How and when to update a clinical practice guideline

Marcello Tonelli
Alberta Kidney Disease Network
Canadian Task Force on Preventive Health Care
Guidelines have a “best before date”
Timeline for 2009 KDIGO CKD-MBD CPG

- **Mar 2006**: Generate PICOD questions
- **Jun 2006**: 1st WG Meeting: September 11-12, 2006
  - Finalize literature search parameters: PICOD
  - Population Intervention Comparator Outcomes Duration
- **Sept 2006**: 2nd WG Meeting: March 6-7, 2007
  - Begin literature review
- **Dec 2006**: 3rd WG Meeting: October 3-4, 2007
  - Craft guideline statements & complete lit review
- **Mar 2007**: 4th WG Meeting: March 3-4, 2008
  - Consensus on strength of GL statement, evidence & wording
- **Sept 2007**: 5th WG Meeting: Jan 19-20, 2009
  - Consensus on GL revisions based on public feedback
- **Dec 2007**: Publication
How long does it take before systematic reviews are out of date?

Shojania, Ann Intern Med 2007

N=100

Noncardiovascular
Cardiovascular

Median Survival (95% CI)
6.6 (5.1–1.4)
2.9 (1.1–5.3)
How long does it take before CPG are out of date?

<table>
<thead>
<tr>
<th>% of Guidelines Still Valid</th>
<th>Time (95% Confidence Interval), y</th>
</tr>
</thead>
<tbody>
<tr>
<td>90</td>
<td>3.6 (2.6, 4.6)</td>
</tr>
<tr>
<td>80</td>
<td>4.4 (3.5, 5.3)</td>
</tr>
<tr>
<td>50</td>
<td>5.8 (5.0, 6.6)</td>
</tr>
</tbody>
</table>

Shekelle, JAMA 2001
How long does it take before CPG are out of date?

Survival appears shorter for broader guidelines e.g., evaluation and care of CHF vs. management of otitis media with effusion.

Shekelle, JAMA 2001
What about guidelines on nephrology topics?

VALIDITY

optimist: our guidelines don’t change quickly

pessimist: our guidelines weren't valid in the first place
When do CPG need updating?

special challenge for virtual organizations

Revising a recommendation simply because you don’t agree with it is not really appropriate!
When do CPG need updating?

When there have been changes in:

- available interventions

These considerations imply a variable lifespan for CPG
(some last longer than others)

- resources available for healthcare

Shekelle, BMJ 2001
How do you know if a guideline needs updating?

- Scheduled review / withdrawal
- Ongoing surveillance – (reasonable accuracy)
- Ad hoc revision

Slide adapted from Paul Shekelle
What are the options for updating CPG?

- Living guideline
- Selective update
- Full review
- Refresh
- Keeping up-to-date

Slide adapted from Roberta James
What are the options for updating CPG?

- **full review**
  - Cons
    - heavy workload
    - slow/inefficient
  - Pros
    - thorough
    - predictable duration
    - robust methods

*start a new guideline from scratch*
What are the options for updating CPG?

living guideline

**Cons**
- difficult to stop
- burnout
- lots of work for little change
- managing audit trail

**Pros**
- up-to-date!
- good stakeholder involvement
- predictable

*constantly review and update guideline*

_Slide adapted from Roberta James_
What are the options for updating CPG?

*quick update (within 6 months) for big ticket change*
  - new evidence affecting ≤2 key questions or
  - policy/licensing change that affects entire CPG and
  - small CPG group

### Cons
- “patchwork” effect
- less comprehensive stakeholder engagement
- not comprehensive

### Pros
- less resource intensive
- quick
- responsive to stakeholders

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*Slide adapted from Roberta James*
What are the options for updating CPG?

update only the parts of the guideline that need to be updated

Cons

- old vs new format
- existing vs new KQ
- managing expectations re. scope

Pros

- quicker
- good stakeholder input
- less resource-intensive than full update
- established methods

selective update

Slide adapted from Roberta James
What are the options for updating CPG?

