KDIGO Clinical Practice Guideline for the Care of Kidney Transplant Recipients

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http://www3.interscience.wiley.com/journal/118499698/toc

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SECTION I: USE OF THE CLINICAL PRACTICE GUIDELINE

This Clinical Practice Guideline document is based upon the best information available as of March 2009. It is designed to provide information and assist decision-making. It is not intended to define a standard of care, and should not be construed as one, nor should it be interpreted as prescribing an exclusive course of management.

Variations in practice will inevitably and appropriately occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every health-care professional making use of these recommendations is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation. The recommendations for research contained within this document are general and do not imply a specific protocol.

SECTION II: DISCLOSURE

Kidney Disease: Improving Global Outcomes (KDIGO) makes every effort to avoid any actual or reasonably perceived conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the Work Group.

All members of the Work Group are required to complete, sign, and submit a disclosure and attestation form showing all such relationships that might be perceived or actual conflicts of interest. This document is updated annually and information is adjusted accordingly. All reported information is published in its entirety at the end of this document in the Work Group members' Biographic and Disclosure Information section, and is on file at the National Kidney Foundation (NKF), Managing Agent for KDIGO.

KDIGO gratefully acknowledges the following sponsors that make our initiatives possible: Abbott, Amgen, Belo Foundation, Coca-Cola Company, Dole Food Company, Genzyme, Hoffmann-LaRoche, JC Penney, NATCO-The Organization for Transplant Professionals, National Kidney Foundation-Board of Directors, Novartis, Robert and Jane Cizik Foundation, Shire, Transwestern Commercial Services, and Wyeth. KDIGO is supported by a consortium of sponsors and no funding is accepted for the development of specific guidelines.

Work Group Membership

Work Group Co-Chairs

Bertram L. Kasiske, MD
Hennepin County Medical Center
Minneapolis, MN

Martin G. Zeier, MD, FASN
University Hospital of Heidelberg
Heidelberg, Germany

Work Group

Jonathan C. Craig, MBChB, MM (Clin Epi), DCH, FRACP, PhD
The Children's Hospital at Westmead
Westmead, Australia

Henrik Ekberg, MD, PhD
Lund University
Malmö, Sweden

Catherine A. Garvey, RN, BA, CCTC
University of Minnesota
Minneapolis MN

Michael D. Green, MD, MPH
Children's Hospital of Pittsburgh
Pittsburgh, PA

Vivekanand Jha, MD, FRCP
Postgraduate Medical Institute
Chandigarh, India

Michelle A. Josephson, MD
University of Chicago
Chicago, IL

Bryce A. Kiberd, MD
Dalhousie University
Halifax, Canada

Henri A. Kreis, MD
Université Paris Descartes &
Hôpital Necker
Paris, France

Ruth A. McDonald, MD
University of Washington
Seattle Children's Hospital
Seattle, WA

John M. Newmann, PhD, MPH
Health Policy Research & Analysis
Reston, VA

Gregorio T. Obrador, MD, MPH
Universidad Panamericana School of Medicine
Mexico City, Mexico

Liaison to The Transplantation Society and the Global Alliance of Transplantation:
Jeremy R. Chapman, MD, FRACP, FRCP
Westmead Hospital
Westmead, Australia

Liaison to the American Society of Transplantation
Flavio G. Vincenti, MD
University of California at San Francisco
San Francisco, CA

Evidence Review Team

Tufts Center for Kidney Disease Guideline Development and Implementation, Tufts Medical Center, Boston, MA, USA:

Ethan M. Balk, MD, MPH, Project Director and Director, Evidence-based Medicine
Martin Wagner, MD, MS, Assistant Project Director
Gowri Raman, MD, Research Fellow
Samuel Abariga, MD, MS, Research Associate
Amy Earley, BS, Project Coordinator

In addition, support and supervision were provided by:

Katrin Uhlig, MD, MS, Director, Guideline Development
Joseph Lau, MD, Methods Consultant

