommendations

- **Supplementation should commence as soon as possible after transplantation to correct hypophosphataemia. (*Grade D recommendation*)**
- **Physicians should be aware that in the late post-transplant period phosphate supplementation has the potential to worsen hyperparathyroidism and may mask phosphorus deficiency. (*Grade D recommendation*)**

## Practice recommendations

- **The treating physician should determine the dose on the basis of serum phosphate concentrations. (*Expert Opinion*)**
- **Kidney transplant recipients should be advised to consume phosphate-rich foods as early as possible after transplantation once good graft function is achieved. (*Expert Opinion*)**
- **Supplementation should commence if hypophosphataemia persists even if dietary phosphate intake appears to be adequate. (*Expert Opinion*)**

## Practice tips

- Whilst to date there have been no studies examining the effect of dietary phosphate intake on hypophosphataemia in kidney transplant recipients, the consensus among experts in Australia and New Zealand is that the intake of phosphate-rich foods should be encouraged as early as possible.
- Well-designed studies on phosphate supplementation after kidney transplantation are required to guide starting point, dosage, side-effect profile or likely response rate. Furthermore, prospective, controlled studies are required to answer whether or not particular increased dietary phosphate intake is effective in preventing or treating hypophosphataemia in adult kidney transplant recipients.

# Guideline 9 - Management of Anaemia

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## Guideline objective:

To ensure that appropriate nutrition interventions are used to prevent or manage anaemia in adult kidney transplant recipients.

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## Clinical question:

What are the appropriate nutritional interventions to prevent or manage anaemia in adult kidney transplant recipients?

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## Evidence statements

## Level of Evidence

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There are no published studies of satisfactory quality examining the efficacy of specific dietary interventions in the management of anaemia in kidney transplant recipients.

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## Evidence-based recommendations

**No evidence-based recommendations possible**

## Practice recommendations

- **All adult kidney transplant recipients should be regularly screened for anaemia. (*Expert Opinion*)**
- **Causes of anaemia, including deficiencies in iron, folate and vitamin B12, should be should be carefully evaluated. (*Expert Opinion*)**
- **A dietitian should be consulted for the management of anaemia if dietary deficiencies are shown to be the cause. (*Expert Opinion*)**
- **Diet may be used in conjunction with pharmacological doses of nutrients to correct anaemia. (*Expert Opinion*)**

## Practice tips

- There is a paucity of published information on the topic of treating post-transplant anaemia and treatment goals but current opinion seems to favour treating persistent anaemia to achieve targets similar to those recommended for patients with chronic kidney disease.
- Ferritin, being an acute phase reactant, does not correlate well with serum iron or haematocrit in adult kidney transplant recipients. (Level II evidence) (94)
- To improve accuracy in measuring iron deficiency in this population, % transferrin saturated with iron and % hypochromic red blood cells (currently the best available marker to identify functional iron deficiency) should be assessed. This is in line with the European Best Practice Guidelines. (186)
- Whilst there are no studies specifically examining the short- or long-term effects of diet or dietary supplements in the treatment of anaemia, one study suggests that oral ferrous sulphate can be safely administered together with the mycophenolate mofetil, having no effect on systemic mycophenolate exposure in stable adult kidney graft recipients. (Level II evidence) (187)

# Guideline 10 - Food Safety

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## Guideline objective:

To ensure that adult kidney transplant recipients are given appropriate food safety advice.

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## Clinical question:

What food safety measures should be recommended to adult kidney transplant recipients?

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## Evidence statements

## Level of Evidence

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1. There is no published data on the efficacy of any food safety measures in reducing the risk of food-borne illness in adult kidney transplant recipients.

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2. There is no evidence that a restricted, low bacteria diet is effective in reducing the incidence of listeria and other food-borne illness in adult kidney transplant recipients.

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## Evidence-based recommendations

**No evidence-based recommendations possible**

## Practice recommendations

- **A consultation with a dietitian is important to identify the most important food safety issues relevant to each individual patient and ensure that dietary requirements are met whilst food safety precautions are followed. (*Expert Opinion*)**
- **It is prudent to provide general food safety advice to kidney transplant recipients as per the food safety guidelines produced by Food Standards Australia New Zealand (188). (*Expert Opinion*)**
- **The patient should understand that, during the early post-transplant period and in periods of acute illness, the likelihood of food-borne infection is high due to a greatly suppressed immune system. (*Expert Opinion*)**

# Guideline Summary

## Nutrition Assessment and Diagnosis

The following table summarises the recommendations contained in this document pertaining to nutrition assessment and diagnosis. The grade of each recommendation is indicated unless the recommendation is based on expert opinion.

Nutrition assessment measures	Nutrition diagnosis: Targets for optimal nutritional status	Grade
<b>Dietary intake</b>	Dietary intake in line with recommendations summarised in <b><i>Nutrition Intervention and Monitoring</i></b> , below.	See below
<ul style="list-style-type: none"> <li>- Diet history</li> <li>- Food diary</li> <li>- 24 hour recall</li> </ul>		
<b>Anthropometry</b>		
<ul style="list-style-type: none"> <li>- Body mass index</li> <li>- Waist circumference</li> </ul>	21-25 m <sup>2</sup> /kg body weight ≤ 90cm males; ≤ 80cm females	C
<b>Biochemical and clinical measures</b>		
<ul style="list-style-type: none"> <li>- Subjective global assessment</li> <li>- Blood pressure</li> </ul>	A (No sign of malnutrition) <130/85 mmHg <125/75 mmHg (with proteinuria >1 g/day)	D
<ul style="list-style-type: none"> <li>- Fasting plasma glucose</li> <li>- HbA1c</li> </ul>		4.4-6.7 mmol/L (with diabetes) <7% (with diabetes)
<ul style="list-style-type: none"> <li>- Total cholesterol</li> <li>- LDL-cholesterol</li> </ul>	<4.0 mmol/L <2.5 mmol/L <2.0 mmol/L (with coronary heart disease)	-
<ul style="list-style-type: none"> <li>- HDL-cholesterol</li> <li>- Triglycerides</li> </ul>		>1.0 mmol/L <1.5 mmol/L
<ul style="list-style-type: none"> <li>- Serum electrolytes</li> <li>- Serum creatinine</li> <li>- Urinary electrolytes</li> </ul>	Within normal range for unit Monitor change Within normal range for unit	-
<ul style="list-style-type: none"> <li>- Haemoglobin</li> <li>- Serum Albumin</li> <li>- Inflammatory markers</li> </ul>	Within normal range for unit Within normal range for unit Note that these markers will affect serum albumin level	-
<ul style="list-style-type: none"> <li>- Fluid balance</li> </ul>	Monitor input and output, particularly early post-transplant	-
<b>Medication review</b>		
<ul style="list-style-type: none"> <li>- Drug-nutrient interactions</li> <li>- Symptom/medication/food diary</li> </ul>	Optimal nutritional intake to counter drug-nutrient interactions Advise against grapefruit consumption	-

## Nutrition Intervention and Monitoring

The following table summarises the recommendations contained in this document pertaining to nutrition interventions and monitoring. The grade of each recommendation is indicated unless the recommendation is based on expert opinion.

Nutrition Interventions	Outcomes to be monitored	Grade
<b>Energy</b>		
Ideal energy intake for age, gender, weight, physical activity	Healthy weight maintained	-
If weight loss is required apply an appropriate energy deficit	Appropriate weight loss	-
	Neutral or positive nitrogen balance	D
<b>Protein</b>		
In the early post-transplant period: 1.3-1.5g/kg/day	Progression to kidney failure slowed	-
With the presence of chronic rejection: 0.7-0.8g/kg/day	Neutral or positive nitrogen balance	D
In patients with stable kidney function: 0.84g/kg/day (males), 0.75g/kg/day (females)		
<b>Fat</b>		
Of total energy intake:		
- total fat should comprise: 30-35%;		-
- saturated and <i>trans</i> fatty acids (FA) total: ≤8%;		
- n-6 polyunsaturated FA: 8-10%;		
- marine sources of n-3 FA eaten twice/week	Prevention/management of dyslipidaemia	
- plant sources of n-3 polyunsaturated FA: 2g/day		
- monounsaturated fatty acids: up to 20%		
<b>Carbohydrate</b>		
Carbohydrate should be consumed predominantly in the form of wholegrains and foods with a low energy density and/or low glycaemic index	Prevention/management of dyslipidaemia and diabetes	-
Daily fibre: 25g (females); 30g (males)		
Include sources of soluble fibre		D
<b>Sodium</b>		
Limit dietary sodium intake to 80-100mmol/day	Management of hypertension	-
<b>Potassium</b>		
No restriction required unless serum levels consistently high	Maintain serum potassium in normal range	-
<b>Magnesium</b>		
Recommended dietary intake for life stage and gender based on Nutrient Reference Values for Australia and New Zealand (157)	Maintain serum magnesium in normal range	-
<b>Phosphate</b>		
Encourage phosphate-rich foods as early as possible after good graft function is achieved	Management of hypophosphatemia	

**(Nutrition Intervention and Monitoring Summary continued)**

**Calcium and vitamin D**

Ensure adequate dietary calcium intake (1000mg/day;1300mg/day post-menopause) and adequate vitamin D intake

If intake inadequate, discuss with treating physician supplementation/ medications to preserve bone mineral density

**Iron, folate, vitamin B12**

Ensure adequate dietary intake of iron, folate and vitamin B12

Possible dietary contributors to post-transplant anaemia should be excluded or addressed

**Fluid**

Ensure appropriate fluid intake as dictated by fluid balance status, in consultation with physician (most important in early post-transplant period)

Alcohol should be limited to 20g/day (males), 10g/day (females) with two alcohol-free days per week

Fluid balance achieved

Management of dyslipidaemia, hypertension and weight

**Food safety**

Food safety precautions in line with guidelines produced by *Food Standards Australia New Zealand* should be discussed

Prevention of food-borne infection

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# Appendices

## Appendix A

### **Key post- transplant health concerns: Results of a survey of kidney transplant recipients and health professionals in Australia and New Zealand**

A survey was conducted between June and August 2006 to determine which post-transplant health issues are of greatest significance to kidney transplant recipients and to the health professionals who care for them.

#### ***The questionnaire***

Data was collected by means of self-completed questionnaires. There were two questionnaires: the first designed for completion by kidney transplant recipients; the second for completion by health professionals who care for kidney transplant recipients. Both questionnaires asked respondents to identify the health issues of greatest concern to adult kidney transplant recipients. The health professionals' questionnaire also collected information on current nutritional management practices, including the referral process, nutrition assessment, dietary interventions and follow-up protocols.

