



# Implementing GRADE-ADOLOPMENT for Clinical Practice Guidelines in Resource-Limited Settings: The AKU Experience

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**Abstract:** In regions grappling with limited resources to support the formulation of evidence-based Clinical Practice Guidelines (CPGs), GRADE-ADOLOPMENT offers a unique pathway to craft guidelines tailored to the specific needs of areas with sparse CPGs. The Aga Khan University in Karachi, Pakistan, used GRADE-ADOLOPMENT to create guidelines for prevalent diseases in Pakistan. An adaptation of the GRADE-ADOLOPMENT methodology was employed in collaboration with the US GRADE working group. ADOLOPMENT is a combination of de-novo creation, adoption (use as is or with minor changes), or adaptation (modification based on local context) of recommendations. After the selection of a source guideline (SG), the recommendations were either adopted, adapted, or excluded. Adaptations were done using the Evidence-To-Decision table. Contextualized CPGs were developed for Pakistan, covering over 25 medical specialties. The article discusses the wide variety of topics and specialties covered using GRADE-ADOLOPMENT in Pakistan for the first time. The lessons learned from this resource-constrained GRADE-ADOLOPMENT experience provide valuable guidance for teams undertaking projects in similar resource-limited settings. The GRADE-ADOLOPMENT experience at AKU in Pakistan serves as a valuable example, showcasing both the challenges and creative solutions in the context of medical guideline development in resource-limited regions.

**Keywords:** Adaptation, Clinical Practice Guidelines, De-novo guidelines, Evidence-to-Decision tables, GRADE-ADOLOPMENT, .

## 1. INTRODUCTION

Clinical practice guidelines (CPGs) play an important role in making healthcare decisions, even though their formation is resource-intensive [1]. The GRADE-ADOLOPMENT methodology offers a cost-effective approach that can provide local CPGs to experts. The process is used to provide a structured assessment of evidence and recommendations that can help healthcare professionals make informed decisions based on the best evidence-based suggestions. It is an extensive approach to guideline development and helps to ensure that recommendations are based on high-quality evidence and are clear about the reliability of those recommendations. This methodology has been proven successful in different regions of the world such as Saudi Arabia [2], Australia [3], the

Eastern Mediterranean region [4], the Asia-Pacific region [5], Mexico [6], and the United Kingdom [7], but remains to be underutilized in lower-middle-income countries (LMICs).

Pakistan, an LMIC, has its major share of healthcare funds being utilized for health and access leading to a scarcity of available CPGs catering to local context. GRADE-ADOLOPMENT's transparency and efficiency make it a compelling choice [2]. Since CPGs play a role in patient care and their outcomes, quality-based evidence is essential to validate their recommendation. The development of CPGs is based on three pathways; adoption, creation, and adaptation [6]. Adoption is done when previously recognized CPG is directly included without any modifications or alterations. Creation refers to the de novo creation of a CPG

with recommendations through an extensive literature review. A PICO (Patient, Intervention, Comparison, and Outcome) question is made and then a systematic review is conducted. After that, an expert panel is involved which ultimately, leads to the creation of a new CPG. Adaptation refers to modifications of already established CPGs to tailor to local context.

While adopting guidelines is an acceptable approach, it is important to keep in mind the limitations associated with this method. The occurrence of different diseases, as well as the ways they are diagnosed and treated, can vary based on regional factors. As a result, CPGs may be influenced by individual physician preferences, which can result in a lack of standardized care. This can lead to a significant number of patients receiving either inadequate or excessive treatment. Hence, our country needs to develop CPGs that are tailored to needs according to local context. This will help ensure consistent and evidence-based healthcare. This paper talks about the Aga Khan University's (AKU) initiative to adopt CPGs for Pakistan by using the GRADE-ADOLOPMENT. We convey our personal experiences and obstacles faced that provide our perspective on developing guidelines in a country with limited resources.

## 2. METHODS

The adoption process was initiated within the vicinity of AKU based on GRADE-ADOLOPMENT. A budget was established for the guideline developing group and was authorized by AKUH's Provost. Finally, the CCBP was created in May 2020. This would help ensure standardized healthcare access in Pakistan which would provide a local perspective. GRADE-ADOLOPMENT is accepted widely for evidence-based CPGs and clinical recommendations. Over 100 organizations have approved this methodology and follow this protocol for quality evidence-based recommendations. In collaboration with the US working group, AKU conducts the process in 8 stages (Table 1).

### 2.1. Creation of a Center for Clinical Best Practices

AKU introduced CCBP to create a platform for

which they can collect the finest clinical practices for Pakistan, with the help of the US GRADE working group as well.

### 2.2. Compiling a Content List

Section heads and department chairs collaborated with CCBP to compile a content list. In AKU, each section head led their respective specialty or subspecialty. They were given the task of providing a list of diagnoses and diseases that were to be emphasized in the development of CPGs.