Work Group Member Expertise and Disclosure Information

Work Group Member	Area of Expertise	Disclosures
Bertram L. Kasiske, MD Work Group Co-Chair; USA	Transplant Nephrologist	*Advisor/Consultant:* *Astellas; LithoLink; Novartis; Wyeth* *Grant/Research Support:* *Bristol-Myers Squibb; Genzyme; Merck-Schering Plough*
Martin G. Zeier, MD, FASN Work Group Co-Chair; Germany	Transplant Nephrologist	*Grant/Research Support:* *Astellas; Novartis; Parexel*
Jeremy R. Chapman, MD, FRACP, FRCP Australia	Transplant Nephrologist; Liaison for The Transplantation Society and the Global Alliance for Transplantation	*Advisor/Consultant:* *Astellas; Hoffmann-LaRoche; Novartis; Wyeth* *Grant/Research Support:* *Bristol-Myers Squibb; Novartis; Wyeth*
Jonathan C. Craig, MBChB, MM (Clin Epi), DCH, FRACP, PhD Australia	Pediatrician, Transplant Nephrologist	*No relevant financial relationships reported.*
Henrik Ekberg, MD, PhD Sweden	Transplant Surgeon	*Advisor/Consultant:* *Astellas; Bristol-Myers Squibb; Hansa Medical; Hoffmann-LaRoche; Life Cycle Pharma; Novartis; Wyeth* *Speaker: Astellas; Hoffmann-LaRoche*
Catherine A. Garvey, RN, BA, CCTC USA	Transplant Coordinator	*No relevant financial relationships reported.*
Michael D. Green, MD, MPH USA	Pediatrician, Transplant Infectious Disease Specialist	*No relevant financial relationships reported.*
Vivekanand Jha, MD, FRCP India	Transplant Nephrologist	*No relevant financial relationships reported.*
Michelle A. Josephson, MD USA	Transplant Nephrologist	*Advisor/Consultant:* *Digitas Health; MKSAP; Wyeth* *Speaker: Hoffmann-LaRoche* *Grant/Research Support:* *Amgen; Astellas; Wyeth*
Bryce A. Kiberd, MD Canada	Transplant Nephrologist	*Speaker: Hoffmann-LaRoche*
Henri A. Kreis, MD France	Transplant Nephrologist	*Advisor/Consultant: Novimmune*
Ruth A. McDonald, MD USA	Pediatrician, Transplant Nephrologist	*No relevant financial relationships reported.*
John M. Newmann, PhD, MPH USA	Transplant Recipient	*Advisor/Consultant:* *Arbor Research Collaborative; Renaissance Health Care*
Gregorio T. Obrador, MD, MPH Mexico	Transplant Nephrologist	*No relevant financial relationships reported.*
Flavio G. Vincenti, MD USA	Transplant Nephrologist; Liaison for the American Society of Transplantation	*Grant/Research Support:* *Astellas; Bristol-Myers Squibb; Genentech; Hoffmann-LaRoche; Novartis; Wyeth*

KDIGO Board Members

Garabed Eknoyan, MD
Norbert Lameire, MD
Founding KDIGO Co-Chairs

Kai-Uwe Eckardt, MD
KDIGO Co-Chair

Bertram L. Kasiske, MD
KDIGO Co-Chair

Omar I. Abboud, MD, FRCP
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Sharon P. Andreoli, MD
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Fred Brown, MBA, FACHE
Jerilynn D. Burrowes, PhD, RD
Evelyn Butera, MS, RN, CNN
Daniel Cattran, MD, FRCPC
Allan J. Collins, MD, FACP
Ricardo Correa-Rotter, MD
William G. Couser, MD
Olivier Coustere
Adrian Covic, MD, PhD
Jonathan C. Craig, MBChB, MM (Clin Epi), DCH, FRACP, PhD
Angel de Francisco, MD
Paul de Jong, MD
Tilman B. Drüeke, MD, FRCP
Denis P. Fouque, MD, PhD
Gordon Guyatt, MD, MSc, BSc, FRCPC
Philip Halloran, MD, PhD
David Harris, MD
Michel Jadoul, MD
Vivekanand Jha, MD, FRCP
Martin K. Kuhlmann, MD
Suhnggwon Kim, MD, PhD
Adeera Levin, MD, FRCPC
Nathan W. Levin, MD, FACP
Philip K.T. Li, MD, FRCP, FACP
Zhi-Hong Liu, MD
Francesco Locatelli, MD
Alison M. MacLeod, MBChB, MD, FRCP
Pablo Massari, MD
Peter A. McCullough, MD, MPH, FACC, FACP, FCCP, FAHA
Rafique Moosa, MD
Miguel C. Riella, MD
Bernardo Rodriquez-Iturbe, MD
Robert Schrier, MD
Trent Tipple, MD
Yusuke Tsukamoto, MD
Raymond Vanholder, MD
Giancarlo Viberti, MD, FRCP
Theodor Vogels, MSW
David Wheeler, MD, FRCP
Carmine Zoccali, MD