The questionnaires were reviewed by dietitians, nurses and transplant physicians (at John Hunter Hospital, Newcastle, NSW and Royal Prince Alfred Hospital, Sydney, NSW) and modified as required prior to distribution.

Questionnaires were anonymous and returned via email or mail.

#### ***Respondents***

Kidney transplant recipients were sourced through transplant coordinators at the 20 kidney transplant units in Australia and New Zealand, *Transplant Australia* and *Kidney Health Australia* were invited to participate.

Health professionals at the 17 adult transplant units in Australia and the 3 in New Zealand were invited to participate in the survey by telephone or email. Questionnaires were then posted or emailed either to individual health professionals directly or to transplant directors and coordinators for distribution to staff at their units. Other dietitians who care for kidney transplant recipients but not based at transplant hospitals were invited to participate in the survey via the Dietitians Association of Australia newsletter and through contact with Renal Interest Groups.

The written information accompanying the questionnaire explained the purpose of the survey in relation to the development of best practice guidelines.

Responses were received from 163 kidney transplant recipients (74% of whom were residents of Australia) and 67 health professionals (75% based in hospitals in Australia), including 20 dietitians, 16 renal transplant physicians, 12 transplant coordinators, 8 transplant nurses, 3 transplant surgeons, 2 pharmacists, 1 social worker, 1 physiotherapist and 1 nephrologist.

#### ***Results***

There was broad agreement (over 75%) among both the surveyed health professionals and transplant recipients that the following issues are of significant concern in the early post-transplantation period:

- Poor wound healing
- Hyperglycaemia (and diabetes)
- Infection risk

Health professionals and transplant recipients generally agreed that the major long-term post-transplant are:

- Excessive weight gain and obesity
- Diabetes
- Dyslipidaemia
- Bone disease
- Hypertension

With respect to nutritional assessment and management practices, there are variations between transplant units:

- *all* new transplant recipients are referred to a dietitian in 88 per cent of transplant units and seen within 2 weeks; in the remaining units, referrals are made for specific problems only;
- there is high variability in the data collected by dietitians in the nutritional assessment of transplant recipients: whilst blood test results, anthropometry and diet history are assessed by all dietitians, exercise, medications and/or social history may or may not be considered in the overall assessment;
- nutritional interventions varied considerably from unit to unit with respect to recommendations regarding energy intake; protein requirement; the type of carbohydrate and fat to include in the diet; sodium, potassium, phosphorus, magnesium requirements; whether or not to recommend vitamin or mineral supplements; and the strictness of food safety instructions;
- in 29 per cent of transplant units, there is a follow-up protocol for dietitians; in the other units, patients may only be seen if they are specifically referred (53 per cent) or may not be seen at all after discharge (18 per cent).

## **Conclusions**

A detailed description of the survey results was made available to all participants: through transplant coordinators at transplant units, *Transplant Australia* and *Kidney Health Australia* for kidney transplant recipients and by emails sent to health professionals at the units.

The survey results confirmed the need for clinical practice guidelines for the nutritional management for kidney transplant recipients.

The topics for inclusion in the guidelines were selected on the basis of the results of the survey and available prevalence and incidence data.

# Appendix B

## Search strategies and search yields

### Search strategy: MEDLINE – 1966 to week 1 September 2006 (Yield: 701)

1. Kidney Transplantation/
2. exp Nutrition Assessment/
3. exp Nutrition Therapy/
4. exp Diet Therapy/
5. Nutritional Status/
6. Nutritional Requirements/
7. ((nutrition\$ or diet\$) and (assess\$ or advic\$ or education\$ or trainin\$ or interven\$)).tw.
8. (diet\$ intervention\$ or nutrition\$ intervention\$).tw.
9. exp Energy Intake/
10. exp Dietary Carbohydrates/
11. carbohydrate\$ diet\$.tw.
12. exp Dietary Proteins/
13. (low protein diet\$ or high protein diet\$).tw.
14. Dietary Fiber/
15. (low fibre diet\$ or low fibre diet\$).tw.
16. (high fibre diet\$ or high fiber diet\$).tw.
17. GI diet\$.tw.
18. Glycemic Index/
19. exp Dietary Fats/
20. (diet\$ and (cholesterol\$ or fat\$)).tw.
21. (low fat diet\$ or high fat diet\$).tw.
22. (low salt diet or high\$ salt diet\$).tw.
23. Potassium, Dietary/
24. exp Sodium, Dietary/
25. (potassium intake\$ or (potassium and diet\$)).tw.
26. Calcium, Dietary/
27. (calcium intake\$ or (calcium and diet\$)).tw.
28. ((low bacteria or neutropeni\$) and diet\$).tw.
29. exp Dietary Supplements/
30. exp Micronutrients/
31. (vitamin\$ and (diet\$ or supplement\$)).tw.
32. (trace element\$ and (diet\$ or supplement\$)).tw.
33. ((diet\$ or nutrition\$) and supplement\$).tw.
34. ((folate or folic acid or magnesium or calcium or "vitamin D" or phosphate\$) and supplement\$).tw.
35. herbal supplement\$.tw.
36. Phytotherapy/
37. exp Plant Oils/
38. (diet\$ and (fruit\$ or vegetable\$)).tw.
39. (diet\$ and (mediterranean\$ or fad\$ or vegetarian\$)).tw.
40. exp Exercise/
41. (exercise or physical activit\$).tw.
42. or/2-41
43. and/1,42
44. animals/ not (animals/ and humans/)
45. 43 not 44
46. (pediatric not adult).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
47. (adolescent not adult).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
48. 46 or 47
49. 45 not 48
50. limit 49 to (english language and abstracts)

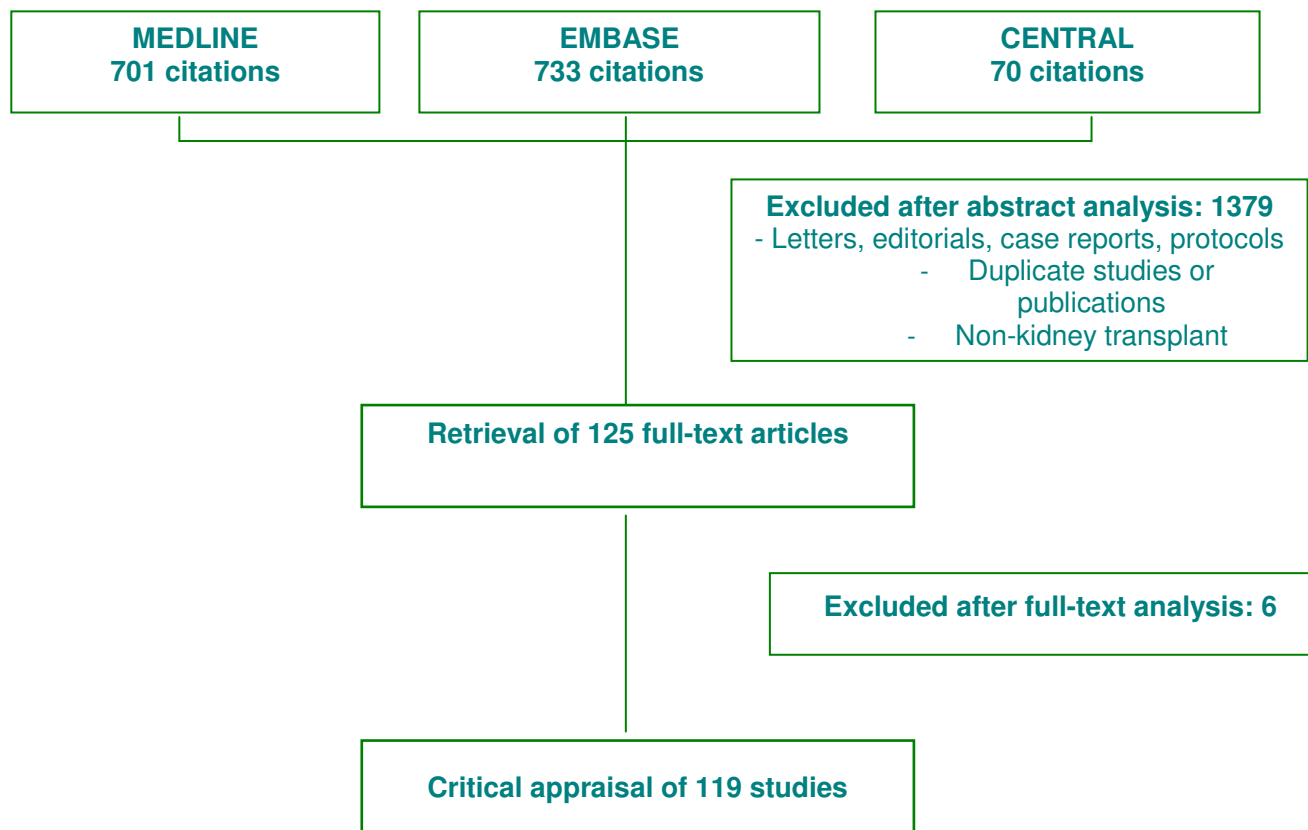
## Search strategy: EMBASE – 1980 to week 1 September 2006 (Yield: 733)

1. exp Kidney Transplantation/
2. kidney pancreas transplantation/
3. 1 not 2
4. exp nutrition/
5. ((nutrition\$ or diet\$) and (assess\$ or advic\$ or education\$ or train\$ or interv\$)).tw.
6. carbohydrate\$ diet\$.tw.
7. (low protein diet\$ or high protein diet\$).tw.
8. (low fibre diet\$ or low fiber diet\$).tw.
9. (high fibre diet\$ or high fiber diet\$).tw.
10. GI diet\$.tw.
11. (diet\$ and (cholesterol\$ or fat\$)).tw.
12. (low fat diet\$ or high fat diet\$).tw.
13. (low salt diet\$ or high salt diet\$).tw.
14. (potassium intake\$ or (potassium and diet\$)).tw.
15. ((low bacteria or neutropeni\$) and diet\$).tw.
16. (calcium intake\$ or (calcium and diet\$)).tw.
17. ((low bacteri\$ or neutropeni\$) and diet\$).tw.
18. (vitamin\$ and (diet\$ or supplement\$)).tw.
19. (trace element\$ and (diet\$ or supplement\$)).tw.
20. ((diet\$ or nutrition\$) and supplement\$).tw.
21. ((folate or folic acid or magnesium or calcium or "vitamin d" or phosphate\$) and supplement\$).tw.
22. herbal supplement\$.tw.
23. phytotherapy/
24. exp Vegetable Oil/
25. (diet\$ and (fruit\$ or vegetable\$)).tw.
26. (diet\$ and (mediterranean\$ or fad\$ or vegetarian)).tw.
27. EXERCISE/
28. (exercis\$ or physical activ\$).tw.
29. or/4-28
30. and/3,29
31. (human not animal).sh,de,hw.
32. (adult not child).sh,de,hw.
33. (letter\$ or editorial\$).pt.
34. 30 and 31
35. 34 and 32
36. 35 not 33
37. limit 36 to english language
38. limit 37 to abstracts

