

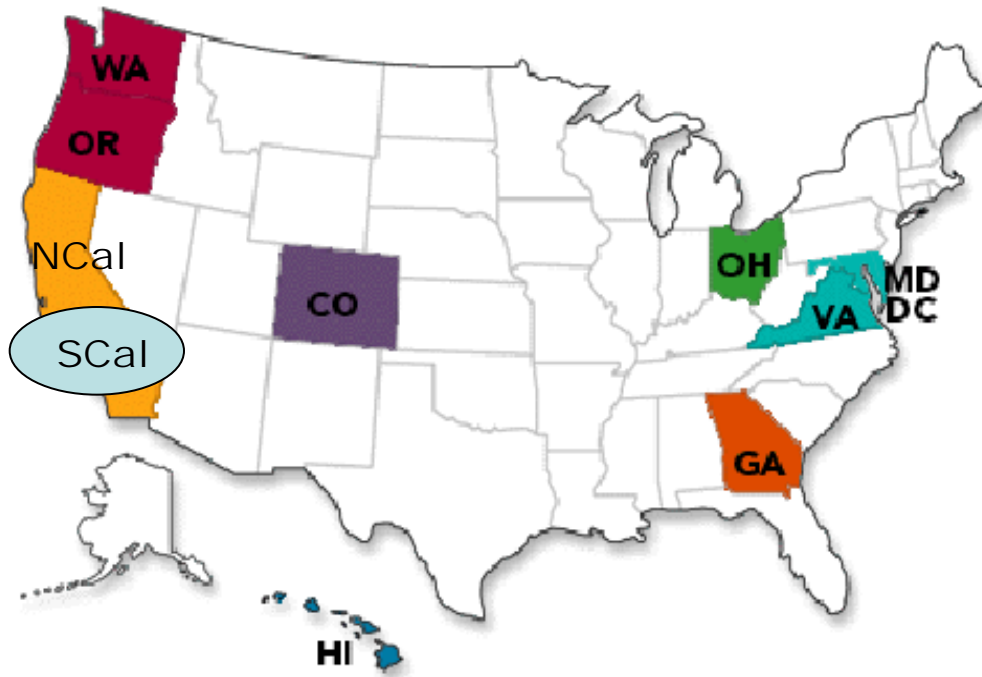
# Using Rapid Reviews to Influence Guidance Development in the Emergency Department Setting



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- I certify that, to the best of my knowledge, no aspect of my current personal or professional situation might reasonably be expected to affect significantly my views on the subject on which I am presenting,
- I am employed by the Southern California Permanente Medical Group (SCPMG), which contracts exclusively with the Kaiser Foundation Health Plan to provide medical services in the U.S.
- All current professional activities are funded by SCPMG and The Permanente Federation



## Description:

- Largest nonprofit health plan in the U.S. (founded 1945)
- Integrated health care delivery system
- Serving 9 states & Dist. of Columbia
- 9.1 million members (3.6 million in So. California Region)
- 17,000+ physicians
- 175,000+ employees
- 37 hospitals and med centers
- 600+ medical offices
- \$50.6 billion operating revenue (2012)
- Active Regional/National Guideline & Technology Assessment Programs

## Kaiser Permanente Structure



- Conducts reviews of scientific studies to support evidence-based clinical and operational decision making within KPSC
- Clinical guideline development ongoing since 1991; rapid reviews in place since 1998
- Currently staffed by 9 Masters-level research analysts with backgrounds in epidemiology, statistics and research methods
- Receive requests via email or “inquiry line”
- Senior leadership promotes a strong evidence-based culture
- Knowledge products generally well-received due to involvement of key clinician leaders in all phases:
  - topic selection, clinical question formulation
  - evidence review/synthesis
  - content development for knowledge products
  - implementation/knowledge translation activities

## ■ Full Systematic Reviews (SRs)

- Follow methodology outlined in systematic evidence review standards developed by the Institute of Medicine, Cochrane Collaboration, AHRQ Effective Healthcare Program, etc.
- Long-term project
- Goals: Rigorous methods, transparency, minimize risk of bias, assess balance of benefits/harms of interventions

## ■ Rapid (Systematic) Reviews

- Follow streamlined, systematic methods and processes
- No universally accepted definition or standards
- Typically take short-cuts or departures from full SR standards, but use defined “systematic” methods/processes to provide a timely response
- Goals: Be as rigorous as possible, yet recognize and be transparent about methods, limitations and potential biases