KDIGO Guideline Development Staff

Kerry Willis, PhD, Senior Vice-President for Scientific Activities
Donna Fingerhut, Managing Director of Scientific Activities
Michael Cheung, Guideline Development Director
Dekeya Slaughter-Larkem, Guideline Development Project Manager
Sean Slifer, Scientific Activities Manager

Abbreviations and Acronyms

ACCORD	Action to Control Cardiovascular Risk in Diabetes
ACE-I	Angiotensin-converting enzyme inhibitor
ADA	American Diabetes Association
ADVANCE	Action in Diabetes and Vascular Disease
AGREE	Appraisal of Guidelines for Research and Evaluation
ALG	Antilymphocyte globulin
ALT	Alanine aminotransferase
ANCA	Antineutrophil cytoplasmic antibody
ARB	Angiotensin II receptor blocker
ATG	Antithymocyte globulin
AUC	Area under concentration-time curve
BCG	Bacillus Calmette-Guérin
BKV	BK polyoma virus
BMD	Bone mineral density
BMI	Body mass index
CAD	Coronary artery disease
CAI	Chronic allograft injury
CAN	Chronic allograft nephropathy
CCB	Calcium-channel blocker
CDC	US Centers for Disease Control and Prevention
CHF	Congestive heart failure
CI	Confidence Interval
CKD	Chronic kidney disease
CKD-MBD	Chronic kidney disease–mineral and bone disorder
CMV	Cytomegalovirus
CNI	Calcineurin inhibitor
COGS	Conference on Guideline Standardization
CsA	Cyclosporine A
CsA-ME	Cyclosporine A microemulsion
CSF	Colony-stimulating factor
CVD	Cardiovascular disease
CYP3A4	Cytochrome P450 3A4
D	Transplant donor
DGF	Delayed graft function
EBV	Epstein-Barr virus
EC-MPS	Enteric-coated mycophenolate sodium
eGFR	Estimated glomerular filtration rate
ELISA	Enzyme-linked immunosorbent assay
ERT	Evidence Review Team
ESA	Erythropoiesis-stimulating agent
FDA	Food and Drug Administration
FOBT	Fecal occult blood testing
FSGS	Focal segmental glomerulosclerosis
GBM	Glomerular basement membrane
GFR	Glomerular filtration rate
HbA_{1c}	Hemoglobin A_{1c}
HBcAb	Antibody to hepatitis B core antigen
HBeAg	Hepatitis B E antigen
HBsAb	Antibody to hepatitis B surface antigen
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HDL-C	High-density lipoprotein cholesterol
HIV	Human immunodeficiency virus
HLA	Human leukocyte antigen
HPV	Human papillomavirus
HSV	Herpes simplex virus
HUS	Hemolytic-uremic syndrome
IgA	Immunoglobulin A
IgG	Immunoglobulin G
IL2	Interleukin 2
IL2-RA	Interleukin-2 receptor antagonist
IF/TA	Interstitial fibrosis and tubular atrophy
KDIGO	Kidney Disease: Improving Global Outcomes
KDOQI	Kidney Disease Outcomes Quality Initiative
KTR	Kidney transplant recipient
LDL-C	Low-density lipoprotein cholesterol
MMF	Mycophenolate mofetil
MPA	Mycophenolic acid
MPGN	Membranoproliferative glomerulonephritis
mTORi	Mammalian target of rapamycin inhibitor(s)
NAT	Nucleic acid testing
NIH	National Institutes of Health
NKF	National Kidney Foundation
NODAT	New-onset diabetes after transplantation
OKT3	Muromonab (anti–T-cell antibody)
PTH	Parathyroid hormone
PCP	*Pneumocystis jirovecii* pneumonia
PPD	Purified protein derivative
PRA	Panel-reactive antibody
PSA	Prostate-specific antigen
PTLD	Post-transplant lymphoproliferative disease
PVD	Peripheral vascular disease
R	Transplant recipient
RCT	Randomized controlled trial
RR	Relative risk
rhGH	Recombinant human growth hormone
SIR	Standardized incidence ratio
TB	Tuberculosis
UKPDS	United Kingdom Prospective Diabetes Study
USPSTF	US Preventive Services Task Force
UTI	Urinary tract infection
VZV	Varicella zoster virus
WHO	World Health Organization

Reference Keys

NOMENCLATURE AND DESCRIPTION FOR RATING GUIDELINE RECOMMENDATIONS

Within each recommendation, the strength of recommendation is indicated as **Level 1**, **Level 2**, or **Not Graded**, and the quality of the supporting evidence is shown as **A**, **B**, **C**, or **D**.