**Search strategy: Cochrane Renal Group's Specialised Register and the Central Register of Controlled Trials (CENTRAL) in the Cochrane Library (at September 2006) (Yield: 70)**

#1 Kidney Transplantation, MESH term  
#2 exp Nutrition Assessment MESH term  
#3 exp Nutrition Therapy MESH term  
#4 exp Diet Therapy MESH term  
#5 Nutritional Status, MESH term  
#6 Nutritional Requirements, MESH term  
#7 exp Energy Intake MESH term  
#8 exp Dietary Carbohydrates MESH term  
#9 exp Dietary Proteins MESH term  
#10 Dietary Fiber, MESH term  
#11 Glycemic Index, MESH term  
#12 exp Dietary Fats MESH term  
#13 Potassium, Dietary, MESH term  
#14 exp Sodium, Dietary MESH term  
#15 Calcium, Dietary, MESH term  
#16 exp Dietary Supplements MESH term  
#17 exp Micronutrients MESH term  
#18 Phytotherapy, MESH term  
#19 exp Plant Oils MESH term  
#20 exp Exercise MESH term  
#21(nutrition\* or diet\*) and (assess\* or advic\* or education\* or train\* or interven\*):ti,ab,kw  
#22(diet\* intervention\* ) or (nutrition\* intervention\*):ti,ab,kw  
#23(carbohydrate\* diet\*):ti,ab,kw  
#24(low fibre diet\*) or (low fiber diet\*):ti,ab,kw  
#25(low protein diet\*) or (high protein diet\*):ti,ab,kw  
#26(high fibre diet\*) or (high fiber diet\*):ti,ab,kw  
#27(low fat diet\*) or (high fat diet\*):ti,ab,kw  
#28(low salt diet\*) or (high salt diet\*):ti,ab,kw  
#29(potassium intake\*) or (potassium and diet\*):ti,ab,kw  
#30(calcium intake\*) or (calcium and diet\*):ti,ab,kw  
#31(low bacteria and diet\*):ti,ab,kw  
#32(neutropenia\* and diet\*):ti,ab,kw  
#33(vitamin\* and (diet\* or supplement\*)):ti,ab,kw  
#34(trace element\* and (diet\* or supplement\*)):ti,ab,kw  
#35(diet\* or nutrition\*) and supplement\*:ti,ab,kw  
#36(folate or folic acid or magnesium or calcium of "vitamin d" or phosphate\*) and supplement\*:ti,ab,kw  
#37(herbal supplement\*):ti,ab,kw  
#38(diet\* and (fruit\* or vegetable\*)):ti,ab,kw  
#39 (diet\* and (mediterranean or fad or vegetarian)):ti,ab,kw  
#40(exercis\* or "physical activit\*"):ti,ab,kw  
#41(#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR  
#15 OR #16 OR #17 OR #18 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27  
OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR  
#39 OR #40)  
#42(#1 AND #41)

Of the **1504 citations** found in the literature search, 1379 did not meet the inclusion criteria and were excluded. Of the **125 full-text articles retrieved**, **119 papers were critically appraised** after further exclusions.



Evidence statements contained in this guideline document are based on the **17 studies** considered to be of sufficiently high quality. The characteristics of the 14 included intervention studies are presented in Appendix C.

The number of studies of satisfactory quality for each guideline topic were:

Nutrition assessment:	2 (Level III-2, IV)
Overweight/obesity:	2 (Level III-3, IV)
Dyslipidaemia:	4 (Level III-1, IV)
Diabetes:	None
Protein requirements:	3 (Level III-1, -2)
Bone disease:	2 (Level I, II)
Hypophosphataemia:	2 (Level III-1, IV)
Hypertension:	2 (Level III-1, -2)
Anaemia:	None
Food safety:	None

# Appendix C

## Characteristics of included studies

### Anthropometric Assessment

**Study:** Gore JL, Pham PT, Danovitch GM, Wilkinson AH, Rosenthal JT, Lipshutz GS, Singer JS. Obesity and outcome following renal transplantation. *American Journal of Transplantation* 2006; 6: 357-363

<b>Methods</b>	Country:	USA
	Setting/design:	Retrospective
	Level of evidence:	III-2 (Aetiology)
	Bias minimisation:	Authors adjusted for factors known to affect graft function and overall graft survival

<b>Participants</b>	<b>Inclusion criteria</b>	Kidney transplant recipients over 18 years transplanted between 1/1/97 and 31/12/99 followed up until 16/7/04 with complete anthropometric and graft outcome data
	Number:	27, 377 (89.5% of total 30, 597 transplants)
	Age in each category (mean age in years +/-SD):	<i>Underweight</i> (BMI: less than 18.5 kg/m <sup>2</sup> ) - 38.5 ± 13.3 <i>Normal weight</i> (BMI: 18.5–24.9 kg/m <sup>2</sup> ) - 43.7 ± 13.2 <i>Overweight</i> (BMI: 25–29.9 kg/m <sup>2</sup> ) - 47.9 ± 12.5 <i>Obese</i> (BMI: 30–34.9 kg/m <sup>2</sup> ) - 48.3 ± 11.7 <i>Morbidly obese</i> (35 or higher kg/m <sup>2</sup> )- 45.8 ± 11.7
	Sex (M/F):	16,339/11,038 (60% males)
	<b>Exclusions:</b>	Multi-organ transplantation or a history of prior renal transplantation

<b>Study end points</b>	Graft outcomes analysed included: the need for blood transfusions postoperatively, the incidence of DGF defined by dialysis requirement in the first week following transplantation, prolonged hospitalization defined as a length of stay greater than 14 days, and early graft loss or recipient mortality, defined as any graft failure or patient death within 30 days of transplantation. Immunologic outcomes included treatment for acute rejection, as reported in the UNOS STAR files, either prior to discharge, within the first 6 months following transplantation, or within the first post-operative year. Overall patient and graft survival were separately analysed. Graft failure was defined as a permanent return to dialysis dependence or death with a functioning graft.
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<b>Outcomes</b>	Among the <i>obese</i> or <i>morbidly obese</i> subjects there was a higher prevalence of the following comorbid conditions: diabetes, hypertension, coronary artery disease, peripheral vascular disease ( $p < 0.001$ ). Obese and morbidly obese recipients were significantly more likely to experience DGF ( $p < 0.001$ ) Morbid obesity is associated with prolonged hospitalisation ( $p < 0.001$ ) and greater likelihood of acute rejection episodes (defined by treatment not biopsy) ( $p = 0.006$ ) and graft failure ( $p < 0.001$ ) For DGF, prolonged hospitalization, early graft loss and death with a functioning graft, a trend was observed where each higher recipient BMI category suffered an increased risk of the adverse outcome. After controlling for other variables, obesity was not independently associated with increased risk of death with a functioning graft.
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## Anthropometric Assessment (continued)

**Study:** Meier-Kriesche HU, Arndorfer JA, Kaplan B: The impact of body mass index on renal transplant outcomes: A significant independent risk factor for graft failure and patient death. *Transplantation* 2002;73:70-74.

<b>Methods</b>	Country: Setting/design: Time frame:  Level of evidence: Bias minimisation:	USA Retrospective From transplant date until graft loss, death or study end date (30/5/98) III-2 Exclusion of patients with incomplete data with respect to chronic allograft failure endpoint
<b>Participants</b>	<b>Inclusion criteria</b>  Number: Age (mean): Sex (M/F):  <b>Exclusions:</b>	Adult renal transplant recipients, registered in the USRDS database between 1988 and 1997 51,927  Paediatric, multiorgan, repeat renal transplant recipients
<b>Study end points</b>	<p>Patient death, death censored graft loss, chronic allograft failure, and overall graft loss (combined endpoint of patient death and graft loss). Additionally, the relationship between BMI and cause-specific death (cardiovascular and infectious death) was investigated.</p> <p>Other endpoints included acute rejection within the first 6 months posttransplantation and delayed graft function defined as the need for renal replacement therapy within the first week posttransplant.</p> <p>Chronic renal allograft failure (CAF) was defined as graft loss secondary to chronic allograft nephropathy or graft loss after 6 months posttransplant, censored for patient death or graft loss secondary to acute rejection, graft thrombosis, infection, surgical complications, or recurrent disease</p>	
<b>Outcomes</b>	<p><b>Patient death with functioning graft:</b> U-shaped association between BMI and death with functioning graft. Beyond the range 22–32 kg/m<sup>2</sup> on both extremes of the BMI distribution there was a significant association with increased risk for patient death. (<math>p &lt; 0.0001</math> overall)</p> <p><b>Chronic allograft failure:</b> (<math>n = 47,514</math> as patients with less than 6-months follow up based on definition were excluded) U-shaped association between BMI and CAF but the increased relative risk for CAF in the lower BMI groups did not reach statistical significance while BMI categories <math>&gt; 30</math> kg/m<sup>2</sup> were associated with a significantly higher CAF risk (<math>p &lt; 0.0001</math> overall)</p> <p><b>Overall graft loss:</b> Compared to the reference category of BMI 24–26 kg/m<sup>2</sup>, these BMI categories were associated with a significantly increased relative risk (RR) for graft loss:</p> <ul style="list-style-type: none"> <li>- BMI of <math>&lt; 18</math> kg/m<sup>2</sup> RR = 1.213, confidence interval [CI] = 1.110–1.326 (<math>p &lt; 0.005</math>)</li> <li>- BMI of 18–20 kg/m<sup>2</sup> RR = 1.114, CI = 1.044–1.189; (<math>p &lt; 0.005</math>)</li> <li>- BMI of 26–28 kg/m<sup>2</sup> RR = 1.071, CI = 1.008–1.136, proceeding toward the higher BMI categories there was an exponential increase in the relative risk for graft loss with a BMI of <math>&gt; 36</math> kg/m<sup>2</sup> associated with a RR = 1.385, CI = 1.300–1.551 (<math>p &lt; 0.005</math>).</li> </ul> <p><b>Cause-specific death:</b></p> <ul style="list-style-type: none"> <li>- <b>Cardiovascular disease</b> – BMI of <math>&lt; 20</math> and <math>&gt; 30</math> significantly increased relative risk of death caused by cardiovascular disease (<math>p &gt; 0.0001</math> overall)</li> <li>- there was a tendency towards higher cardiovascular risk less than a BMI of 22 kg/m<sup>2</sup> and above a BMI of 26 kg/m<sup>2</sup>; from the lowest relative risk in the BMI group of 22–24 kg/m<sup>2</sup> toward the most elevated risk in the BMI group above 36 kg/m<sup>2</sup> there was an exponential increase in the relative risk for cardiovascular death.</li> <li>- <b>Infectious causes</b> – there was a strong association with very low and elevated BMI and the relative risk for this end point (1614 events), a U-shaped curve was observed with an interval without significant risk increase between BMI 22–30 kg/m<sup>2</sup>.</li> </ul> <p><b>Acute rejection in first 6 months:</b> no significant association found between BMI and the odds ratio for acute rejection episodes within the first 6 months posttransplantation</p> <p><b>Delayed graft function:</b> BMI <math>&lt; 18</math> kg/m<sup>2</sup> was associated with a significantly lower risk for delayed graft function as compared to the reference group (RR = 0.78, CI 0.60–0.98). The relative risk for delayed graft function increased gradually with increasing BMI with the most elevated risk at BMI above 36 kg/m<sup>2</sup> (RR = 1.51, CI 1.27–1.85).</p>	