# Rapid Review Product Deliverables and Timeframes

	Time Sensitive Assessment (1-10 Business Days)	Detailed Assessment (4-12 weeks)
<b>Request Type</b>	<ul style="list-style-type: none"> <li>• Patient-specific inquiries</li> <li>• Patient appeal w/short due date (regulatory requirement)</li> <li>• Other time-sensitive general request</li> </ul>	<ul style="list-style-type: none"> <li>• General requests for in-depth systematic evidence search on a new technology</li> </ul>
<b>Scope of evidence review</b>	<p>High-level search for:</p> <ul style="list-style-type: none"> <li>• Systematic reviews</li> <li>• Technology assessments</li> <li>• Clinical guidelines</li> <li>• Clinical trials published after SR date</li> </ul>	<ul style="list-style-type: none"> <li>• Systematic evidence search</li> <li>• Review of all relevant studies</li> <li>• Summary of findings in narrative and/or evidence table format</li> <li>• Critical evaluation of quality and sufficiency of body of evidence</li> </ul>
<b>Product description</b>	<p>E-mail or brief report with an overview of literature search results and high-level summary of body of evidence (e.g., number and type of studies, conclusions from SRs and clinical trial abstracts, etc.)</p>	<p>Detailed report with background information on medical condition and technology; critical appraisal/quality assessment of body of evidence; grey literature sources (FDA/CMS, medical policies, guidelines).</p>

- Previously, all patients admitted into ED for any abdominopelvic (AP) pain received computed tomography (CT) with oral contrast
- Oral contrast is used to help differentiate small bowel from other viscera or pathology
- Issues with oral contrast:
  - Impairs the assessment of the bowel wall and lumen, precluding visualization of abnormal mucosal enhancement and GI bleeding
  - Increases ER time by an average of 3 hours
  - Increases costs
- Many institutions have eliminated oral CT for routine AP pain
  - Mayo Clinic ER, UCSF, Stanford, Duke, Yale, Mt. Sinai (NY)
- Benefits of eliminating oral contrast:
  - Could reduce risk of contrast-induced neuropathy, allergic reactions, ER delays, costs, and overall LOS in ED

- Program was piloted in San Diego Kaiser: May 15, 2011- August 15, 2011
  - N = 1800 patients
  - IV contrast only for all ED patients undergoing AP CT imaging for abdominal pain
  - Outcomes incl. turn-around times, LOS, quality, safety, efficacy, cost-savings
- N = 1782 patients included
- Turn-around time (time from order to completion of study) prior to pilot ~144 mins; after new protocol, turn-around-time dropped to 90 minutes ( $p < 0.01$ )
- LOS for discharged patients decreased by one hour ( $p < 0.01$ ); admitted patients decreased by an average of 46 mins ( $p < 0.05$ ).
- Estimated annualized cost savings from protocol change was +\$500,000
- 10 patients (0.56%) had repeat CT with oral contrast performed with only one patient having a modification in their management.
- No adverse outcomes were identified by not using oral contrast.



# KPSC Rapid Review 5-Step Process:

## 1. Communicating with Key Stakeholders to determine PICOTS



<b>Patients</b>	<b>ED patients with undifferentiated abdominal/pelvic pain (suspected appendicitis and/or any other abdominal condition/disease)</b>
<b>Intervention</b>	<b>Abdominal CT screening with no oral contrast</b>
<b>Comparison</b>	<ul style="list-style-type: none"><li>• <b>CT screening with... oral contrast alone; rectal alone; oral contrast + IV contrast; oral contrast + rectal contrast; rectal alone; IV alone</b></li><li>• <b>Non-contrast (no oral or IV or rectal)</b></li></ul>
<b>Critical Outcomes</b>	<b>Mortality/Morbidity from abdominal disease (e.g., appendicitis or other abdominal/pelvic disease) Diagnostic performance of CT screening tests (sensitivity, specificity, PPV, NPV)</b>
<b>Timing and Settings</b>	<b>Upon presentation into ED</b>

- **1) Does CT screening with oral contrast vs. CT screening without oral contrast (i.e., no contrast, IV contrast, rectal contrast or combinations) reduce morbidity/mortality from abdominal/pelvic disease in ED patients with abdominal/pelvic pain?**
- **2) What is the diagnostic accuracy of CT screening with oral contrast vs. CT without oral contrast (i.e., no contrast, IV contrast, rectal contrast or combinations) in the emergency department (ED) evaluation of adults with abdominal/pelvic pain?**
- **3) Does CT screening with oral contrast vs. CT screening without oral contrast (i.e., no contrast, IV contrast, rectal contrast or combinations) reduce length of stay (LOS) in the emergency department (ED)?**