Grade*	Implications		
	Patients	**Clinicians**	**Policy**
Level 1 'We recommend'	Most people in your situation would want the recommended course of action and only a small proportion would not.	Most patients should receive the recommended course of action.	The recommendation can be adopted as a policy in most situations.
Level 2 'We suggest'	The majority of people in your situation would want the recommended course of action, but many would not.	Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences.	The recommendation is likely to require debate and involvement of stakeholders before policy can be determined.

* The additional category 'Not Graded' was used, typically, to provide guidance based on common sense or where the topic does not allow adequate application of evidence. The most common examples include recommendations regarding monitoring intervals, counseling, and referral to other clinical specialists. The ungraded recommendations are generally written as simple declarative statements, but are not meant to be interpreted as being stronger recommendations than Level 1 or 2 recommendations.

A: High quality of evidence. We are confident that the true effect lies close to that of the estimate of the effect.
B: Moderate quality of evidence. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
C: Low quality of evidence. The true effect may be substantially different from the estimate of the effect.
D: Very low quality of evidence. The estimate of effect is very uncertain, and often will be far from the truth.

Conversion Factors of Metric Units to SI Units

Parameter	Metric Units	Conversion Factor	SI Units
Albumin	g/dL	10	g/L
Calcium	mg/dL	0.2495	mmol/L
Cholesterol	mg/dL	0.02586	mmol/L
Creatinine	mg/dL	88.4	µmol/L
Creatinine clearance	mL/min	0.01667	mL/s
Glucose	mg/dL	0.05551	mmol/L
Hemoglobin	g/dL	10	g/L
High-density lipoprotein cholesterol (HDL-C)	mg/dL	0.02586	mmol/L
Insulin	µU/mL	7.175	pmol/L
Low-density lipoprotein cholesterol (LDL-C)	mg/dL	0.02586	mmol/L
Neutrophil count	#/µL	1×10^6	#/L
Parathyroid hormone	pg/mL	1	ng/L
Phosphate (as inorganic phosphorus)	mg/dL	0.3229	mmol/L
Platelet count	#/µL	1×10^6	#/L
Protein, total	g/dL	10	g/L
Titers	copies/mL	1000	copies/L
Triglycerides	mg/dL	0.01129	mmol/L
Uric acid	mg/dL	59.48	µmol/L
Urinary oxalate excretion	mg/dL	11.11	µmol/d
Urinary protein excretion	g/dL	1000	mg/dL
Vitamin D, 25-Hydroxyvitamin D	ng/mL	2.496	nmol/L

Note: Metric unit x conversion factor = SI unit.

American Journal of Transplantation 2009; 9 (Suppl 3): S1–S157
Wiley Periodicals Inc.

doi: 10.1111/j.1600-6143.2009.02834.x

Abstract

The 2009 Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guideline on the monitoring, management, and treatment of kidney transplant recipients is intended to assist the practitioner caring for adults and children after kidney transplantation. The guideline development process followed an evidence-based approach, and management recommendations are based on systematic reviews of relevant treatment trials. Critical appraisal of the quality of the evidence and the strength of recommendations followed the Grades of Recommendation Assessment, Development, and Evaluation (GRADE) approach. The guideline makes recommendations for immunosuppression, graft monitoring, as well as prevention and treatment of infection, cardiovascular disease, malignancy, and other complications that are common in kidney transplant recipients, including hematological and bone disorders. Limitations of the evidence, especially on the lack of definitive clinical outcome trials, are discussed and suggestions are provided for future research.

Keywords: Guideline; KDIGO; kidney transplant recipient care; immunosuppression; graft monitoring; infectious diseases; cardiovascular disease; malignancy; mineral and bone disorder; hematological complications; hyperuricemia; gout; growth; sexual function; fertility; mental health

In citing this document, the following format should be used: Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group. KDIGO clinical practice guideline for the care of kidney transplant recipients. *American Journal of Transplantation* 2009; 9(Suppl 3): S1–S157.

Foreward

Since the first successful kidney transplantation in 1954, there has been an exponential growth in publications dealing with the care of kidney transplant recipients (KTRs). In addition, the science of conducting and interpreting both clinical trials and observational studies has become increasingly controversial and complex. Caring for KTRs requires specialized knowledge in areas as varied as immunology, pharmacology, nephrology, endocrinology and infectious disease. The last two comprehensive clinical practice guidelines on the care of KTRs were published in 2000 by the American Society of Transplantation and the European Best Practices Guidelines Expert Group. Both of these guidelines were based primarily on expert opinion, not rigorous evidence review. For these reasons, the international consortium of kidney guideline developers, Kidney Disease: Improving Global Outcomes (KDIGO), concluded that a new comprehensive evidence-based clinical practice guideline for the care of KTRs was necessary.