## Anthropometric Assessment (continued)

**Study:** Micozkadioglu H, Ozdemir FN, Sezer S, Arat Z, Haberal M: Weight gain after living-related renal transplantation affects long-term graft function. *Transplant Proc* 2005;37:1029-1032

<b>Methods</b>	Country: Setting/design: Time frame: Level of evidence: Bias minimisation:	Turkey Retrospective Two years post-transplantation III-2
<b>Participants</b>	<b>Inclusion criteria</b>  Number: Age (mean): Sex (M/F):  <b>Exclusions:</b>	Adult patients who received living-related renal transplants between January 1996 and December 1999, and who were still living at the time of the study  93 33.78 +/-9.78 65/28  HBsAg positivity, repeat renal transplant, graft loss in the first year, delayed graft function, and a diagnosis of cyclosporine toxicity.
<b>Study end points</b>	Occurrence of chronic allograft nephropathy (which was diagnosed when a patient's creatinine level remained >2 mg/dL and all other possible reasons for this rise were excluded, or if there were positive findings on renal biopsy) and risk factors including: number of HLA mismatches, PRA levels, delayed graft function, acute rejection, suboptimal immunosuppression. In each case, BMI, calculated using the formula of weight (kg)/height (m <sup>2</sup> ) was recorded at 6 months after transplantation and yearly thereafter. A recipient was considered to exhibit abnormal weight gain if the BMI rose >10% and remained at this level throughout at least 2 years posttransplantation. Patients were divided into two groups: abnormal weight gain (group 1) versus normal or no weight gain (group 2).	
<b>Outcomes</b>	Patients with a 10% increase in body mass index sustained throughout at least 2 years posttransplantation were categorized as group 1 (abnormal weight gain; <i>n</i> = 65) and the others were categorized as group 2 (no or normal weight gain; <i>n</i> =28). Chronic allograft nephropathy was more frequent among group 1 (84.4% vs 15.6%, respectively <i>p</i> <.03).  Logistic regression and backward stepwise analyses were performed to evaluate risk factors for the development of CAN. The results showed that the most important risk factor for the development of CAN was the occurrence of an acute rejection episode (OR = 5.39, 95% CI: 2.07 to 14.03, <i>P</i> < .001). This episode increased the risk for development of CAN fivefold. Among patients without an acute rejection episode, the most important risk factor was abnormal weight gain after renal transplantation, a threefold higher risk of developing CAN (OR = 3.04, 95% CI:1.01 to 9.69, <i>P</i> <.04).  Since abnormal weight gain was identified as a risk factor for development of CAN, the two groups were compared with respect to immunologic and nonimmunologic risk factors for CAN. Analysis indicated no significant differences regarding to other risk factors for development of CAN between the two groups ( <i>P</i> <.05 for all)	

## Anthropometric Assessment (continued)

**Study:** Djukanović L, Ležaić V, Blagojević R, Radivojević D, Stošović M, Jovanović N, Ristić S, Simić-Ogrizović S: Co-morbidity and kidney graft failure - two main causes of malnutrition in kidney transplant patients. *Nephrol Dial Transplant* 2003;18:v68-70.

<b>Methods</b>	Country: Setting/design: Level of evidence: Bias minimisation:	Yugoslavia Cross-sectional IV Note: Randomly selection method not described
<b>Participants</b>	<b>Inclusion criteria</b>  Number: Age (range): Sex (M/F):	Randomly-selected patients from the 452 transplant patients followed up at the outpatient clinic 47 13-54 years 29/18
	<b>Exclusions:</b>	
<b>Study end points</b>	Nutritional status was determined by anthropometric parameters (body weight, the mid-arm muscle circumference, skinfold thickness, BMI) as well as by determination of several biochemical parameters (serum protein, albumin, cholesterol, red blood cell count).  Co-morbidity of the examined patients was assessed using the Index of Coexistent Diseases.	
<b>Outcomes</b>	<p>The selected patients had received a kidney graft 6–180 months previously, the majority from living related donors. The immunosuppression consisted of cyclosporin, steroids and azathioprine.</p> <p>Subjects were allocated to three groups according to BMI</p> <ul style="list-style-type: none"><li>- BMI &lt;21kg/m<sup>2</sup> (group 1) n=11;</li><li>- BMI 21-25 kg/m<sup>2</sup> (group 2) n=20; and</li><li>- BMI &gt;25 kg/m<sup>2</sup> n=17</li></ul> <p>Only groups 1 and 2 were compared in the analysis.</p> <p>The comparison of the biochemical parameters between patients in groups 1 and 2 showed that patients with a BMI of &lt;21kg/m<sup>2</sup> had significantly lower levels of protein (66 vs 77 g/l), albumin (33 vs 39 g/l) and haemoglobin (102 vs 121 g/l) compared with patients with a BMI of 21-25kg/m<sup>2</sup> (<math>p&lt;0.05</math>).</p> <p>Patients with a BMI of &lt;21kg/m<sup>2</sup> had significantly higher serum creatinine levels (<math>p&lt;0.05</math>). There were significantly more females with a BMI of &lt;21kg/m<sup>2</sup> (<math>p&lt;0.05</math>).</p> <p>No significant differences were found in age at transplantation, pre-transplantation time on dialysis, donor origin, early post-transplant course, immunosuppressive therapy, number of rejection episodes and duration of post-transplant period between the group 1 and group 2 patients.</p>	

## Anthropometric Assessment (continued)

**Study:** Van den Ham ECH, Kooman JP, Christiaans MHL, Nieman FHM, van Kreel BK, Heidendal GAK, van Hooff JP: Body composition in renal transplant patients: Bioimpedance analysis compared to isotope dilution, dual energy x-ray absorptiometry, and anthropometry. *J Am Soc Nephrol* 1999;10:1067-1069.

<b>Methods</b>	Country: Setting/design: Level of evidence: Bias minimisation:	The Netherlands Cross-sectional IV All patients were receiving immunosuppressive therapy, which consisted of combinations of prednisolone, azathioprine, and cyclosporine
	<b>Inclusion criteria</b>	Renal transplant patients with a stable renal function and maintenance immunosuppressive therapy for at least 2 years
	Number: Age (range): Sex (M/F):	77 51.0 +/- 11.7 years 42/45
	<b>Exclusions:</b>	Presence of insulin-dependent diabetes mellitus, metal implants (prostheses or pacemakers), and recent complications ( <i>e.g.</i> , malignancies or surgery).
<b>Study end points</b>	Body composition was measured by isotope dilution (deuterium (D2O) and potassium bromide (KBr)), DEXA, anthropometry, and MF-BIA	
<b>Outcomes</b>	<p>Isotope dilution (deuterium (D2O) data for 73 patients were available (data for 4 patients lost in laboratory analysis). MF-BIA measurements were performed in 10 subjects (5 males) (mean age of 59.0 +/- 13.1 yrs). Bromide dilution data are available for 72 subjects (data of 5 patients were lost during laboratory analysis). DEXA total body scans were available for 75 subjects. Anthropometric data are available for 74 renal transplant patients (in three patients it was not possible to measure skinfold thickness of the iliac crest because of multiple scars).</p> <p><b>Estimating total body water:</b> <i>TBWD2O</i> compared with <i>TBWMF-BIA</i> is 34.2+/-6.1 L versus 33.5+/-5.9 L (<math>p&lt;0.05</math>). <i>TBWD2O</i> is highly and significantly correlated to <i>TBWMF-BIA</i> (<math>r=0.943</math>, <math>p&lt;0.001</math>).</p> <p><b>Estimating extracellular water:</b> <i>ECWKBr</i> compared with <i>ECWMF-BIA</i> is 15.5+/-2.9 L versus 18.7+/-3.6 L (<math>P&lt;0.05</math>). <i>ECWKBr</i> is highly and significantly correlated to <i>ECWMF-BIA</i> (<math>r=0.865</math>, <math>p&lt;0.001</math>).</p> <p><b>Estimating body fat:</b></p> <ul style="list-style-type: none"> <li>- <i>BFDEXA</i> compared with <i>BFMF-BIA</i> is 30.3+/-10.5% versus 33.7+/-9.2% (<math>p&lt;0.05</math>). <i>BFDEXA</i> and <i>BFMF-BIA</i> are highly and significantly correlated (<math>r=0.895</math>, <math>p&lt;0.001</math>). In patients with a BMI &lt;22.5 kg/m<sup>2</sup>, patients with cystic kidneys and patients with a high waist-to-hip ratio, method agreement appears to be below the predetermined lowest acceptable method agreement.</li> <li>- <i>BFanthr</i> compared with <i>BFMF-BIA</i> is 27.9 +/-10.2% versus 33.4+/-9.2% (<math>p&lt;0.05</math>). <i>BFanthr</i> is highly and significantly correlated to <i>BFMF-BIA</i> (<math>r=0.860</math>, <math>p&lt;0.001</math>). However the intraclass correlation coefficient for method agreement of BF by anthropometry and by MF-BIA (<i>ICCBF-A</i>) is 0.856; because this ICC lies only a fraction above the predetermined lowest acceptable method agreement, method agreement between anthropometry and MF-BIA for measuring body fat appears to be questionable.</li> <li>- <i>BFDEXA</i> compared with <i>BFanthr</i> is 30.2 6 10.7% versus 28.1 6 10.3% (<math>p&lt;0.05</math>). <i>BFDEXA</i> is highly and significantly correlated to <i>BFanthr</i> (<math>r=0.913</math>, <math>p&lt;0.001</math>). The</li> </ul>	

