

Critical Appraisal of International Clinical Practice Guidelines in Kidney Transplantation Using the Appraisal of Guidelines for Research and Education (AGREE) II Tool: A Systematic Review

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AUTHORSHIP PAGE

Authorship

KO, RR, SK, JO, PM and LP were involved in the concept and design of the systematic review. KO and LP designed the search strategy. KO and RR screened search results for relevant full-texts and these were checked by LP. KO and RR performed the data extraction. All authors were involved in the critical appraisal of guidelines with AGREE II. KO wrote the initial drafts of the manuscript and these were revised by LP. All authors critically revised the final draft of the manuscript. KO had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. KO is guarantor.

Disclosure

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and the authors declare no conflicts of interest.

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ABBREVIATIONS PAGE

AGREE II - Appraisal of Guidelines for Research and Evaluation II

CPG – Clinical Practice Guideline

Ktx – Kidney Transplantation

NHS - National Health Service

NICE - National Institute for Health and Care Excellence

UK – United Kingdom

WHO - World Health Organization

ABSTRACT

Background: Whilst Clinical Practice Guidelines (CPGs) are used for the development of local protocols in kidney transplantation (Ktx), the quality of their methodology is variable. This systematic review aimed to critically appraise international CPGs in all aspects of Ktx using the Appraisal of Guidelines for Research and Evaluation (AGREE) II tool. **Methods:** CPGs in Ktx and donation published between 2010 and 2017 were identified from MEDLINE, Embase, National Guideline Clearinghouse, NHS and NICE Evidence Searches, and the websites of transplant societies. Using AGREE II, 3 appraisers assessed the quality of CPGs. Interrater reliability was measured using the intraclass correlation coefficient (ICC). **Results:** Searches identified 3,168 records and 115 CPGs were included. The highest scoring AGREE II domain was 'Scope and Purpose' (80%; Range 30-100%), followed by 'Clarity of Presentation' (77%; Range 43-98%), 'Editorial independence' (52%; Range 0-94%), 'Rigour of Development' (47%; Range 6-97%) and 'Stakeholder Involvement' (41%; Range 11-85%). The poorest scoring domain was 'Applicability' (31%; Range 3-74%). Most CPGs were recommended for future use either with (63%) or without modifications (18%). A small number were not recommended for future use (14%) or reviewers did not agree on recommending the CPG (5%). The overall mean CPG quality score was 4 out of 7 (Range 2-7). The mean ICC of 0.74 indicated substantial agreement between reviewers. **Conclusions:** The quality of international CPGs in Ktx was variable, and most CPGs lacked key aspects of methodological robustness and transparency. Improvements in methodology, patient involvement and strategies for implementation are required.

Introduction

Kidney donation and transplantation are complex and evolving fields. Over 84,000 kidney transplants were estimated as carried out globally in 2015, based on the Global Observatory on Donation and Transplantation data, produced by the WHO-ONT collaboration.¹ Clinical Practice Guidelines (CPGs), defined as “systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances”² are essential for the development of protocols in transplant centres. CPGs should be evidence-based and of high quality to ensure these protocols reflect a good standard of clinical care and drive improvements in patient and clinical outcomes.

Variability in the quality of United Kingdom (UK) CPGs in all aspects of kidney transplantation however has been previously identified.³ Using the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument, the methodological rigour and transparency of 13 UK CPGs published between 2010 and 2017 were critically assessed. UK CPGs scored satisfactorily overall but considerable variation in domain scores both within and across CPGs were identified. In another study, also using AGREE II, the quality of 13 CPGs for malignancy screening among solid organ transplant recipients were shown to demonstrate considerable variability and weakness in quality.⁴ The quality of 10 evidence-based CPGs and consensus statements focussed on the screening and follow-up of living kidney donors published between 1996-2010 from Australia, UK, United States, Continental Europe, and Canada were also shown to lack methodological rigour when examined with AGREE, an earlier model of the AGREE II.⁵

The aim of this systematic review was to critically appraise international CPGs on all aspects of kidney transplantation and donation. The AGREE II was used to assess the methodological rigour and transparency of the guideline development process.

Methods

Identification of CPGs

This systematic review of international CPGs was registered with the PROSPERO database of systematic review protocols (PROSPERO ID: CRD42015027356). The review was reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The methods for this systematic review have been previously described.³ Briefly, relevant CPGs published from 2010 until April 2017 were identified via MEDLINE, Embase, and the National Guideline Clearinghouse and the National Health Service (NHS) and National Institute for Health and Care Excellence (NICE) evidence search platform. The full search strategy is provided in Materials and Methods, SDC, <http://links.lww.com/TP/B574>. Searches included keywords and MeSH terms for kidney transplantation, combined with terms for CPGs and were limited to the English language. In addition, 1 author (KO) manually searched the websites of international transplantation and nephrology societies, the United States Public Health Service and the World Health organization (WHO). A full list of included societies is available in Materials and Methods, SDC, <http://links.lww.com/TP/B574>. Included CPGs from these searches were checked by a second author (LP).

CPGs and consensus statements published by international societies or experts where the main aim of the paper was to provide guidelines and/or recommendations specific to kidney transplantation or kidney donation were included. Where multiple versions of a CPG were identified, the most recent full publication was included. Papers not aimed specifically for kidney transplantation were included if they comprised a chapter designated to kidney transplantation. Two authors (KO and RR) independently reviewed the abstracts of all potentially eligible studies and made the final selection of studies to include based on their full texts. The same 2 authors independently extracted the following data from all included

studies: author, year, title, organisation, funding body and whether patients had been involved in the preparation of the guideline. Patient involvement was considered met if the guideline explicitly described that a patient representative was included in the working group and contributed to the development of the CPG.