# KPSC Rapid Review 5-Step Process:

## 2. Conduct Comprehensive Evidence Search



- First priority: Search for existing high-quality systematic reviews from recognized sources (AHRQ, Cochrane Collaboration, public/private tech assessment and guideline groups, top-tier medical journals, etc.)
- If no high-quality SRs available, conduct search for high-quality studies from bibliographic and other databases (e.g., PubMed, CINAHL, Psych/Social Science, Clinical Trials.gov, TRIP, etc.)
- Supplement with searches of:
  - Professional society evidence reviews/guidelines/policies
  - Regulatory and payor sources – FDA, CMS, health plan medical policies, etc.
  - Internet search engines (e.g., Google)

Site Searched	Search Terms/ Limits	Results
Cochrane Database (OVID) <a href="http://cl.kp.org/portal/site/cal/?epi_menuitemID=7996b20213a837f8401fdf702a71eea0">http://cl.kp.org/portal/site/cal/?epi_menuitemID=7996b20213a837f8401fdf702a71eea0</a>	Oral contrast Barium sulfate	0/41
PUBMED (access via KP Clinical Library - cl.kp.org)	Barium Sulfate [MH] OR "oral contrast" AND "emergency department"  (((("CT scan" OR "CT" OR computed tomography OR computerized axial tomography) AND (contrast OR "oral contrast" OR iodine* OR barium-sulfate OR barium*) AND (Humans[Mesh] AND (Clinical Trial[ptyp] OR Meta-Analysis[ptyp] OR systematic[sb] OR Randomized Controlled Trial[ptyp] OR Practice Guideline[ptyp] OR Guideline[ptyp] OR Technical Report[ptyp]) AND English[lang]))) AND (emergency department* OR emergency room* AND (Humans[Mesh] AND (Clinical Trial[ptyp] OR Meta-Analysis[ptyp] OR systematic[sb] OR Randomized Controlled Trial[ptyp] OR Practice Guideline[ptyp] OR Guideline[ptyp] OR Technical Report[ptyp]) AND English[lang])))	Used: 9

### **Overview of Search Methods**

**A comprehensive search was conducted on July 16, 2012 to identify evidence-based guidelines, systematic reviews and clinical trials evaluating abdominal CT scanning with and without the use of oral contrast. A search of Pubmed/MEDLINE ([www.pubmed.gov](http://www.pubmed.gov)) and the Cochrane database used various combinations of the following search term(s): (See Appendix A for additional search strategy details)**

**"computed tomography" "oral contrast" "abdominal or pelvic pain"**

**AMSTAR was used to assess the methodological quality of systematic reviews (See Appendix D).**

# KPSC Rapid Review 5-Step Process:

## 3. Selecting and Abstracting Data



- Single screening, selecting and abstracting
- Stay mindful of limitations including deadlines
- No dual review
- Studies are selected if they fall under inclusion/exclusion criteria
  - Including language, study design, patient population

**Inclusion/Exclusion Criteria:** Studies that specifically studied abdominal trauma patients, children, or patients stratified by body mass index were not included. Studies evaluating the effects of abdominal CT scans for identifying any abdominal disease or abdominal pain, and not limited to appendicitis, were included. Studies were included provided the reported effects of scanning on morbidity/mortality. Studies were also included if they reported on the diagnostic characteristics (sensitivity, specificity, positive predictive value, negative predictive value) of abdominal CT screening protocols (i.e. with and without contrast).

# KPSC Rapid Review 5-Step Process:

## 4. Evaluating the Literature

- Information is often tabled for clarity
- Quality of literature is assessed using appropriate grading guideline
  - Diagnostic studies were evaluated with Risk of Bias and Applicability Judgments from QUADAS-2 tool
  - Individual studies evaluating LOS in ED were evaluated with the AHRQ checklist for assessing risk of bias

### APPENDIX B. Evidence Tables

Table 3. Comparing the Effects of IV vs. IV+Oral Contrast in Adults with Non-Traumatic Abdominal Pain in the Emergency Department