## Biochemical and Clinical Assessment

**Study:** Sezer S, Ozdemir FN, Afsar B, Colak T, Kizay U, Haberal M: Subjective global assessment is a useful method to detect malnutrition in renal transplant patients. *Transplant Proc* 2006;38:517-520

<b>Methods</b>	Country: Setting/design: Level of evidence: Bias minimisation:	Turkey Cross-sectional IV All patients underwent subjective global assessment by a single dietitian. Triceps skinfold thickness (TSF) was measured in triplicate.
<b>Participants</b>	<b>Inclusion criteria</b>  Number: Age (range): Sex (M/F):  <b>Exclusions:</b>	47 37.6 +/- 10.2 years 37/10  Recipients with advanced liver disease, malignancy, or severe diabetic complications, such as gastroparesis, or those unwilling to participate
<b>Study end points</b>	Number of hospitalizations in the preceding year, presence of chronic allograft failure and mean laboratory values of the last 6 months: haemoglobin, serum creatinine, albumin, pre-albumin phosphorus, C-reactive protein levels, and lipid profile. Also serum levels of albumin and C-reactive protein at the time of transplantation were determined from the medical records.	
<b>Outcomes</b>	<p>Patients were classified into 3 nutritional groups: A (n=31, 66%), B (n=11, 23.4%), and C (n=5, 10.6%). Statistical analysis compared group A (no malnutrition, n=31, 66%) with groups B/C (moderate or severe malnutrition, n=16, 34%).</p> <p>Comparison of the 2 groups revealed the serum albumin (<math>P &lt; 0.0001</math>), body mass index (<math>p &lt; 0.02</math>), and mid-arm circumference (<math>p &lt; 0.02</math>) to be higher in group A than groups B/C. Group B/C patients showed higher levels of C-reactive protein (<math>p &lt; 0.0001</math>).</p> <p>When compared to the pretransplantation period, 83.8% of patients in group A had increased body mass index (from 21.8 +/- 3.8 to 24.6 +/- 3.6 kg/m<sup>2</sup> after transplantation compared to 18.7% patients in groups B/C (<math>P &lt; 0.0001</math>). The mean BMI decreased in groups B/C from 23.2 +/- 3.6 to 21.9 +/- 3.6 kg/m<sup>2</sup>.</p> <p>The hospitalization rates were significantly lower in group A (<math>p &lt; 0.02</math>).</p> <p>Patients in group A tended to have a lower frequency of chronic allograft rejection when compared to group B/C subjects (<math>p &lt; 0.13</math>).</p> <p>The difference in chronic rejection rates between group A and group B/C was not significant (<math>P = 0.13</math>).</p> <p>There were significantly more patients in group A hospitalized in the previous year compared to group B/C (<math>p &lt; 0.02</math>).</p>	

## Dietary Protein Requirements

**Study:** Whittier FC, Evans DH, Dutton S, Ross G, Luger A, Nolph KD, Nauer JH, Brooks CS, Moore H. Nutrition in renal transplantation. American Journal of Kidney Diseases, 1985; 6(6): 405-411.

<b>Methods</b>	Country:	USA
	Setting/design:	Randomised, controlled study
	Time frame:	Immediately post-transplant for four weeks
	Level of evidence:	III-1
	Randomisation method:	Not described
	Blinding:	No
	Follow-up period:	Four weeks
<b>Participants</b>	<b>Inclusion criteria</b>	Non-diabetic renal transplant recipients, immediately post-transplant
	<b>Treatment group</b>	
	Number:	6
	Age (mean):	33 years
	Sex (M/F):	4/2
	<b>Control group</b>	
	Number:	6
	Age (mean):	32 years
	Sex (M/F):	5/1
	<b>Exclusions:</b>	Patients over 55 years or with diabetes
<b>Interventions</b>	Treatment group (mean+/-SD):	1941 +/-122 kCal (~ 28-30kcal/kg)/d; 2.2g protein/kg/d; ranging from 1.4 to 3.0g/kg
	Control group (mean+/-SD):	2097 +/- 291 kCal (~ 28-30kcal/kg)/d, 1.1g protein/kg/d
	Co-intervention:	All patients received same care until day 4 post-transplant when randomised to treatment or control group. Both groups given: 800ml fluid plus urine output, 2g Na, 80mEq K, 800-1200mg Ca, daily vitamin supplement
<b>Outcomes</b>	Nitrogen balance proportional to daily nitrogen intake in all 12 subjects. Muscle mass changes: loss in control group versus gain in treatment group (p<0.005), with one patient in control group excluded from analysis due to high protein intake (see below).	
<b>Notes</b>	Diets were designed to provide: 28-30kCal/kg with experimental diet providing 210g protein (3g/kg) and control diet providing 70g protein (1g/kg). Actual intakes varied from this, with means shown in above interventions. One patient in the control group was excluded in the analysis as their protein intake was double the mean of the others in the control group. High protein diet converted negative nitrogen balance to positive in the 28 day study period.	
<b>Quality checklist</b>	Allocation concealment	No
	Blinding	No
	Intention to treat analysis	Yes
	Completeness of follow-up	100%

## Dietary Protein Requirements (continued)

**Study:** Cogan MG, Sargent JA, Yarborough SG, Vincenti F, Amend Jr. WJ. Prevention of prednisone-induced negative nitrogen balance. *Annals of Internal Medicine*, 1981; 95: 158-161.

<b>Methods</b>	Country: Setting/design: Time frame: Level of evidence: Randomisation method: Blinding: Follow-up period:	USA Single centre, prospective, non-randomised 9 months IV None None 10-14 day treatment period (until spontaneous diuresis or acute rejection episode occurred)
<b>Participants</b>	<b>Inclusion criteria</b>  <b>Treatment group</b> Number: Age (mean): Sex (M/F):  <b>'Control' group</b> Number: Age (mean): Sex (M/F):  <b>Non-transplant group</b> Number: Age (mean): Sex (M/F):  <b>Exclusions:</b>	Kidney transplant recipients with acute tubular necrosis for at least one week post-transplant requiring haemodialysis  8 43+/-5 years 4/4  7 34+/-9 years 5/2  (Not receiving prednisone) 6 Not stated Not stated  Not stated
<b>Interventions</b>	Treatment group: Control group: Co-intervention:	1.3 +/- 0.06 g protein/kg; 33+/-3 kcal/kg; approx 2g Na, 3g K 0.73+/-0.03g protein/kg/d; 20+/-2kcal/kg/d; 2g Na; 2g K Prednisone: 120mg/d tapered to 70-90mg/d (both groups)
<b>Outcomes</b>	Treatment and Control Groups started in negative nitrogen balance, whilst, non-transplant group (not receiving prednisone) were in nitrogen balance, confirming that prednisone induces negative nitrogen balance. Treatment group achieved neutral nitrogen balance (with no change in urea production) after higher protein diet provided. Control group remained in a stable state of negative nitrogen balance and had a higher rate of urea production (muscle breakdown). The rate of urea generation and haemodialytic requirements for prednisone-treated transplant recipients are not raised when protein and calorie intake are increased sufficiently to eliminate negative nitrogen balance.	
<b>Notes</b>	Comparison of treatment and control groups with respect to the effect of protein intake on nitrogen balance was not possible as there was a significant difference in mean energy intake of each group. Hence with respect to NHMRC levels of evidence this study was graded IV.	
<b>Quality checklist</b>	Allocation concealment Blinding Intention to treat analysis Completeness of follow-up	No No Yes 100%

## Dietary Protein Requirements (continued)

**Study:** Rosenberg ME, Salahudeen AK, Hostetter TH. Dietary protein and the renin-angiotensin system in chronic renal allograft rejection. *Kidney International*, 1995; 48(Suppl 52): S102-S106

<b>Methods</b>	Country: Setting/design: Time frame:  Level of evidence: Randomisation method: Blinding: Follow-up period:	USA Single centre, randomised cross-over design 4-8 weeks 11 day diet; 1-4 week washout period; 11 day diet III-1 Not described No Until completion of two diet periods
<b>Participants</b>	<b>Inclusion criteria</b>  <b>Treatment group</b> Number: Age (mean): Sex (M/F):  <b>Exclusions:</b>	Kidney transplant recipients with biopsy-proven chronic rejection, proteinuria, elevated serum creatinine, stable immunosuppressive regimen, no ACE inhibitor for 2 months preceding study  14 37+/-4 years 1:1  Evidence of proteinuria from a native kidney
<b>Interventions</b>	Diet 1: Diet 2: Co-intervention:	0.55g protein/kg body weight 2.0g protein/kg body weight Both diets contained: 35 kcal/kg/d (carbohydrate kilojoules substituted for protein kilojoules on the lower protein diet); 80mmol/d Na; 100mmol/d K Thirteen of the patients treated with antihypertensives to reduce mean arterial blood pressure to the same degree in both groups by 5-10mmHg. Daily P intake similar at start.
<b>Outcomes</b>	Fractional clearance of albumin and IgG on low protein diet was consistent with improved glomerular permselectivity. Serum total protein, albumin and transferrin were significantly lower at the end of the LP diet compared to the HP diet.	
<b>Notes</b>	Follow-up period not long enough to assess the effects of dietary protein on long-term changes in glomerular filtration rate or progression of chronic renal failure. Study results suggest that 0.55g protein/kg body weight may be below safe level of protein restriction.	
<b>Quality checklist</b>	Allocation concealment Blinding Intention to treat analysis Completeness of follow-up	No No Yes 100%

## Dietary Protein Requirements (continued)

**Study:** Bernardi A, Biasia F, Pati T, Piva M, D'Angelo A, Bucciante G. Long-term protein intake in kidney transplant recipients: Effect in kidney graft function and in nutritional status. *American Journal of Kidney Diseases*, 2003; 41(3): S146-152.