Critical Appraisal with AGREE II

The AGREE II and the method used to critically appraise CPGs with AGREE II has been previously described in detail.³ Briefly, the AGREE II consists of 23 items organised into the following 6 quality domains: i) Scope and Purpose, ii) Stakeholder Involvement, iii) Rigour of Development, iv) Clarity of Presentation, v) Applicability, and vi) Editorial Independence (see Materials and Methods, SDC, <http://links.lww.com/TP/B574>), in addition to 2 overall items. Each of the 23 items are scored on a 7 point Likert scale from 1 (strongly disagree) to 7 (strongly agree) and a domain score is calculated which involves summing up all of the scores of the individual items in a domain and scaling the total as a percentage of the maximum possible score for that domain (Range: 0-100%). For the first overall item, appraisers rate the quality of the entire CPG on the same Likert scale. For the second overall item, appraisers decide whether they would consider the CPG appropriate for future use, and answer with either 'Yes', 'Yes with Modifications', or 'No'.⁶

Each CPG was critically evaluated by 3 appraisers, including 1 transplant clinician and 2 methodologists using AGREE II. All appraisers completed the AGREE II Tutorial and Practice Exercise before commencing the critical appraisal of CPGs.

Appraisers were asked to review and where appropriate revise their initial ratings on any item where their score differed to the other 2 appraisers' scores by ≥ 5 points (ie, 1 or 2 versus 7 and 1 versus 6). Initial and adjusted scores were calculated and results presented are those of adjusted scores.

Interrater Reliability

The Intraclass Correlation Coefficient (ICC) was used to calculate interrater reliability.⁷ Two-way mixed model statistical analyses were performed using MedCalc for Windows, version 15.11.0.⁸ The ICC analysis included average measures for absolute agreement and the degree of agreement was quantified using the following definitions: ICC= <0.20, slight agreement; ICC=0.21-0.40, fair agreement; ICC=0.41-0.60, moderate agreement; ICC=0.61-0.80, substantial agreement; 0.81-1.00, almost perfect agreement.⁹

Results

Included Studies

Systematic searches resulted in 3168 records of which 115 CPGs were subsequently included in this systematic review.¹⁰⁻¹²⁵ A literature flow diagram is shown in Figure 1.

CPGs were developed in the following countries; Australia (n=35), Australia & New Zealand (n=2), Brazil (n=1), Canada (n=4), Denmark (n=1), Europe (n=9), Europe & USA (n=1), France (n=2), Germany (n=2), India (n=2), International (n=7), Iran (n=1), Italy (n=1), Japan (n=3), Nordic Countries (n=1), Spain (n=6), United Kingdom (n=16), USA (n=20) and USA & Canada (n=1). The majority of CPGs were from developed countries (97%) according to the International Statistical Institute World Bank Country Classifications¹²⁶ with a small minority from the developing countries Brazil, Iran and India (3%).

The highest number CPGs were published in 2010 (n=25), the remainder in 2011 (n=19), 2012 (n=9), 2013 (n=15), 2014 (n=13), 2015 (n=15), 2016 (n=16) and 2017 (n=3).

CPGs were categorised according to their main topic, and most CPGs were published on living donation (n=22). Other categories included infections (n=18), recipient care (n=15), recipient assessment (n=9), deceased donation (n=9), nutrition (n=9), cardiovascular and lipid complications (n=6), antibodies (n=4), immunosuppression (n=3), mixed aspects of

transplantation including CPGs reporting on multiple aspects of transplantation (n=6), imaging and biopsies (n=5), and other aspects of transplantation (n=9).

Domain Scores

Domain scores and overall scores, including mean and ranges are shown in Table 1. The highest domain score across all CPGs was 'Scope and Purpose' (80%; range 30-100%), followed by 'Clarity of Presentation' (77%; range 43-98%), 'Editorial independence' (52%; range 0-94%), 'Rigour of Development' (47%; range 6-97%), 'Stakeholder Involvement' (41%; range 11-85%) and 'Applicability' (31%; range 3-74%). Domain scores and overall scores for all CPGs are plotted in Figure 2. 'Editorial independence' had the largest range of scores, whilst 'Clarity of Presentation' had the smallest range.

Overall Scores

The overall score ranged from 2-7 out of 7 across CPGs. 51 CPGs scored ≥ 5 (44%), whilst 64 scored < 5 (56%).

Overall, 72 CPGs were recommended for future use with modifications (63%), 21 were recommended for use without modifications (18%), 16 were not recommended (14%) and for 6 CPGs, appraisers did not agree whether the CPG should be recommended (5%).

Individual Item scores

The highest and lowest scoring individual items are shown in Table 2. Mean compliance to AGREE items ranged from 28% to 86%. The largest range in appraiser scores for 1 item was for 'a procedure for updating the guideline is provided' (10-100%).

Patient Involvement and Funding Body

Only 6 CPGs explicitly described in the guideline document that a patient representative was included in the working group and had contributed to the development of the guideline.

The majority of CPGs (n=71) did not describe sources of funding for the development of the CPG. Of those that described funding sources (n=44), the majority were funded by nonindustry (n=27), followed by industry (n=7), a mixture of industry and nonindustry (n=4), whilst 6 CPGs stated that no funding was received.

Interrater Reliability

The Intraclass Correlation Coefficient across CPGs ranged from 0.28 to 0.92 indicating a fair to almost perfect level of interrater agreement. The average interrater reliability was substantial at 0.74.

Original scores

Ninety-three item score adjustments occurred across CPGs. Score adjustments most commonly occurred in the domain 'Editorial Independence', specifically for item 22 (The views of the funding body have not influenced the content of the guideline). Item score adjustments did not alter the average domain scores across CPGs, and there was only 1 difference in the order from highest to lowest scoring items. Item 10 (The methods for formulating the recommendations are clearly described) moved up from from 15th to 14th position and item 22 moved down from 14th to 15th position. There were no adjustments across CPGs for the 2 overall ratings.

Discussion

Variability in the methodology and quality of 115 CPGs in kidney transplantation was found in this systematic review. The highest scoring domain was ‘Scope and Purpose’ followed by ‘Clarity of presentation’, which is consistent with previous international studies where these domains have also scored highest.^{3-5,127,128} These 2 domains are important because they look at the overall language, structure, and format of the guideline as well as the overall aim, health questions, and target population. Simple, easy to understand CPGs appear to be the most accessed by clinicians and more likely to be implemented.¹²⁹⁻¹³¹ The majority of CPGs adhered well to the items within these domains, indicating that guideline developers worldwide may understand the value and importance of these components. It may also be that the fulfilment of these components does not require a large amount of resources.¹³² It is encouraging that guideline developers are getting these aspects correct, as without adherence to these domains, CPGs may form cumbersome, complex documents that are likely ineffectual in clinical practice.