Scanning Protocol	Name, year Design, N	Objective	Inclusion/Exclusion Criteria	Risk of Bias/Other Study Limitations	Author Reported Results
IV vs. IV and Oral Contrast	Hekimoglu et al., 2011 RCT N=200	To compare MDCT with IV alone to MDCT with IV and oral contrast (IVO) in adult patients with suspected appendicitis.	Patients 18 years and older with non-traumatic abdominal pain. Patients with possible contrast allergy, pregnancy, and traumatic cause of abdominal pain were excluded.	<b>Risk of Bias: Moderate</b> -Sequence Generation: No -Allocation Concealment: No -Blinding: No -Incomplete outcome data addressed: Unclear -Selective outcome reporting: No -Other limitations: Small sample size, potential confounders, incorrect calculations, unknown length of follow up for readmission/diagnosis accuracy, study completed in a foreign academic hospital, no power calculations mentioned.	<ul style="list-style-type: none"> <li>• Group 1, Reader 1 (oral and IV) had a sensitivity of 96.9% and a specificity of 98.5%; 97% PPV and 98.6% NPV</li> <li>• Group 2, Reader 1 (IV only) had a sensitivity of 93.4% and specificity 97%; 93.7% PPV and 97% NPV</li> <li>• Group 1, Reader 2 (oral and IV)</li> <li>• Group 2, Reader 2 (IV only)</li> <li>• The difference between the two readers in each group was not statistically significant</li> </ul>
IV vs. IV and Oral Contrast	Keener et al., 2012 RCT N=227 (IV [N = 114] and IVO [N = 113])	To compare CT with IV alone to CT with IV and oral contrast (IVO) in adult patients with suspected appendicitis.	Patients 18 years and older with signs and symptoms suggestive of appendicitis were included; confirmed pregnancy, allergy to IV or oral contrast, creatinine level of 1.5 or greater patients were excluded.	<b>Risk of Bias: Unclear</b> -Sequence Generation: No -Allocation Concealment: No -Blinding: No -Incomplete outcome data addressed: Unclear -Selective outcome reporting: Unclear -Other limitations: Small sample size, incorrect power calculations, academic hospital.	<ul style="list-style-type: none"> <li>• 80 (35.2%) patients with positive CT scans for appendicitis. Of these patients, 42 were IV and 38 were IVO (p = .612).</li> <li>• Both IV (n = 114) and IVO (n = 113) scans had 100% sensitivity (95% confidence interval [CI], 89.9-100 and 87.4-100, respectively)</li> <li>• NPV: 100% (95% CI, 93.7-100 and 93.9-100, respectively) for appendicitis.</li> <li>• Specificity of IV and IVO scans was 98.6 and 94.9 (95% CI, 91.6-99.9 and 86.9-98.4, respectively), respectively PPV: 97.6 and 89.5 (95% CI, 85.9-99.9 and 74.2-96.6).</li> </ul>
IV vs. IV and Oral Contrast	Anderson et al., 2009 RCT N=303 (151	To compare the diagnostic accuracy of IV contrast-enhanced 64-	Patients with acute non-traumatic AB pain and clinical suspicion of	<b>Risk of Bias: High</b> -Sequence Generation: No -Allocation Concealment: No -Blinding: No -Incomplete outcome data	<ul style="list-style-type: none"> <li>• Of the 303 patients enrolled, 151 patients (50%) were randomized to group 1 and the remaining 152 (50%) were randomized to group 2.</li> <li>• The combined reader performance for the diagnosis of appendicitis in group 1 was a sensitivity of 100% (95% CI, 76.8-100%) and specificity of 97.1% (95% CI, 92.7-</li> </ul>

# 4. Evaluating the Literature (cont.)

## QUADAS-2 tool

DOMAIN	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING
Description	Describe methods of patient selection: Describe included patients (prior testing, presentation, intended use of index test and setting):	Describe the index test and how it was conducted and interpreted:	Describe the reference standard and how it was conducted and interpreted:	Describe any patients who did not receive the index test(s) and/or reference standard or who were excluded from the 2x2 table (refer to flow diagram): Describe the time interval and any interventions between index test(s) and reference standard:
Signaling questions (yes/no/unclear)	Was a consecutive or random sample of patients enrolled?	Were the index test results interpreted without knowledge of the results of the reference standard?	Is the reference standard likely to correctly classify the target condition?	Was there an appropriate interval between index test(s) and reference standard?
	Was a case-control design avoided?	If a threshold was used, was it pre-specified?	Were the reference standard results interpreted without knowledge of the results of the index test?	Did all patients receive a reference standard?
	Did the study avoid inappropriate exclusions?			Did all patients receive the same reference standard?
				Were all patients included in the analysis?
Risk of bias: High/low/unclear	Could the selection of patients have introduced bias?	Could the conduct or interpretation of the index test have introduced bias?	Could the reference standard, its conduct, or its interpretation have introduced bias?	Could the patient flow have introduced bias?
Concerns regarding applicability: High/low/unclear	Are there concerns that the included patients do not match the review question?	Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Are there concerns that the target condition as defined by the reference standard does not match the review question?	