<b>Methods</b>	Country: Setting/design: Time frame: Level of evidence: Randomisation method: Blinding: Intention-to-treat: Follow-up period:	Italy Single-centre, prospective observational study 1989 to 2002 IV None No N/A 12 years
<b>Participants</b>	<b>Inclusion criteria</b>  Number: Age (mean): Sex (M/F): <b>Exclusions:</b>	All kidney transplant recipients who entered the centre for control of graft failure and chronic rejection between 1989 and 2002 48 43.43 +/- 12.42 years (m) 41.45 +/- 22.69 years (f) 36/12 None
<b>Interventions</b>	All subjects were given the same advice: 30kcal/kg; 0.7-0.8g protein/kg/d; 3g/d sodium; <30% total E from fat; reduced sulphur-rich amino acids 2-monthly: weighed food diary for 2 days and diet interview performed  Group divided into two, on the basis of compliance to dietary advice: Group 1: 0.73+/-0.11g/kg (n=30) Group 2: 1.4+/-0.23g/kg (n=13)	
<b>Outcomes</b>	<ol style="list-style-type: none"> <li>1. <i>Serum creatinine:</i> Stable in Group 1; increasing in Group 2 (p&lt;0.001)</li> <li>2. <i>GFR:</i> Stable in Group 1; progressive decline in Group 2 (p&lt;0.0001)</li> <li>3. <i>24 hour urinary protein excretion:</i> Reduced in Group 1 (p&lt;0.002) but not significant in Group 2</li> </ol>	
<b>Notes</b>	No information presented on similarities or differences between Group 1 and 2 subjects.	
<b>Quality checklist</b>	Allocation concealment Blinding Intention to treat analysis Completeness of follow-up	N/A N/A N/A 90% (5 of the 48 died during study period)

## Management of Overweight and Obesity

**Study:** Patel, MG. The effect of dietary intervention on weight gains after renal transplantation. *Journal of Renal Nutrition*, 1998; 8(3): 137-141.

<b>Methods</b>	Country: Setting/design: Level of evidence: Randomisation method: Blinding: Intention-to-treat: Follow-up period:	USA Comparative study with historical controls (clinical records) III-3 None N/A N/A 1 year
<b>Participants</b>	<b>Inclusion criteria</b>  <b>Treatment group</b> Number: Age (mean): Sex (M/F): <b>Retrospective control group</b> Number: Age (mean): Sex (M/F):  <b>Exclusions:</b>	Adult kidney transplant recipients with stable functioning grafts, immediately post-transplant  11 Not stated 9/2 22 Not stated 14/4  Not stated
<b>Interventions</b>	Treatment group:  Control group: Co-intervention:	Intensive, individualised verbal and written dietary advice described in detail (incl. info on P, F, C, fluid, Ca, Fe, Na, hygiene, weight loss and exercise with a meal plan Follow-up weekly for 1 <sup>st</sup> month then monthly to 4 months Who gave dietary advice is not stated. No dietary advice or follow-up None
<b>Outcomes</b>	<p><i>1. BMI change</i> Significant increase for Treatment Group from 4 months to 1 year (<math>p=0.02</math>) Significant increase Control Group from baseline to 4 months (<math>p&lt;0.001</math>), from baseline to 1 year (<math>p&lt;0.001</math>) and from 4 months to 1 year (<math>p&lt;0.001</math>)</p> <p><i>2. BMI difference between groups</i> Treatment Group vs Control Group at 4 months and 1 year, <math>p=0.003</math>, <math>0.006</math> respectively.</p> <p><i>3. Actual weight gained</i> Less weight gain in Treatment Group than Control Group at 4 months and 1 year (<math>p=0.01</math>, <math>0.01</math> respectively) (1.4kg vs 7.1kg in first 4 months; 5.5kg vs 11.8kg over one year, Treatment and Control Groups respectively)</p>	
<b>Notes</b>	Potentially difficult to conduct with a concurrent control group for ethical reasons. Suggests that early intervention and regular follow-up is important in preventing excessive weight gain after transplantation.	
<b>Quality checklist</b>	Allocation concealment Blinding Intention to treat analysis Completeness of follow-up	No No No 100%

## Management of Overweight and Obesity (continued)

**Study:** Lopes IM, Martin M, Errasti P, Martinez JA. Benefits of a dietary intervention on weight loss, body composition, and lipid profile after renal transplantation. *Nutrition*, 1999; 15:7-10.

<b>Methods</b>	Country: Setting/design: Time frame: Level of evidence: Randomisation method: Blinding:	Spain Single centre, prospective, case series, pre- and post-test 6 months IV None No
<b>Participants</b>	<b>Inclusion criteria</b>  <b>Treatment group</b> Number: Age (mean): Sex (M/F):  <b>Exclusions:</b>	Stable renal function (serum creatinine <2mg/dL), BMI>27, three immunosuppressive drugs (prednisone, cyclosporin, azathioprine)  23 42+/-14 yrs 7/16  Diabetes, myxedema, nephrotic syndrome, hyperlipidemia due to thyroid or liver disease, cholesterol or weight-lowering agents
<b>Interventions</b>	Monthly individualised dietary instruction American Heart Association "Step One Diet" (<30% energy from fat; <10% saturated fat, <300mg cholesterol/day) with an restriction of ~30% of total estimated energy expenditure	
<b>Outcomes</b>	<p><i>1. Dietary intake</i> Decreased total and saturated fat and cholesterol intake (p&lt;0.001, &lt;0.01, 0.01 respectively) Increase in CHO (p&lt;0.001)</p> <p><i>2. Blood lipids</i> Total cholesterol decreased significantly (p&lt;0.05) LDL-cholesterol decreased significantly in males (p&lt;0.05)</p> <p><i>3. Body composition</i> Weight loss of 3.2 +/- 2.9kg (p&lt;0.001) Fat loss (p&lt;0.05)</p>	
<b>Quality checklist</b>	Allocation concealment Blinding Intention to treat analysis Completeness of follow-up	No No Yes 100%

## Management of Dyslipidaemia

**Study:** Stachowska E, Weslowska T, Safranow K, Domanski L, Rac M, Dziedziejko V, Ciechanowski K, Chlubek D. Simple dietary interventions reduce the risk factors of atherosclerosis in renal graft recipients. *Journal of Renal Nutrition*, 2005; 15(3): 291-297.

<b>Methods</b>	Country:	Poland
	Setting/design:	Single centre, randomised controlled study
	Time frame:	6 months
	Level of evidence:	III-1
	Randomisation method:	Not described
	Blinding:	
	- Participants:	No
	- Investigators:	Unclear
	- Outcome assessors:	Unclear
	- Data analysis:	Unclear
	Follow-up period:	6 months
<b>Participants</b>	<b>Inclusion criteria</b>	Kidney graft recipients with stable graft function
	<b>Treatment group</b>	
	Number:	21
	Age (mean):	41+/-12.5
	Sex (M/F):	15 males, 6 females
	<b>Control group</b>	
	Number:	16
	Age (mean):	46+/-9.5
	Sex (M/F):	10 males, 6 females
	<b>Exclusions:</b>	Not stated
<b>Interventions</b>	Treatment group:	“Modified Mediterranean diet” – low glycaemic index carbohydrates, 30ml cold-pressed olive oil, rapeseed oil for cooking, foods rich in n-3 and alpha-tocopherol (nuts, grains, linseeds), fresh vegetables with every meal, daily animal protein 25-50g (males), 23-46g (females) Given weekly menus (4 week cycle) Diet provided: 47% CHO, 38% fat (SMP=10:22:6), 15% protein. Compliance assessed every 4 weeks by 24hr food diaries and monitoring oleic acid content in plasma triglycerides
	Control group:	Low-fat diet, typical of Central European pattern – isocaloric Diet provided: 57% CHO; 26% fat (PUFA-dominant), 17% protein. Higher glycaemic index/lower fibre and lower fruit and vegetable content than treatment diet.
<b>Outcomes</b>	Study outcomes	
	1. <i>Total serum cholesterol:</i>	Reduction only in Treatment Group 230 to 210mg/dL (p<0.02)
	2. <i>Serum triglycerides:</i>	Reduction only in Treatment Group 194 to 152mg/dL (p<0.0007)
	3. <i>Weight and body fat:</i>	No significant change in either group
<b>Notes</b>	Patients treated the same apart from treatment: immunosuppressive and antihypertensive regimens not changed; no antilipemic drugs administered before or during study	
<b>Quality checklist</b>	Allocation concealment	No
	Blinding	No
	Intention to treat analysis	Yes
	Completeness of follow-up	100%

## Management of Dyslipidaemia (continued)

**Study:** Barbagallo CNM, Cefalu AB, Gallo S, Rizzo M, Noto D, Cavera G, Rao Camemi A, Marino G, Caldarella R, Notarbartolo A, Averna MR. Effect of Mediterranean diet on lipid levels and cardiovascular risk in renal transplant recipients. *Nephron* 1999; 82: 199-204.

<b>Methods</b>	Country: Setting/design: Level of evidence: Randomisation method: Blinding: Follow-up period:	Italy Case series IV N/A No 10-12 weeks
<b>Participants</b>	<b>Inclusion criteria</b>  <b>Treatment group</b> Number: Age (mean): Sex (M/F):  <b>Exclusions:</b>	Stable kidney transplant recipients with serum creatinine <2mg/dl  78 42+/-10 years 51/27  Not stated
<b>Interventions</b>	Treatment group:	24 weeks on usual diet followed by 10-12 weeks on the American Heart Association Step One Diet, modified to include a higher proportion of wholegrain carbohydrates and monounsaturated fatty acids. Strictly individualised with intensive counselling before starting diet, with 4-weekly follow-up to assess compliance.
<b>Outcomes</b>	Trend in first 24 weeks (no dietary intervention): increasing serum lipid levels. Post-diet: significant reduction in total cholesterol, LDL-cholesterol, triglycerides, LDL-C: HDL-C ratio.	
<b>Quality checklist</b>	Allocation concealment Blinding Intention to treat analysis Completeness of follow-up	No No Yes 100%



## Management of Hypertension

**Study:** Keven K, Yalçın S, Canbakan B, Kutley S, Sengül S, Erturk S, Erbay B. The impact of daily sodium on posttransplant hypertension in kidney allograft recipients. *Transplantation Proceedings* 2006; 38: 1223-1326.