The poorest scoring domain was ‘applicability’ which is consistent with previous studies.^{3-5,127} All items in this domain scored poorly across CPGs. The ‘applicability’ domain examines whether CPGs have provided advice or tools for putting recommendations into practice, described facilitators and barriers in implementation, considered the resource implications of applying recommendations and presented monitoring or auditing criteria. Unlike other domains, adhering to the aspects of ‘applicability’ may require a larger amount of resources via the implementation of pilot testing, economic evaluations, educational tools and patient leaflets.⁶ Useful CPGs however are those that can be adapted to clinical practice, not those that merely excel in theoretical content, and CPGs that are not clinically applicable arguably waste time and resources when recommendations are not utilised by the intended health practices.¹³⁰ Decision making at the point of care may be compromised as without

accessibility to reliable and replicable guidance, uncertainty remains. Treatment may be potentially delayed and the emergence of inconsistencies which creates difficulty when assessing outcomes. A lack of proper consideration of the underlying evidence or poor clarity in presentation will also affect clinician's confidence in the guidelines, meaning that adherence is less likely. Moreover, there is the potential harm to healthcare systems when limited resources are expended on prescribed interventions that are unaffordable, or compromise operating efficiency.¹³³ Despite this, developers continuously overlook the applicability of CPGs. Organisations might need to consider refraining in developing CPGs unless they have the necessary funding and resources to address these aspects.

Comparatively, the domains 'Rigour of Development' and 'Stakeholder Involvement' scored slightly better, although still averaged poorly overall. Described as the strongest indicator for guideline quality, the domain 'rigour of development' examines the processes used to gather and synthesise the evidence.¹²⁷ CPGs based on poor quality evidence risk the recommendation of suboptimal, ineffective or even harmful practices.¹³³ The use of systematic methods in the searching and selection of evidence are scrutinised in this domain, as well as reporting the strengths and limitations of evidence used to inform recommendations via specific instruments such as GRADE and the Jadad scale. Informal tools may also be utilised, but the essential component is transparently reporting all methods used in the identification, inclusion, and utilisation of the evidence. Many CPGs are developed with low-level evidence or without the inclusion of evidence, instead based on expert opinion.^{134,135} The rationale behind this is that they provide continuity to clinical practice where there is a need for guidance and the evidence is poor. Reporting all methodological aspects is therefore particularly essential to allow the users of CPGs to judge the validity of the content.

Also examined within this domain, is the undertaking of external reviews and including a procedure and date for CPG revision, items where CPGs again scored poorly. The external review is an important aspect as those individuals not directly involved in the process of CPG development have an opportunity to examine recommendations. Lack of awareness, familiarity and agreement of CPGs have been identified as barriers to their usage and adherence to recommendations.^{131,136} The inclusion of clinicians as external reviewers may encourage those within their practice to be more engaged with the implementation of guidance.¹³⁷ Involving those outside the working group may also help to ensure that recommendations are relevant, reliable and free from bias. According to AGREE II, external reviewers should consist of both clinical and methodological experts. Also recommended is publicly documenting the methodology utilised, as well as all reviewer criticisms, and the rationale for any modifications that did or did not occur to ensure transparency.¹³⁸

There does not appear to be consensus on the timeframe for CPG review, possibly because this is largely dependent on the content of the CPG and how regularly new, relevant evidence materialises.¹³⁹ Studies examining the validity of CPGs in health care show variable results where a fifth of CPGs developed in the Spanish National Health System were out of date within 5 years.¹⁴⁰ Half of CPGs published by the US Agency for Healthcare Research and Quality were obsolete after 5.8 years, and 86% of CPGs developed by the UK National Institute for Health and Clinical Excellence were still up to date 3 years after publication.^{141,142} The challenge for CPG developers is to ensure recommendations are valid, reliable and up to date without wasting time and resources in identifying new evidence if there is no significant change, or the evidence does not warrant changes to current recommendations.¹⁴² The Transplant Library is a resource that provides quick access to high quality evidence that could warrant changes to recommendations.¹⁴³ For improvements in this item, developers should document the proposed date for CPG review detailing clearly the

intended methodology, monitor the literature regularly, and update recommendations when new evidence suggests the need for modification.

The poorest scoring item across CPGs was seeking the views and preferences of the target population, which is 1 of 3 items included in the domain 'stakeholder involvement'. The importance of patient preferences to clinical decision-making has gained steady momentum and has led to advocating the involvement of patient and public representatives in the development of CPGs.^{144,145} A collaborative approach is recommended which allows the formulation of CPGs that are not only evidence-based but that are more likely to be adhered to by patients and therefore useful in clinical practice. The incorporation of a patient representative in the working group and in the development of CPGs was examined in this systematic review. Disappointingly, very few CPGs included a patient representative. Similar findings are reported in a systematic review spanning 2 decades between 1980 and 2007 highlighting that little progress has been made with improving this area.¹²⁷ The Guideline International Network provide a useful online toolkit which details practical support for obtaining patient perspectives via 3 main strategies; consultation, participation and communication.¹⁴⁶ Guideline developers would benefit from incorporating such examples in the development of CPGs to ensure they are clinically applicable to the target population.

The domain 'editorial independence' examines competing interests declarations and whether recommendations may be biased by the views of funding bodies or CPG developers. CPGs performed moderately in this domain and the majority of CPGs did not describe details of funding. CPG developers may underestimate the importance of addressing and declaring all competing interests and financial aid. Alternatively, excluding this information may be a sinister way of concealing the exchange of professional or financial gains for the promotion of specific recommendations. CPGs are widely distributed and have the power to influence

clinical practice protocols and unethical or unsafe recommendations must not be put forward for personal or organisational gain. Preventing competing interests in CPG development is a difficult and complex task. Excluding individuals with conflicts of interest in the involvement of CPG development is a possible solution, however this is dependent on self-reporting and evidence suggests that many individuals are not transparent, or even aware of their own conflicts of interest.¹⁴⁷ It may also be difficult to exclude certain individuals' with conflicts of interest as their expertise is not replaceable.¹⁴⁸ Similarly, considerable time and resources are involved in the development of CPGs and funding may not be available from nonconflicting organisations. Conflicts of interest and involvement of funders in CPG development should be reduced as much as possible to avoid biased guidelines.¹⁴⁸ CPG users would benefit from explicit, publicly accessible details of funding and conflicts of interest, which will increase their confidence about the reliability of CPGs for clinical practice.