### 2.3. Identification of Source Guidelines

Source guidelines were selected; those that were based on the GRADE methodology were preferred and relevant recommendations were selected. For every CPG on the list, CCBP collaborated with each section head to modify the recommendation(s) according to local relevance. A source guideline is already a pre-existing guideline that is relevant to the topics identified from the content list. These could be national or Society-Based. Original evidence-to-decision tables were made by contacting the committee chair or members who were involved in the CPGs for the source guidelines.

### 2.4. Table of Recommendations (ToR)

The recommendations were extracted from the source guidelines and were arranged in the form of a table as seen in Table 2. The recommendations were categorized as adopted, adapted, or excluded. Adopted points are the recommendations that are accepted as it is, without any modifications or very minor changes. Adapted points are those points that are modified to tailor local relevance. Excluded recommendations are those that are removed from the final CPGs due to multiple reasons such as lack of availability in Pakistan, if they were not applicable under these settings, or if the recommendations advise advanced and modern technological interventions for a particular purpose that would not be sufficient in the Pakistani population and so on.

### 2.5. Evidence to Decision (EtD) Table

The adapted recommendations are then further evaluated by the CCBP team to create the Evidence

**Table 1.** A step-by-step guide for the development of CPGs.

Tasks	Steps
<b>Creation of a Centre for Clinical Best Practices (CCBP)</b>	
Create a centre for clinical CPG development	<ol style="list-style-type: none"> <li>1. Establishment of Clinical and Translational Research Incubator (CITRIC)</li> <li>2. Creation of CCBP within CITRIC</li> <li>3. Formation of a core team comprising a director, manager, and methodologists</li> <li>4. Collaboration with the US GRADE working group</li> </ol>
<b>Compiling a Content List</b>	
Create a ‘problem list’ to prioritize for CPG creation/adaptation	<ol style="list-style-type: none"> <li>1. Collaboration with all section heads and department chairs</li> <li>2. Identification of a list of diagnoses to be prioritized for the CPG manual.</li> <li>3. Review as well as share the list with the entire section faculty before finalizing</li> </ol>
<b>Identification of Source Guidelines</b>	
Identify a source guideline to modify a CPG for local context	<ol style="list-style-type: none"> <li>1. CCBP collaboration with each section head on one guideline from the list</li> <li>2. Precise identification of the source guideline(s)</li> <li>3. Extraction of the original evidence to decision tables via contacting SG’s committee chair/members</li> </ol>
<b>Creation of Table of Recommendations (ToR)</b>	
Create a table of recommendations for CPG development	<ol style="list-style-type: none"> <li>1. Selection of all recommendations from each identified source CPG</li> <li>2. Categorization of each recommendation as adopted, adapted, or excluded.</li> <li>3. Review by the CCBP team</li> <li>4. All recommendations marked as “to be adapted” selected for the next stage</li> </ol>
<b>Creation of Evidence to Decision Table (EtD)</b>	
Use the GRADEPro software to create the EtD	<ol style="list-style-type: none"> <li>1. Collaboration between CCBP methodologist and section head to extract all relevant information addressing each domain of the EtD.</li> <li>2. Inclusion of the 12 domains in the GRADEPro EtD</li> <li>3. A comprehensive review by the section heads and US GRADE working group.</li> <li>4. Sharing of finalized tables electronically with the group of experts</li> </ol>
<b>Expert panel review</b>	
Review of the EtD by an expert panel to determine the strength of recommendations and finalize EtD	<ol style="list-style-type: none"> <li>1. Information session with all panelists to comprehensively explain the EtD domains, the questions to be addressed, and the process of utilizing GRADEPro panel voice.</li> <li>2. Incorporation of all suggestions by expert panels into the EtD</li> <li>3. A panel meeting to determine the strength of recommendations.</li> <li>4. A final “consensus” meeting to finalize EtD</li> </ol>
<b>Formulation of CPGs</b>	
Formulate the final version of the CPGs for dissemination	<ol style="list-style-type: none"> <li>1. Formatted CPG document shared with a graphic designer to condense it into a pre-decided template.</li> <li>2. Approval of the final version by section heads and panel members</li> </ol>
<b>Internal and External Boards</b>	
To give their valuable feedback(s) in improving these guidelines	<ol style="list-style-type: none"> <li>1. These experts were provided with the liberty to assess and modify the guidelines.</li> <li>2. Changes or suggestions made by the members were considered and incorporated after discussions with the guidelines development team.</li> </ol>
<b>9. Dissemination of CPG</b>	
To disseminate the CPGs ensuring their availability and accessibility across Pakistan	<ol style="list-style-type: none"> <li>1. Dissemination across AKUH health centers all over Pakistan</li> <li>2. Dissemination at a district and provincial level</li> </ol>

**Table 2.** A template of the table of recommendations (ToR).

S. No.	Recommendations	To Adopt	To Adapt/Modify	To exclude
1				
2				
3				

for Decision (EtD) table to serve as the key tool in the presentation of evidence and corresponding results. These tables were created using GRADEPro software which in turn, summarizes research evidence. For the recommendations that were adapted into the final CPGs, the methodologists in the CCBP department and the respective section heads collected information through local data literature, expert input, and Mini-Systematic Reviews. The EtD tables are carefully evaluated and finalized by the respective section heads.