<b>Methods</b>	Country: Setting/design: Time frame: Level of evidence: Randomisation method: Blinding: - Participants: - Investigators: - Outcome assessors: - Data analysis: Follow-up period:	Turkey Prospective, randomised controlled study January 2004-December 2004 III-1 Not described Not possible Physician who arranged antihypertensive meds was blinded No No 3 months
<b>Participants</b>	<b>Inclusion criteria</b>  <b>Treatment group</b> Number: Age (mean): Sex (M/F):  <b>Control group</b> Number: Age (mean): Sex (M/F):  <b>Exclusions:</b>	Stable allograft function (serum creatinine <2.5mg/dL), providing written, informed consent  18 40 +/- 14 years 13 male, 5 female  14 43 +/- 9 years 12 male, 2 female  Evidence of renal artery stenosis
<b>Interventions</b>	Treatment group:  Control group: Co-intervention:	3-month sodium-restricted diet (80-100mmol/day) arranged by a dietitian at the beginning of the study Seen by the same dietitian at 4,8,12 weeks. Normal treatment Antihypertensive medications adjusted according to blood pressure levels
<b>Outcomes</b>	<p>1. <i>Urinary sodium</i> Significantly lower in treatment group (p=0.001) at 3 months</p> <p>2. <i>Systolic and diastolic blood pressure</i> Significantly lower in treatment group (p=0.001) at 3 months Clinically significant: 146/89 to 116/72 mmHg</p>	
<b>Notes</b>	<p>Maintenance immunosuppressive treatment:</p> <ul style="list-style-type: none"> <li>- prednisolone, azathioprine/mycophenolate mofetil and tacrolimus/cyclosporin (n=29)</li> <li>- prednisolone and azathioprine mycophenolate mofetil (n=3)</li> </ul> <p>12 of the 18 patients on the low sodium diet were on cyclosporine, 5 were on tacrolimus and 1 received neither. No analysis with respect to immunosuppressive regimen.</p>	
<b>Quality checklist</b>	Allocation concealment Blinding Intention to treat analysis Completeness of follow-up	No Some Yes 91% Non-compliance with study visits n=1 Long-term hospitalisation due to chronic diarrhoea n=1 Development of chronic allograft nephropathy n=1

## Management of Hypertension (continued)

**Study:** Curtis JJ, Luke RG, Jones P, Diethelm AG. Hypertension in cyclosporine-treated renal transplant recipients is sodium dependent. American Journal of Medicine 1988; 85: 134-138.

<b>Methods</b>	Country: Setting/design: Level of evidence: Randomisation method: Blinding: Follow-up period:	USA Single-centre, prospective, comparative study III-2 No (matched controls used) Not stated 10 days
<b>Participants</b>	<b>Inclusion criteria</b>  <b>Group A</b> (on Cyclosporine) Number: Age (mean): Sex (M/F):  <b>Group B</b> (on Azathioprine) Number: Age (mean): Sex (M/F):  <b>Exclusions:</b>	Stable kidney transplant recipients with serum creatinine <2mg/dL with hypertension (arterial pressure>105mmHg)  15 37+/-2.4 years 10/5  15 39+/-2.7 years 10/5  Native kidney bilateral nephrectomy Renal artery stenosis diagnosed as cause of hypertension
<b>Interventions</b>	Both groups received the same dietary sodium treatment: 4 days 150mEq sodium diet; 12.5mg dose captopril 4 days sodium restriction: 9mEq sodium diet 3 days: 3.8mEq/kg body weight sodium diet	
<b>Outcomes</b>	<p>1. <i>Mean arterial pressure with sodium restriction of 9mEq</i> Significant decrease in mean arterial pressure in Group A (<math>p&lt;0.01</math>); Compared to Group B, significantly greater change (<math>p&lt;0.001</math>)</p> <p>2. <i>Mean arterial pressure with sodium loading of 3.8mEq/kg body weight</i> No difference between Group A and B</p>	
<b>Notes</b>	Sodium restriction of 9mEq is extreme and not practical outside of experimental, short-term conditions, however study suggests that patients on Cyclosporine are more likely to respond to a sodium restriction than those on Azathioprine.	
<b>Quality checklist</b>	Allocation concealment Blinding Intention to treat analysis Completeness of follow-up	No No Yes 100%

## Management of Diabetes Mellitus

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**Study:** Mathew JT, Rao M, Job V, Ratnaswamy S, Jacob CK. Post-transplant hyperglycaemia: a study of the risk factors. *Nephrology Dialysis Transplantation* 2003; 18: 164-171.

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<b>Methods</b>	Country: Setting/design: Time frame: Level of evidence: Follow-up period: Completeness to follow-up:	India Prospective cohort study 2 years (June 1996 to May 1998) <b>II</b> 25.6 months (+/- 12.8 months) 100%
<b>Participants</b>	<b>Inclusion criteria</b>  - Number: - Age (mean): - Sex (male/female):  <b>Exclusions:</b>	Consecutive, non-diabetic adult ESRF patients awaiting kidney transplantation 174 32.9 +/- 9.7 years 83.6% males  Not described
<b>Study end points</b>	Development of post-transplant diabetes mellitus (PTDM) or impaired glucose tolerance (IGT)	
<b>Outcomes</b>	21.4% (n=38) developed PTDM (74.4% in first 3 months, 90% in first year) 24.1% had IGT after transplant 20.7% had transient abnormality in glucose tolerance after transplant Greater age significantly associated with PTDM Higher rise in BMI significantly associated with PTDM Higher proportion of patients with IGT developed PTDM	

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## Management of Bone Disease

**Study:** El-Agroudy AE, El-Husseini AA, El-Sayed M, Ghoneim MA. Preventing bone loss in renal transplant recipients with vitamin D. *Journal of the American Society of Nephrology* 2003;14(11): 2975-2979

<b>Methods</b>	Country:	Egypt
	Setting/design:	Single Centre
	Time frame:	Not stated
	Level of evidence:	II
	Randomisation method:	Randomised at time of transplantation
	Blinding:	- Participants: No - Investigators: Yes - Outcome Assessors: Not stated - Data analysis: Not stated
	Intention-to-treat:	No
	Follow-up period:	12 months
	Loss to follow-up:	0% lost to follow-up
<b>Participants</b>	<b>Inclusion criteria</b>	Live-donor renal transplant recipients, greater than 20 years, no diabetes, no steroids before transplantation, haemodialysis for not more than 2 years
	<b>Treatment group</b>	
	Number:	20
	Age (mean):	31.4 ± 10.1
	Sex (M/F):	Not stated
	<b>Control group</b>	
	Number:	20
	Age (mean):	31.6 ± 10.7
	Sex (M/F):	Not stated
	<b>Exclusions:</b>	Impaired graft function (serum creatinine >0.18 mmol/L, previous fractures, presence of any other endocrine abnormalities, intake of fluoride, vitamin D or hormones
<b>Interventions</b>	Treatment group:	Alfacalcidol (1-alpha-Hydroxycholecalciferol) 0.5 mg PO
	Control group:	No treatment
	Co-intervention:	Calcium carbonate 500mg
<b>Outcomes</b>	<p>Bone mineral density was increased by 2.1%, 1.8%, and 3.2% at lumbar spine, femoral neck, and forearm, respectively, in treatment group, whereas it decreased by 3.2%, 3.8%, and 1.8% at the same sites in the control group (<math>p &lt; 0.05</math>).</p> <p>Serum intact parathyroid hormone level decreased significantly in treatment group compared with the control group (<math>p = 0.003</math>).</p> <p>Serum calcium values increased significantly in the control group (<math>p &lt; 0.05</math>) and in treatment group (<math>p &lt; 0.001</math>). There was a statistically significant difference between both groups at the end of the study (<math>p &lt; 0.001</math>).</p> <p>iPTH values decreased significantly in treatment group (<math>p &lt; 0.003</math>) compared with the control group (<math>p &lt; 0.09</math>).</p> <p>Hypercalcemia occurred in 1 patient (5%) in the treatment group, which necessitated a reduction in the alfacalcidol dose.</p> <p>The difference between treatment and control groups with respect to serum creatinine values did not reach statistical significance (<math>p = 0.18</math>).</p>	
<b>Notes</b>	No exclusions described	
<b>Quality checklist</b>	Allocation concealment	Unclear
	Blinding	Only the investigators
	Intention to treat analysis	No
	Completeness of follow-up	100%

## Management of Bone Disease (continued)

**Study:** Palmer SC, McGregor DO, Strippoli GFM. Interventions for preventing bone disease in kidney transplant recipients. Cochrane Database of Systematic Reviews 2005, Issue 2.

<b>Methods</b>	Country: Setting/design: Level of evidence:	N/A Systematic Review I
<b>Inclusion criteria</b>	All randomised controlled trials (RCTs) and quasi-RCTs (in which allocation to treatment was obtained by alternation, use of alternate medical records, date of birth or other predictable methods) looking at the treatment options for bone disease following kidney transplantation were included.	
<b>Criteria</b>	Participants:  Interventions:  Outcome measures:	Kidney transplant recipients of any age, receiving any immunosuppression regimen. Recipients of any other transplant were excluded. Bisphosphonates, vitamin D or derivatives, calcitonin and gonadal replacement, fluoride, anabolic steroids; calcium supplementation could also be taken Fracture at any site after transplantation Absolute changes in bone mineral density, presence of low bone turnover, acute graft rejection, end of treatment plasma creatinine, overall mortality. Potential harms of treatment
<b>Conclusions</b>	<ol style="list-style-type: none"> <li>1. Administration of bisphosphonates, vitamin D analogues (with or without calcium) and calcitonin has been the most extensively studied agents.</li> <li>2. No RCT was powered to demonstrate a reduction in the risk of fracture at any site following transplantation.</li> <li>3. Treatment with bisphosphonates, vitamin D analogue and calcitonin all had beneficial effect on the percentage change in bone mineral density at the lumbar spine. Similar results seen at femoral neck (excepting calcitonin).</li> <li>4. Reported toxicity related to treatment was uncommon, and interventions appeared to be well-tolerated.</li> </ol>	
<b>Quality checklist</b>	<ol style="list-style-type: none"> <li>1. Adequate search strategy used.</li> <li>2. Appropriate inclusion criteria applied in an unbiased way.</li> <li>3. Quality assessment of studies undertaken.</li> <li>4. Characteristics of individual studies appropriately summarised.</li> <li>5. Methods for pooling data appropriate.</li> <li>6. Sources of heterogeneity explored.</li> </ol>	

## Management of Bone Disease (continued)

**Study:** Torres A, Garcia S, Gomez A, Gonzalez A, Barrios Y, Concepcion MT, et al. Treatment with intermittent calcitriol and calcium reduces bone loss after renal transplantation. *Kidney Int.* 2004;65(2):705.