This systematic review has limitations. Included CPGs were published in English only, the majority of which were developed in Australia and the USA. Therefore, the overall mean results were largely influenced by the CPG development procedures in place in these countries. Systematic searches located CPGs published in journals however, manual searches were constrained to include international transplantation societies that would be producers of CPGs. The majority of these societies were located in developed countries indicating that the quality of CPGs in developing countries are likely underrepresented in this systematic review. A study that surveyed international members of The Transplantation Society on the uptake of a CPG on cytomegalovirus management in solid organ transplantation reported that 20% of respondents were from developing countries.¹⁴⁹ It may be that CPGs from developing countries are sparse and this community relies on CPGs published by other national and international organisations. A large portion of CPGs included in this systematic review were produced in 2010 and 2011 and could be considered out of date. However, as these CPGs

have not been updated and are currently available for use in clinical practice, the inclusion of these CPGs is relevant to the overall quality of international CPGs. CPGs on all aspects of kidney transplantation and kidney donation were included in the systematic review, enabling an extensive range of topic areas to be covered. However due to this variability, recommendations could not be compared across CPGs.

A strength of the systematic review is the use of 3 appraisers for all CPGs, which included individuals with a methodological background and kidney transplant clinicians. The rationale for inclusion of both was to ensure that the examination and interpretation of CPGs was representative of differences in clinical and methodological opinion. Appraisals were completed individually and multiple appraisers with differing affiliations were utilised to limit the influence of confirmation bias. All appraisers completed the training module before appraising any CPGs and the ICC demonstrates that there was a good cohesion between all appraisers.

The AGREE II instrument incorporates specific criteria for all 23 items, however is limited by a lack of guidance on how to make the overall assessments. Appraisers could have rated these differently depending on which aspects of CPG development they felt were most representative of overall CPG quality.¹²⁷ There is also no cut-off to distinguish between high and low quality clinical practice guidelines, an aspect identified as important to many users.¹⁵⁰ The number of items in each domain is not consistent and items attributed to ‘rigour of development’ or ‘applicability’ will have less of an effect on the overall domain score compared to items in the ‘editorial independence’ domain. As with all critical appraisals, the AGREE II is also dependent on methodological reporting. CPG developers may have used utilised methods not described in the document.

Conclusion

The quality of international CPGs in kidney transplantation requires significant improvement. Only a small number of CPGs scored well overall and were recommended for future use without modifications. The majority scored poorly overall and required modification, and a small number were not recommended for future use. All CPGs demonstrated variability in domain and item scores with most performing well in the domains 'scope and purpose' and 'clarity of presentation' and poorly in the domain 'applicability'. CPG developers should pay closer attention to the components of the AGREE II and endeavour to incorporate them into CPGs. Many aspects could be easily improved without an additional burden on time and resources. High-quality CPGs will support evidence-based decision-making and will ultimately lead to better outcomes for kidney transplant recipients.

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TABLES

Table 1: AGREE II Domain Scores and Overall Scores for all CPGs by category

Table 2: Mean compliance to AGREE II items for all CPGs (Range)