## 2.6. Expert Panel Review

An expert panel is established which is led by the section head and consists of a group of experts, who were selected by the section head, in the respective specialty and included AKU faculty and national experts as well from the relevant clinical fields. The GRADEPro Panel voice feature was used to review EtD in real-time and provide necessary feedback. Suggestions and feedback from the panelists were incorporated and then were followed by revision and modification of the final EtD table. The panelists were invited to a final panel consensus meeting to determine the strength of the recommendations. The final decision was based on the comments of all the panel members after which the final EtD was made.

## 2.7. Formulation of CPGs

After reviewing from the panelists, the recommendations were adapted and then compiled in a formatted CPG document. The final version was then further refined and approved by section heads, department chairs, and panel members.

## 2.8. Internal and External Boards

The guidelines went through an extensive review

process, which involved both internal and external reviewers. The internal reviewers comprised healthcare professionals from AKU itself and external members included healthcare professionals from Pakistan who were affiliated other than AKU. Both these experts were provided with the liberty to assess and modify the guidelines. Any changes or suggestions that were made in the process were carefully considered and incorporated after discussions with the guidelines development group.

## 2.9. Dissemination

CPGs will be disseminated internally across AKU health centers in Pakistan, and then later followed by dissemination at district and provincial levels. Dissemination planning involves in publication of these CPGs in peer-reviewed journals and amalgamation into AKU's electronic health resource (EHR) for increasing availability.

## 3. RESULTS

With the collaboration between CCBP and the section heads, several contextualized CPGs for Pakistan were developed. These CPGs covered 25 medical specialties which include the following subjects; Cardiology, Dermatology, Gastroenterology, Internal Medicine, Nephrology, Neurology, Pulmonology, Endocrinology, Rheumatology, Infectious Disease, Breast, Dental, General Surgery, Neurosurgery, Ophthalmology, Orthopedics, ENT, Urology, Vascular Surgery, Gynecology, Emergency Medicine, Family Medicine, Psychiatry, Anesthesia and Palliative Medicine.

## 4. DISCUSSION

Starting the guideline development by utilizing already existent evidence syntheses, particularly

those that are employed in the guidelines, disqualifies the need to conduct extensive systematic reviews regarding health impacts for many questions. This approach is beneficial as it significantly reduces the resource burden associated with guideline development and also aligns with the vision for better guideline development [8]. One of the few advantages of our practice is that the GRADE-ADOLOPMENT process provides a systemic approach for various healthcare and region-specific settings as it uses already existent evidence-based guidelines while involving local stakeholders to systematically and transparently participate in the modification of the guidelines. The purpose of this methodology is to help organizations and healthcare professionals adapt guidelines and choose what suits their needs best.

The guidelines developed involved a vast area of topics, and with the help of EtDs and tools such as GradePro, the CPGs were modified according to Pakistan's healthcare settings. Policymakers can keep certain factors under consideration such as availability of time, availability of manpower and financial resources, experience in using a specific structure, and the ability to build a group in the framework of interest. EtDs play a role in determining the criteria that may revise the strength or course of a recommendation. By focusing on questions and using EtDs, the process uses an already-existent source guideline and conducts an extensive systematic search for evidence-based recommendations as mentioned in the methodology section. Our searches for patients' values and preferences according to local context as well as availability of limited resources and facilities were well received by panelists but provided limited data. The inclusion of local experts and internal and external board members helped modify and identify relevant recommendations for the guidelines. International organizations such as WHO can benefit from this approach as the process can often develop recommendations that may require a local touch and context.

Guideline adaptation gives us an understanding of how different variables such as culture, organization of care, epidemiology, and social values can contribute to evidence-based clinical practice guidelines for clinical, public, and healthcare practices.

## 5. CONCLUSIONS

AKU developed an adaptation protocol to create evidence-based with regards to local context using the GRADE-ADOLOPMENT methodology. The aim is to ensure the delivery of uniform care to all areas of Pakistan. This methodology gives the impression that this process can be utilized worldwide, especially in resource-limited regions as well as to modify guidelines. Another aim to increase dissemination of the guidelines is by introducing a Guideline Manual Book that every physician can carry with them wherever they go to provide quality patient care. It is also important that CPGs should be reevaluated every few years and adapted whenever needed to keep up with modern medicine and practices.

## 6. CONFLICT OF INTEREST

The authors declared no conflict of interest.

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