# 4. Evaluating the Literature (cont.)

## Cochrane Risk of Bias tool

Risk of bias	Criterion	RCTs	CCTs or cohort	Case-control	Case series	Cross-sectional
Selection bias	Was the allocation sequence generated adequately (e.g., random number table, computer-generated randomization)?	x				
	Was the allocation of treatment adequately concealed (e.g., pharmacy-controlled randomization or use of sequentially numbered sealed envelopes)?	x				
	Were participants analyzed within the groups they were originally assigned to?	x	x			
	Did the study apply inclusion/exclusion criteria uniformly to all comparison groups?		x			x
	Were cases and controls selected appropriately (e.g., appropriate diagnostic criteria or definitions, equal application of exclusion criteria to case and controls, sampling not influenced by exposure status)?				x	
	Did the strategy for recruiting participants into the study differ across study groups?			x		
	Does the design or analysis control account for important confounding and modifying variables through matching, stratification, multivariable analysis, or other approaches?	x	x	x	x	x
Performance bias	Did researchers rule out any impact from a concurrent intervention or an unintended exposure that might bias results?	x	x	x	x	x
	Did the study maintain fidelity to the intervention protocol?	x	x	x	x	
Attrition bias	If attrition (overall or differential nonresponse, dropout, loss to follow-up, or exclusion of participants) was a concern, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?	x	x	x	x	x
Detection bias	In prospective studies, was the length of follow-up different between the groups, or in case-control studies, was the time period between the intervention/exposure and outcome the same for cases and controls?	x	x	x		
	Were the outcome assessors blinded to the intervention or exposure status of participants?	x	x	x	x	x
	Were interventions/exposures assessed/defined using valid and reliable measures, implemented consistently across all study participants?	x	x	x	x	x
	Were outcomes assessed/defined using valid and reliable measures, implemented consistently across all study participants?	x	x	x	x	x
	Were confounding variables assessed using valid and reliable measures, implemented consistently across all study participants?			x	x	x
Reporting bias	Were the potential outcomes prespecified by the researchers? Are all prespecified outcomes reported?	x	x	x	x	x

\*Cases and controls should be similar in all factors known to be associated with the disease of interest, but they should not be so uniform as to be matched for the exposure of interest.





# KPSC Rapid Review 5-Step Process:

## 5. Translating Results for Clinical/Operational Decision Making



	Sensitivity	Specificity
<b>Oral Contrast (Oral alone, oral + rectal, oral + IV)</b>	<b>75-100%</b>	<b>83-100%</b>
<b>No Oral Contrast (Non-contrast, rectal only, IV only, rectal +IV)</b>	<b>76-100%</b>	<b>90-100%</b>

Contrast Protocol	Sensitivity	Specificity
<b>Rectal contrast</b>	<b>94-100%</b>	<b>89-100%</b>
<b>Oral contrast alone</b>	<b>76-93%</b>	<b>94-97%</b>
<b>Rectal + Oral contrast</b>	<b>95-97%</b>	<b>94-100%</b>
<b>Oral + IV contrast</b>	<b>90-100%</b>	<b>83-100%</b>
<b>Non-contrast</b>	<b>85-97%</b>	<b>86-100%</b>
<b>IV contrast alone</b>	<b>76-100%</b>	<b>93-98.6%</b>

- Moderate-quality evidence that abdominal CT scanning protocol without oral contrast (e.g., IV or rectal contrast) may be as sensitive and specific as abdominal CT scanning with oral contrast
- Appears to be a trend towards reduced LOS when eliminating oral contrast in the ED for both appendicitis and undifferentiated abdominal pain patients

- Coupled with the results from pilot study, decision-makers implemented regional goal to use IV CT only on all patients >18 for all suspected diagnoses

- KP Southern California's rapid reviews are intended to inform clinical judgment, not replace it.
- Given time constraints for decision making, a modestly robust summary of available evidence is preferable to no evidence at all.
- Transparency is critical and end users should be informed of the methods and limitations of rapid reviews.
- Definitive conclusions should be made cautiously when the evidence base is complex or there is high uncertainty.
- Rapid review methods are continually evolving, and standards are in development