FIGURE LEGEND

Figure 1: Literature flow diagram

Figure 2: AGREE II Domain Scores and Overall Scores for all CPGs

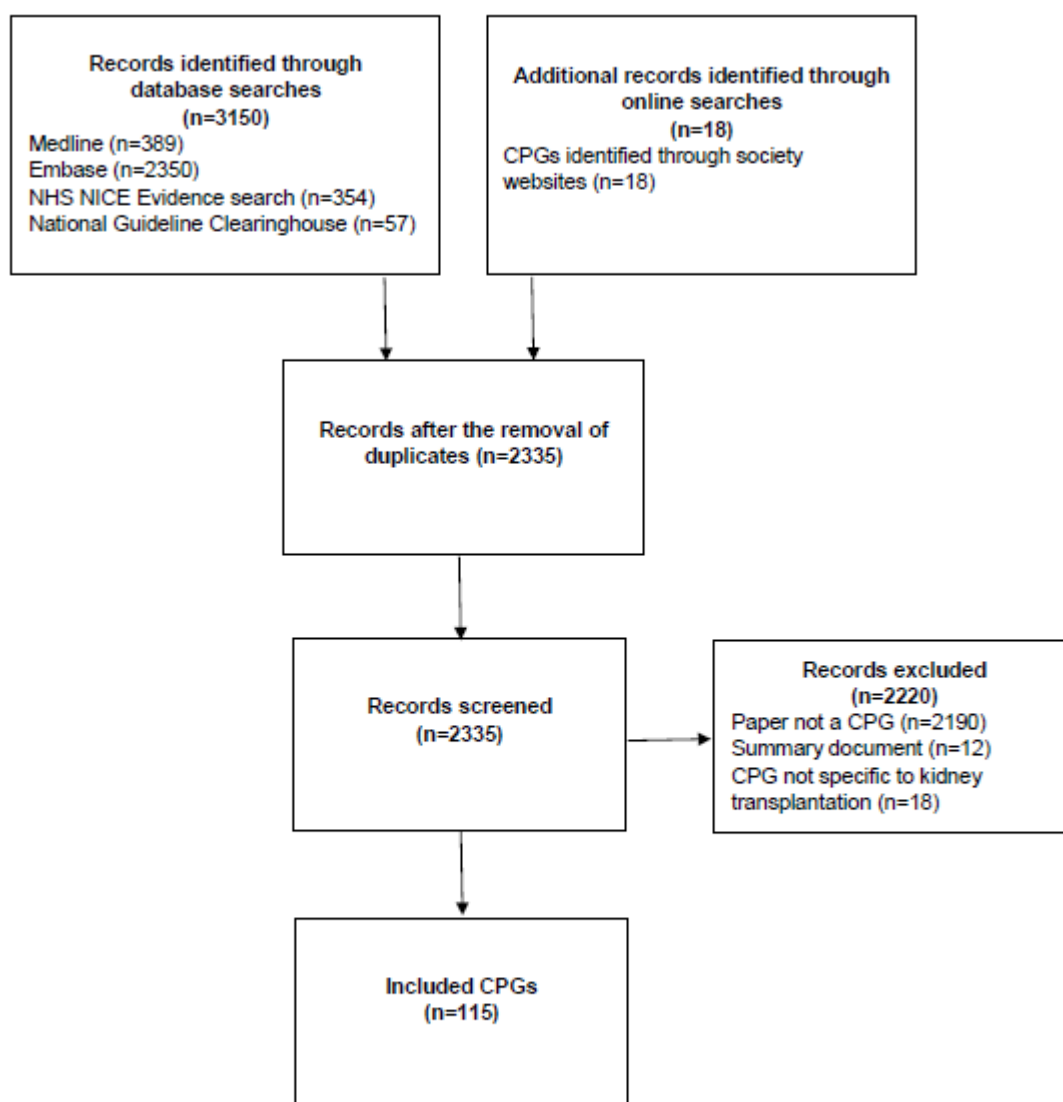


Figure 1: Literature flow diagram

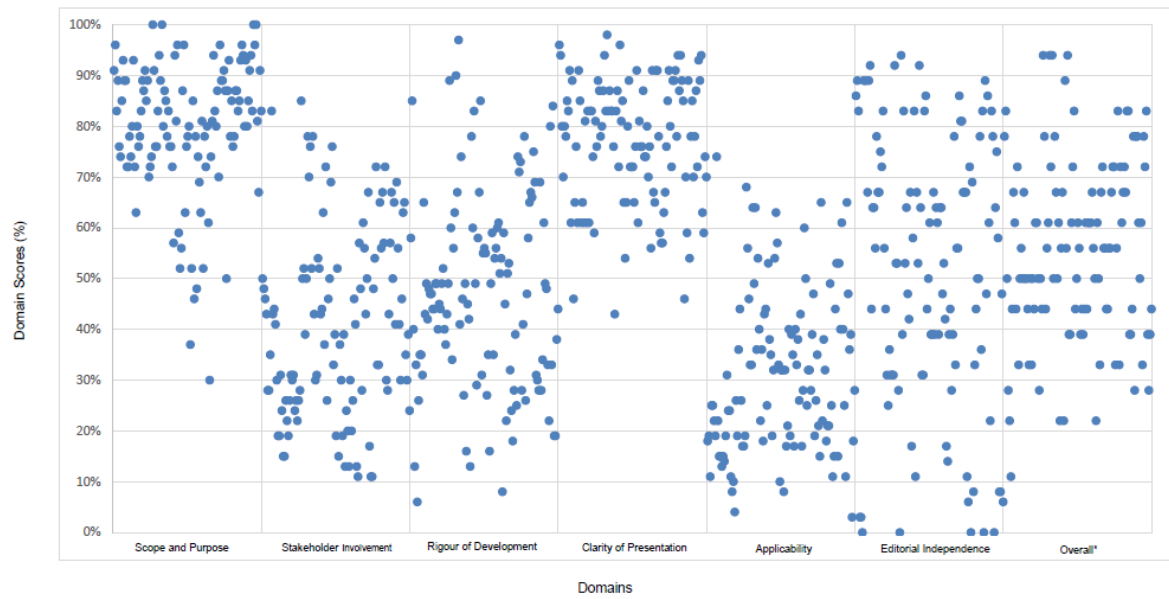


Figure 2: AGREE II Domain Scores and Overall Scores for all CPGs. Each dot within a domain represents a CPG. *Overall scores were converted to percentages using My AGREE PLUS.⁶

Table 1. AGREE II Domain Scores and Overall Scores for all CPGs by category

Domain												
CPGs	Year	Scope & Purpose (%)	Stakeholder Involvement (%)	Rigour of Development (%)	Clarity of Presentation (%)	Applicability (%)	Editorial Independence (%)	Overall score	Recommended for future use	ICC	Country	Funding
Living donation												
The CARI guidelines. Potential child-bearing donors. [10]	2010	78	19	49	65	15	44	4	Yes with Mods	0.82	Australia	Not described
The CARI guidelines. Assessment of donor kidney anatomy. [11]	2010	74	19	42	76	14	64	4	Yes with Mods	0.77	Australia	Not described
The CARI guidelines. Psychosocial care of living kidney donors. [12]	2010	80	31	48	61	19	64	4	Yes with Mods	0.81	Australia	Not described
The CARI guidelines. Justification for living donor kidney transplantation. [13]	2010	93	24	47	91	31	56	5	Yes	0.87	Australia	Not described
The CARI guidelines. Donor renal function. [14]	2010	91	31	49	83	36	31	5	Yes with Mods	0.81	Australia	Not described
The CARI guidelines. Donors at risk: obesity. [15]	2010	85	24	52	83	44	25	5	Yes with Mods	0.77	Australia	Not described
The CARI guidelines. Donors at risk: hypertension. [16]	2010	89	26	40	74	26	36	4	Yes with Mods	0.87	Australia	Not described
The CARI guidelines. Donors at risk: haematuria. [17]	2010	70	22	37	59	17	31	3	No	0.77	Australia	Not described
The CARI guidelines. Donors at risk: proteinuria. [18]	2010	72	26	43	81	17	31	4	Yes with Mods	0.85	Australia	Not described