It is our hope that this document will serve several useful purposes. Our primary goal is to improve patient care. We hope to accomplish this in the short term by helping clinicians know and better understand the evidence (or lack of evidence) that determines current practice. By making this guideline broadly applicable, our purpose is to also encourage and enable the establishment and development of transplant programs worldwide. Finally, by providing comprehensive evidence-based recommendations, this guideline will also help define areas where evidence is lacking and research is needed. Helping to define a research agenda is an often neglected, but very important function of clinical practice guideline development.

We used the GRADE system to rate the strength of evidence and the strength of recommendations. In all, there were only 4 (2%) recommendations in this guideline for which the overall quality of evidence was graded 'A,' whereas 27 (13.6%) were graded 'B,' 77 (38.9%) were graded 'C,' and 90 (45.5%) were graded 'D.' Although there are reasons other than quality of evidence to make a grade 1 or 2 recommendation, in general, there is a correlation between the quality of overall evidence and the strength of the recommendation. Thus, there were 50 (25.3%) recommendations graded '1' and 148 (74.7%) graded '2.' There were 3 (1.5%) recommendations graded '1A,' 16 (8.1%) were '1B,' 18 (9.1%) were '1C,' and 13 (6.6%) were '1D.' There was 1 (0.5%) graded '2A,' 11 (5.6%) were '2B,' 59 (29.8%) were '2C,' and 77 (38.9%) were '2D.' There were 45 (18.5%) statements that were not graded.

Some argue that recommendations should not be made when evidence is weak. However, clinicians still need to make clinical decisions in their daily practice, and they often ask 'what do the experts do in this setting'? We opted to give guidance, rather than remain silent. These recommendations were often rated with a low strength of recommendation and a low strength of evidence, or were not graded. It is important for the users of this guideline to be cognizant of this (see Disclaimer). In every case these recommendations are meant to be a place for clinicians to start, not stop, their inquiries into specific management questions pertinent to the patients they see in daily practice.

We wish to thank Martin Zeier, Co-Chair, along with all of the Work Group members who volunteered countless hours of their time developing this guideline. We also thank the Evidence Review Team members and staff of the National Kidney Foundation who made this project possible. Finally, we owe a special debt of gratitude to the many KDIGO Board members and individuals who volunteered time reviewing the guideline, and making very helpful suggestions.

Kai-Uwe Eckardt, MD
KDIGO Co-Chair

Bertram L. Kasiske, MD
KDIGO Co-Chair

Guideline Scope and Intended Users

This guideline describes the prevention and treatment of complications that occur after kidney transplantation. We do not include pretransplant care. Specifically, we do not address issues pertinent to the evaluation and management of candidates for transplantation, or the evaluation and selection of kidney donors.

Although many of the issues that are pertinent to KTRs are also pertinent to recipients of other organ transplants, we intend this guideline to be for KTRs only. We cover only those aspects of care likely to be different for KTRs than for patients in the general population. For example, we deal with the diagnosis and treatment of acute rejection, but not with the diagnosis and treatment of community-acquired pneumonia. We also make recommendations pertinent to the management of immunosuppressive medications and their complications, including infections, malignancies, and cardiovascular disease (CVD).

This guideline ends before the kidney fails, either by death of the recipient with a functioning graft, return to dialysis, or retransplantation. We do not deal with the preparation of KTRs for return to dialysis or retransplantation.

This guideline was written for doctors, nurses, coordinators, pharmacists, and other medical professionals who directly or indirectly care for KTRs. It was not developed for administrative or regulatory personnel per se. For example, no attempts were made to develop clinical performance measures. Similarly, this guideline was not written for patients directly, although carefully crafted explanations of guideline recommendations could potentially provide useful information for patients.

This guideline was written for transplant-care providers throughout the world. As such, it addresses issues that are important to the care of KTRs in both developed and developing countries, but nowhere was the quality of care compromised for utilitarian purposes. Nevertheless, we recognize that, in many parts of the world, treatment of end-stage kidney disease (chronic kidney disease [CKD] stage 5) with dialysis is not feasible, and transplantation can only be offered as a life-saving therapy if it is practical and cost-effective. Therefore, in providing a comprehensive, evidence-based guideline for the care of the KTRs, we were cognizant of the fact that programs in some areas of the world may need to adopt cost-saving measures in order to make transplantation possible.