<b>Methods</b>	Country: Setting/design: Time frame: Level of evidence: Randomisation method: Blinding:  Intention-to-treat: Follow-up period: Loss to follow-up:	Spain Four centres Not stated I Randomisation at time of transplantation - Participants: Yes - Investigators: Yes - Outcome Assessors Yes - Data Analyses: Yes No 12 months 27%
<b>Participants</b>	<b>Inclusion criteria</b>  <b>Treatment group</b> Number: Age (mean): Sex (M/F):  <b>Control group</b> Number: Age (mean): Sex (M/F):  <b>Exclusions:</b>	Recipient of a first or second renal allograft, older than 20 years  45 46.7 ± 12.2 37/8 Diabetes %: 14(31) Post-menopausal %: 3(7)  41 51.1 ± 11.9 30/11 Diabetics %: 8(20) Post-menopause %: 7(17) Previous parathyroidectomy
<b>Interventions</b>	Treatment group:  Control group:	Calcitriol 0.5 ug alternate days and calcium 1.5 g daily for 3 months then calcium alone for 9 months Calcium 1.5 g daily for 12 months
<b>Outcomes</b>	Serum calcium, phosphorus and creatinine (no significant difference between treatment and control groups)	
<b>Quality checklist</b>	Allocation concealment Blinding Intention to treat analysis Completeness of follow-up	Adequate Yes No 73%

## Management of Hypophosphataemia

**Study:** Ambuhl PM, Meier D, Wolf B, Dydak U, Boesiger P, Binswanger U. Metabolic aspects of phosphate replacement therapy for hypophosphatemia after renal transplantation: impact on muscular phosphate content, mineral metabolism, and acid/base homeostasis. *American Journal of Kidney Diseases* 1999; 34(5): 875-883.

<b>Methods</b>	Country: Setting/design: Level of evidence: Randomisation method: Blinding: - Participants: - Investigators: - Outcome assessors: - Data analysis: Follow-up period:	Switzerland Randomised, controlled trial III-1 Not described Not stated Yes No No No 12 weeks
<b>Participants</b>	<b>Inclusion criteria</b>  <b>Treatment group</b> Number: Age (mean): Sex (M/F):  <b>Control group</b> Number: Age (mean): Sex (M/F):  <b>Exclusions:</b>	Adult stable kidney transplant recipients (with creatinine clearance >30ml/min) with hypophosphataemia (0.3-0.75mmol/L) on at least 2 consecutive occasions without prior phosphate supplementation within 2 weeks of entry to study  14 43.9+/-3.6 10/4 in both groups  14 46.3+/-3.6 10/4  Not stated
<b>Interventions</b>	Treatment group:  Control group: Co-intervention:	Oral neutral phosphate supplementation (Na <sub>2</sub> HPO <sub>4</sub> :NaH <sub>2</sub> PO <sub>4</sub> , with a ratio 4:1) Given NaCl (182mg) instead of phosphate Diet was unrestricted but all patients were encouraged to consume products rich in phosphorus (eg. meat and dairy)
<b>Outcomes</b>	In Treatment Group: corrected serum phosphate, restored muscle phosphate content, increased tissue ATP levels, improved metabolic acidosis. No adverse effects noted	
<b>Notes</b>	No information on dietary phosphate intake	
<b>Quality checklist</b>	Allocation concealment Blinding Intention to treat analysis Completeness of follow-up	No Single (participants only) Yes 100%

## Management of Hypophosphataemia (continued)

**Study:** Caravaca F, Fernández MA, Ruiz-Calero R, Cubero J, Aparico A, Jimenez F, García MC. Effects of oral phosphorus supplementation on mineral metabolism of renal transplant recipients. *Nephrology Dialysis Transplantation*, 1998; 13: 2605-2611.

<b>Methods</b>	Country: Setting/design: Time frame: Level of evidence: Randomisation method: Blinding: Follow-up period:	Spain Single-centre, prospective, pre/post-test Jan-Feb 1997 IV N/A None After 15 days of supplementation
<b>Participants</b>	<b>Inclusion criteria</b>  <b>Treatment group</b> Number: Age (mean): Sex (M/F): Time since transplant:  <b>Exclusions:</b>	Stable graft function, consistent serum creatinine <2mg/dL, serum phosphate <3.5mg/dL at time of study  32 50+/-12 years 17/15 41 +/- 18 months (range: 7-74 months)  Chronic inflammatory infectious, tumoral or liver diseases, diabetes, proteinuria 1g/24h
<b>Interventions</b>	Treatment group:	1 month washout (supplements withdrawn) 750mg Phosphorus Sandoz™ bd, after meals for 15 days No patient received vitamin D, antacids, anticonvulsants, allopurinol or other medications known to affect bone mineral metabolism
<b>Outcomes</b>	1. <i>Serum calcium</i> Decreased in both those with optimal and suboptimal renal function ( $p=0.0003$ ) 2. <i>Serum phosphate</i> Decreased in both those with optimal and suboptimal renal function ( $p=0.0001$ ) 3. <i>Parathyroid hormone concentration</i> Increased in both those with optimal and suboptimal renal function ( $p=0.0001$ ) 4. <i>Serum bicarbonate</i> Decreased ( $p=0.0025$ ) 5. <i>Serum 1,25(OH)<sub>2</sub>D</i> Decreased ( $p=0.0006$ ) 6. <i>Urinary Ca</i> Decreased ( $p=0.0001$ ) 7. <i>Urinary P</i> Increased ( $p=0.0001$ )	
<b>Notes</b>	Suggests potentially negative effect of phosphate supplements.	
<b>Quality checklist</b>	Allocation concealment Blinding Intention to treat analysis Completeness of follow-up	No No Yes 100%

## Management of Anaemia

**Study:** Lorenz M, Wolzt M, Weigel G, Puttinger H, Hörl WH, Födinger M SW, et al. Ferrous sulfate does not affect mycophenolic acid pharmacokinetics in kidney transplant patients. *Am J Kidney Dis.* 2004;43(6):1098.

<b>Methods</b>	Country: Setting/design: Time frame: Level of evidence: Randomisation method: Blinding: - Participants: - Investigators: - Outcome assessors: - Data analysis: Follow-up period:	Austria Single-centre, controlled, randomised, crossover trial May 5, 2002, to June 14, 2002. II Computer-generated sequence Yes Yes Yes Yes N/A
<b>Participants</b>	<b>Inclusion criteria</b>  Number: Age (mean): Sex (M/F):  <b>Exclusions:</b>	Adult kidney transplant recipients with functional iron-deficiency defined as a proportion of hypochromic red blood cells above 2.5%, 2 no current erythropoiesis stimulating therapy, a stable transplant function (estimated creatinine clearance $\geq 30$ mL/min/1.73 m <sup>2</sup> [0.50 mL/s/1.73 m <sup>2</sup> ]), 7,8 no recent acute allograft rejection (within at least 2 months), and time after transplantation of at least 6 months.  10 59 years 6/4  Pregnancy or lactation, hemochromatosis, hemolytic anemia, and preexisting gastrointestinal pathologies that may impair the absorption of MMF or iron
<b>Interventions</b>	Patients were enrolled by 1 of the investigators and randomized to a permuted sequence of the study days A (MMF only), B (MMF only), C (MMF _ ferrous sulfate simultaneously), and D (MMF _ ferrous sulfate after 4 hours). The washout period between study days was 3 to 14 days.	
<b>Outcomes</b>	The primary outcome was defined as the AUC from 0 to 12 hours (AUC <sub>0-12</sub> ) of mycophenolic acid. A reduction of the bioavailability of mycophenolic acid by 66% as assessed from the change in AUC <sub>0-12</sub> following coadministration of ferrous sulfate with MMF was regarded as a clinically relevant pharmacokinetic interaction. Secondary outcome variables included AUC from 0 to 4 hours (AUC <sub>0-4</sub> ), AUC from 4 to 12 hours AUC (AUC <sub>4-12</sub> ), the absorption rate constant (k <sub>a</sub> ), the maximum plasma concentration (C <sub>max</sub> ), and the time of C <sub>max</sub> after peroral administration of MMF (t <sub>max</sub> ) of mycophenolic acid.	
<b>Notes</b>	According to the study results, a single dose of oral ferrous sulfate (Ferro-Gradumet) administered together with MMF has no effect on systemic mycophenolate exposure in stable adult kidney graft recipients.	
<b>Quality checklist</b>	Allocation concealment Blinding	Yes Yes

## Management of Anaemia (continued)

**Study:** Lorenz M, Kletzmayr J, Perschl A, Furrer A, Horl WH, Sunder-Plassman G. Anemia and iron deficiencies among long-term renal transplant recipients. *J Am Soc Nephrol.* 2002;13(3):794-7.

<b>Methods</b>	Country:	Austria
	Setting/design:	Prospective cross-sectional, single centre (outpatient service)
	Time frame:	4 weeks
	Level of evidence:	II

<b>Participants</b>	<b>Inclusion criteria</b>	Adult kidney transplant recipients with stable graft function who visited the outpatient service during the four week study period. Anaemia defined as serum haemoglobin level <12g/dL (females); <13g/dL (males)
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Number:	438
Age (mean):	51.6
Sex (M/F):	261/177

<b>Exclusions:</b>	Not described
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<b>Outcomes</b>	Prevalence of anaemia: n=174 (39.7%) – 37.9% of males; 42.4% of females
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Iron-deficiency indicated by hypochromic red blood cells (HRBC) (>2.5%) was present in 20.1% of all patients ( 14.9% of males; 27.7% of females).

Among anaemic patients, HRBC elevations were more frequent than hypoferritinaemia or decreased transferrin saturation (TSAT). The majority of patients with severe anaemia (Hb<11g/dL) presented with HRBC values in the highest quartile.

Only 10.1% of severely anaemic patients presented with serum ferritin levels of <12ug/L and just 29% of severely anaemic patients presented with TSAT levels of <15%.

In contrast 52.2% of patients with severe anaemia presented with HRBC values of >2.5%.

The authors question the validity of using ferritin and TSAT to screen for iron deficiency.

<b>Notes</b>	Suggests potentially negative effect of phosphate supplements.
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<b>Quality checklist</b>	Allocation concealment	No
	Blinding	No





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