The CARI guidelines. Donors at risk: impaired glucose tolerance. [19]	2010	83	31	49	76	36	67	5	Yes with Mods	0.82	Australia	Not described
The CARI guidelines. Surgical techniques in living donor nephrectomy. [20]	2010	81	37	60	81	38	53	4	Yes with Mods	0.81	Australia	Not described
Single-port laparoscopic nephrectomy. Interventional procedures guidance [IPG414]. [21]	2011	56	50	58	65	54	31	5	Yes with Mods	0.28	UK	Not described
Living Donor Kidney Transplantation (Third Edition). [22]	2011	85	65	58	78	32	8	5	Yes with Mods	0.80	UK	Not described
Dynamic challenges inhibiting optimal adoption of kidney paired donation: findings of a consensus conference. [23]	2013	93	83	35	83	74	89	5	Yes with Mods	0.81	USA	Mixed
Considerations for screening live kidney donors for endemic infections: a viewpoint on the UNOS policy. [24]	2014	85	30	16	61	17	39	3	Yes with Mods	0.82	USA	Not described
Living-Donor Kidney Transplantation: Reducing Financial Barriers to Live Kidney Donation. [25]	2015	83	61	24	59	32	56	4	Yes with Mods	0.67	USA	Non Industry
Living Donor Kidney Transplantation: Improving Efficiencies in Live Kidney Donor Evaluation. [26]	2015	80	56	18	57	32	56	4	Yes with Mods	0.77	USA	Non Industry

Living Donor Kidney Transplantation: Facilitating Education about Live Kidney Donation. [27]	2015	87	43	28	57	28	86	4	Yes with Mods	0.81	USA	Non Industry
Living Donor Kidney Transplantation: Improving Education Outside of Transplant Centers about Live Donor Transplantation. [28]	2015	70	50	39	63	39	81	4	Yes with Mods	0.62	USA	Non Industry
Consensus conference on best practices in live kidney donation: Recommendations to optimize education, access, and care. [29]	2015	96	67	25	67	47	81	4	Yes with Mods	0.86	USA	Non Industry
Living Donor Kidney Transplantation: Overcoming Disparities in Live Kidney Donation in the US. [30]	2015	93	65	34	78	53	86	6	Yes with Mods	0.84	USA	Non Industry
UK Guidelines for Living Organ Donation from Prisoners. [31]	2015	87	48	28	80	21	11	3	Yes with Mods	0.85	UK	Not described
Recipient assessment												
HIV, HBV and HCV infection. [32]	2011	78	19	56	72	32	61	5	Yes with Mods	0.58	Australia	Not described
Paediatric recipient. [33]	2011	46	19	49	81	21	64	4	Yes with Mods	0.62	Australia	Not described
Malignancy. [34]	2011	78	39	59	76	40	61	5	Yes with Mods	0.57	Australia	Not described
Cardiovascular Disease. [35]	2011	63	13	60	74	17	47	5	Yes with Mods	0.83	Australia	Not described
Obesity in renal transplantation. [36]	2011	52	20	51	70	33	42	4	Yes with Mods	0.62	Australia	Not described
Diabetes Mellitus. [37]	2011	61	13	45	67	17	44	4	Yes with Mods	0.79	Australia	Not described

Renal Association Clinical Practice Guideline on the assessment of the potential kidney transplant recipient. [38]	2011	78	33	47	91	38	69	6	Yes	0.81	UK	Not described
Guideline development group. Clinical Practice Guideline on management of patients with diabetes and chronic kidney disease stage 3b or higher (eGFR <45 mL/min). [39]	2015	100	85	89	89	68	92	7	Yes	0.47	Europe	Non Industry
Criteria for and Appropriateness of Renal Transplantation in Elderly Patients With End-Stage Renal Disease. [40]	2016	94	41	33	87	25	78	5	Yes with Mods	0.89	Europe	No funding
Recipient care												
The CARI guidelines. Donor-specific transfusions. [41]	2010	74	28	49	76	19	31	4	Yes with Mods	0.78	Australia	Not described
Canadian Society of Transplantation and Canadian Society of Nephrology commentary on the 2009 KDIGO clinical practice guideline for the care of kidney transplant recipients. [42]	2010	81	48	53	91	50	78	5	Yes with Mods	0.70	Canada	No funding

Routine and emergency management guidelines for the dental patient with renal disease and kidney transplant. Part 1. [43] Routine and emergency management guidelines for the dental patient with renal disease and kidney transplant. Part 2. [44]	2011	76	54	16	43	18	17	2	No	0.81	UK	Not described
KHA-CARI guideline: KHA-CARI adaptation of the KDIGO Clinical Practice Guideline for the Care of Kidney Transplant Recipients. [45]	2012	80	41	59	91	43	39	5	Yes with Mods	0.72	Australia	Not described
KDIGO Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. [46]	2012	96	76	85	89	57	86	6	Yes	0.76	International	Mixed
Chronic renal dysfunction in kidney transplant recipients. Consensus Document. [47]	2012	72	30	43	46	13	92	3	No	0.71	Spain	Industry
ACR Appropriateness Criteria® Renal Transplant Dysfunction. [48]	2012	52	46	29	54	32	31	3	Yes with Mods	0.46	USA	Non Industry
Diagnosis, management and treatment of glucometabolic disorders emerging	2013	85	35	26	85	19	89	4	Yes with Mods	0.89	Scandinavia	No funding

after kidney
transplantation. [49]

Management of the Failing Kidney Transplant. [50]	2014	78	67	67	87	21	44	5	Yes	0.82	UK	Not described
Solid organ transplantation from hepatitis B virus-positive donors: consensus guidelines for recipient management. [51]	2015	76	39	56	80	33	28	4	No consensus	0.73	USA & Canada	Not described
Vitamin D in patients with chronic kidney disease. [52]	2016	91	39	38	74	18	47	3	No	0.74	Italy	Not described
Vaccination guidelines in patients with chronic kidney disease and renal transplant recipients travelling abroad. [53]	2016	67	30	19	59	3	8	3	No consensus	0.76	India	Not described
Guidelines for vaccination in kidney transplant recipients. [54]	2016	83	30	22	72	11	0	3	No	0.90	India	Not described
Practical Recommendations for Long-term Management of Modifiable Risks in Kidney and Liver Transplant Recipients. [55]	2017	94	67	69	89	53	89	6	Yes	0.86	Europe	Industry
Post-Operative Care in the Kidney Transplant Recipient. [56]	2017	87	72	78	89	65	72	6	Yes	0.53	UK	Not described

Infections

Guidelines for the prevention and management of Mycobacterium tuberculosis infection and disease in adult patients with chronic kidney disease. [57]	2010	94	63	78	96	53	67	6	Yes	0.81	UK	Not described
Treatment of Cytomegalovirus disease in renal transplant recipients. [58]	2011	76	39	55	72	10	50	4	Yes with Mods	0.73	Australia	Not described
Prophylaxis for Cytomegalovirus infection in patients following renal transplantation. [59]	2011	81	30	61	80	40	53	5	Yes with Mods	0.62	Australia	Not described
Diagnostic tests for Cytomegalovirus in renal transplantation. [60]	2011	74	24	54	87	39	64	5	Yes with Mods	0.61	Australia	Not described
Preemptive treatment of Cytomegalovirus. [61]	2011	69	20	56	74	35	64	5	Yes with Mods	0.60	Australia	Not described
GESITRA-SEIMC/REIPI recommendations for the management of cytomegalovirus infection in solid-organ transplant patients. [62]	2011	72	43	42	87	44	83	5	Yes with Mods	0.77	Spain	Mixed
The Prevention and Management of CMV Disease after Solid Organ Transplantation. [63]	2011	74	57	51	91	60	39	5	Yes with Mods	0.72	UK	Not described
Donor-derived fungal infections in organ transplant recipients. [64]	2012	78	30	27	83	22	42	4	Yes with Mods	0.74	USA	Not described

Cytomegalovirus in solid organ transplantation. [65]	2013	30	11	22	65	28	28	3	No	0.80	USA	Not described
Urinary tract infections in solid organ transplantation. [66]	2013	48	13	35	76	19	39	4	Yes with Mods	0.72	USA	Not described
BK polyomavirus in solid organ transplantation. [67]	2013	37	15	27	76	8	39	3	Yes with Mods	0.81	USA	Not described
Clinical practice guidelines for antimicrobial prophylaxis in surgery. [68]	2013	87	78	74	87	54	64	6	Yes with Mods	0.46	USA	Non Industry
Consensus document on the management of renal disease in HIV-infected patients. [69]	2014	91	50	58	96	18	86	6	Yes	0.88	Spain	Industry
Clinical practice guideline for the management of chronic kidney disease in patients infected with HIV. [70]	2014	96	48	85	94	19	89	6	Yes	0.90	USA	Non Industry
Management of urinary tract infection in solid organ transplant recipients. [71]	2015	100	65	84	94	36	58	6	Yes with Mods	0.77	Spain	Not described
Kidney & Pancreas Transplantation in Patients with HIV. Second Edition. [72]	2015	87	57	66	94	21	50	5	Yes with Mods	0.81	UK	Not described
Antimicrobial prophylaxis for pneumocystis jiroveci pneumonia (PCP) after solid organ transplantation (SOT).	2015	100	46	80	93	65	64	6	Yes with Mods	0.80	USA	Not described

[73]

Essential Japanese guidelines for the prevention of perioperative infections in the urological field: 2015 edition. [74]	2016	83	24	44	70	28	6	4	No consensus	0.67	Japan	Not described
Deceased donation												
Guidelines for potential multiple organ donors (adult). Part III: organ-specific recommendations. [75]	2011	78	26	54	76	38	17	4	Yes with Mods	0.79	Brazil	Not described
DTG procurement guidelines in heart beating donors. [76]	2011	57	44	13	72	25	11	2	No	0.66	Germany	Not described
Transplantation from deceased donors after circulatory death. [77]	2013	76	56	65	94	18	33	5	Yes with Mods	0.78	UK	Not described
How France launched its donation after cardiac death program. [78]	2014	63	33	31	72	33	44	4	Yes with Mods	0.59	France	Not described
Spanish consensus document for acceptance and rejection of kidneys from expanded criteria donors. [79]	2014	83	46	40	80	11	83	4	Yes with Mods	0.89	Spain	Industry
Surgical Technique for Deceased Donor Abdominal Organ Procurement. [80]	2015	72	46	8	56	26	14	2	No	0.87	Australia & New Zealand	Not described

Management of the Potential Organ Donor in the ICU. [81]	2015	91	50	60	87	56	53	6	Yes	0.69	USA	Non Industry
Clinical Guidelines for Organ Transplantation from Deceased Donors Version 1.0. [82]	2016	85	69	49	70	61	22	5	Yes with Mods	0.51	Australia & New Zealand	Not described
Recommendations for donation after circulatory death kidney transplantation in Europe. [83]	2016	80	41	61	85	40	61	6	Yes	0.59	Europe	No funding
Nutrition												
The CARI guidelines. Nutritional management of dyslipidaemia in adult kidney transplant recipients. [84]	2010	72	15	47	85	24	78	4	No consensus	0.88	Australia	Non Industry
The CARI guidelines. Nutritional management of hypertension in adult kidney transplant recipients. [85]	2010	63	15	44	61	24	67	4	No consensus	0.78	Australia	Non Industry
The CARI guidelines. Nutritional management of overweight and obesity in adult kidney transplant recipients. [86]	2010	80	26	44	65	11	67	4	Yes with Mods	0.83	Australia	Non Industry
The CARI guidelines. Nutritional management of hypophosphataemia in adult kidney transplant recipients. [87]	2010	76	22	49	61	8	75	3	No	0.86	Australia	Non Industry

The CARl guidelines. Nutritional interventions for the prevention of bone disease in kidney transplant recipients. [88]	2010	78	19	49	81	10	72	4	No consensus	0.88	Australia	Non Industry
The CARl guidelines. Nutritional management of anaemia in adult kidney transplant recipients. [89]	2010	83	26	40	61	4	83	3	Yes with Mods	0.89	Australia	Non Industry
The CARl guidelines. Nutritional management of diabetes mellitus in adult kidney transplant recipients. [90]	2010	89	31	45	83	26	56	4	Yes with Mods	0.74	Australia	Non Industry
The CARl guidelines. Food safety recommendations for adult kidney transplant recipients. [91]	2010	87	30	44	61	19	44	4	Yes with Mods	0.73	Australia	Non Industry
The CARl guidelines. Protein requirement in adult kidney transplant recipients. [92]	2010	59	26	49	65	19	64	3	Yes with Mods	0.71	Australia	Non Industry
Cardiovascular and lipid complications												
Danish guidelines for lipid-lowering treatment in patients with chronic renal failure. [93]	2014	76	28	33	80	25	3	2	No	0.45	Denmark	Not described

Cardiac disease evaluation and management among kidney and liver transplantation candidates. [94]	2012	72	41	65	89	15	89	5	Yes with Mods	0.86	USA	Non Industry
KDIGO Clinical Practice Guideline for Lipid Management in Chronic Kidney Disease. [95]	2013	94	78	90	94	64	94	7	Yes	0.51	International	Mixed
Cardiovascular disease: revascularisation. [96]	2013	89	17	74	76	19	67	5	Yes	0.71	Australia	Not described
Medical management of coronary artery disease (excluding lipid-lowering therapy). [97]	2012	89	11	71	85	26	67	5	Yes	0.72	Australia	Not described
Heart Failure. [98]	2013	91	11	73	91	35	67	5	Yes	0.75	Australia	Not described
Antibodies												
Consensus guidelines on the testing and clinical management issues associated with HLA and non-HLA antibodies in transplantation. Transplantation. [99]	2013	89	43	35	91	22	89	5	Yes with Mods	0.83	International	Non Industry
Guidelines for Antibody Incompatible Transplantation (Third Edition). [100]	2016	87	72	75	89	49	50	5	Yes	0.85	UK	Not described
The detection and characterisation of clinically relevant antibodies in allotransplantation. [101]	2014	50	54	41	72	15	6	4	Yes with Mods	0.56	UK	Not described

The use of immunoglobulin therapy for patients undergoing solid organ transplantation: an evidence-based practice guideline. [102]	2010	96	72	83	85	35	92	7	Yes	0.83	Canada	Industry
Immunosuppression												
Generic immunosuppression in solid organ transplantation: a Canadian perspective. [103]	2012	80	52	55	65	32	39	4	Yes with Mods	0.85	Canada	Not described
Advagraf®, a once-daily prolonged release tacrolimus formulation, in kidney transplantation: literature review and guidelines from a panel of experts. [104]	2016	85	28	31	46	11	36	3	No	0.73	France	Not described
Therapeutic Drug Monitoring of Everolimus. [105]	2016	96	63	33	89	47	75	5	Yes with Mods	0.85	International	Industry
Imaging and biopsies												
Imaging recommendations in paediatric uroradiology, part V: childhood cystic kidney disease, childhood renal transplantation and contrast-enhanced ultrasonography in children. [106]	2012	89	44	31	61	15	67	4	No	0.75	Europe	Not described

Tissue pathway for medical renal biopsies [G061]. [107]	2013	87	69	67	80	63	83	5	Yes	0.62	UK	No funding
AJUM practice guideline for the performance of an ultrasound examination of solid-organ transplants. [108]	2014	89	43	13	70	25	3	3	Yes with Mods	0.87	USA	Not described
German recommendations for pretransplantation donor kidney biopsies. [109]	2016	80	50	28	54	15	47	3	No	0.83	Germany	Not described
Standard method for ultrasound evaluation of renal arterial lesions. [110]	2016	81	35	19	63	39	8	3	No	0.71	Japan	Not described
Mixed aspects of transplantation												
ERBP Guideline on the Management and Evaluation of the Kidney Donor and Recipient. [111]	2013	100	76	97	98	64	83	7	Yes	0.58	Europe	Non Industry
Guidelines on Renal Transplantation. [112]	2014	52	37	35	91	32	67	4	Yes with Mods	0.28	Europe	Non Industry
Kidney donor and recipient perioperative evaluation.[113]	2014	74	28	6	78	22	0	2	No	0.78	Iran	Not described
Canadian Forum on Combined Organ Transplantation. [114]	2016	93	43	30	70	15	83	3	Yes with Mods	0.88	Canada	No funding
Guide to the quality and safety of organs for transplantation 6th Edition. [115]	2016	96	57	28	59	44	0	4	Yes with Mods	0.80	Europe	Not described

Does preemptive transplantation versus post start of dialysis transplantation with a kidney from a living donor improve outcomes after transplantation? A systematic literature review and position statement by the Descartes Working Group and ERBP. [116]	2016	83	30	69	85	25	78	6	Yes with Mods	0.91	Europe	Non Industry
Other aspects of transplantation												
Clinical practice guidelines for the management of atypical haemolytic uraemic syndrome in the United Kingdom. [117]	2010	93	33	26	89	22	0	3	No	0.92	UK	Not described
Spanish Society of Nephrology recommendations for controlling mineral and bone disorder in chronic kidney disease patients (S.E.N-M.B.D) [118]	2011	76	52	45	83	43	58	4	Yes with Mods	0.67	Spain	Not described
Expert guidelines for the management of Alport syndrome and thin basement membrane nephropathy. [119]	2013	85	43	46	83	40	47	5	Yes	0.54	International	Not described
Clinical practice guideline for the management of chronic kidney disease-mineral and	2013	80	52	41	83	36	53	4	Yes with Mods	0.52	Japan	Not described

bone disorder. [120]

Proposed guidelines for the diagnosis and management of methylmalonic and propionic acidemia. [121]	2014	89	70	67	83	49	39	5	Yes with Mods	0.58	Europe & USA	Non Industry
Consensus statement on screening, diagnosis, classification and treatment of endemic (Balkan) nephropathy. [122]	2014	76	52	34	78	46	53	4	Yes with Mods	0.69	International	Non Industry
Guidelines on the management of AL amyloidosis. [123]	2015	83	50	63	87	33	0	5	Yes with Mods	0.80	UK	Not described
An international consensus approach to the management of atypical hemolytic uremic syndrome in children. [124]	2016	94	28	32	78	25	33	4	Yes with Mods	0.89	International	Not described
Integrating APOL1 Gene Variants Into Renal Transplantation: Considerations Arising From the American Society of Transplantation Expert Conference. [125]	2017	91	56	48	78	40	83	4	Yes with Mods	0.63	USA	Industry
Mean (Range)		80 (30-100)	41 (11-85)	47 (6-97)	77 (43-98)	31 (3-74)	52 (0-94)	4 (2-7)		0.74 (0.28-0.92)		

*Table is based on adjusted scores; Yes with Mods - Yes with modifications; ICC - Intraclass Correlation Coefficient