- living guideline
- selective update
- full review
- refresh

keeping up-to-date

with new areas?
without new areas?

Slide adapted from Roberta James
Once you’ve decided which approach to take, what next?
Analytical framework

KQ1a. What is the evidence for the benefit of screening for depression in asymptomatic adults 18 years of age or over from the general population not at high risk for depression in (i) primary care or (ii) other outpatient settings to improve critical outcomes?

KQ1b. What is the evidence for the benefit of screening for depression in adults at high risk for depression in (i) primary care, (ii) other outpatient settings, or (iii) specialty clinic setting to improve critical outcomes?

KQ2a. What is the evidence for the harms of screening for depression in asymptomatic adults 18 years of age or over from the general population not at high risk for depression in (i) primary care or (ii) other outpatient settings?

KQ2b. What is the evidence for the harms of screening for depression in adults at high risk for depression in (i) primary care, (ii) other outpatient settings, or (iii) specialty clinics?

CTFPHC, 2013
does screening per se improve outcomes?

Adults aged ≥18 y at average risk of depression or high risk of depression

Screening

Depression

Harms

Accuracy of Screening Tools

Critical outcomes:
- Quality-of-life
- Suicidality rate (attempts or ideation)
- All-cause mortality
- Depression related mortality
- Hospitalization rates
- Symptoms of depression (response or remission)
Analytical framework

Adults aged ≥18 y at average risk of depression or high risk of depression

Screening

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does screening cause harm?
Analytical framework

1. Adults aged ≥18 y at average risk of depression or high risk of depression
   - Screening

2. Harms

3. Accuracy of Screening Tools
   - Critical outcomes:
     - Quality-of-life
     - Suicidality rate (attempts or ideation)
     - All-cause mortality
     - Depression related mortality
     - Hospitalization rates
     - Symptoms of depression (response or remission)

Can we identify the target condition?
Analytical framework

if we identify it, can we treat it?

Adults aged ≥18 y at average risk of depression or high risk of depression

Screening

Depression

1

Critical outcomes:
- Quality-of-life
- Suicidality rate (attempts or ideation)
- All-cause mortality
- Depression related mortality
- Hospitalization rates
- Symptoms of depression (response or remission)

Harms

2

Accuracy of Screening Tools

3

KDIGO

CTFPHC, 2013
### The KDIGO approach: interventions

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Screening criteria</th>
<th>Articles in summary tables</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>CKD stages 3-5</td>
</tr>
<tr>
<td>Treatment targets</td>
<td></td>
<td></td>
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<tr>
<td>CKD stages 3-5, 5D, or 1-5T</td>
<td></td>
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<tr>
<td>RCTs⁹</td>
<td>N ≥ 25 per arm (&gt;10 per arm for bone biopsy)</td>
<td>0</td>
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<tr>
<td>F/U ≥ 6 months</td>
<td></td>
<td></td>
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<tr>
<td>Any P Binder vs placebo/active control (except Ca vs placebo)⁹</td>
<td></td>
<td>1</td>
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<tr>
<td>Phosphate binders</td>
<td></td>
<td></td>
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<tr>
<td>RCTs⁹</td>
<td>N ≥ 25 per arm (&gt;10 per arm for bone biopsy)</td>
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<tr>
<td>F/U ≥ 6 months</td>
<td></td>
<td></td>
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<tr>
<td>Vitamin D</td>
<td></td>
<td></td>
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<tr>
<td>RCTs⁹</td>
<td>N ≥ 25 per arm (&gt;10 per arm for bone biopsy)</td>
<td>7</td>
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<tr>
<td>F/U ≥ 6 months</td>
<td></td>
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<tr>
<td>Calcimimetics</td>
<td></td>
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<tr>
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<td>N ≥ 25 per arm (&gt;10 per arm for bone biopsy)</td>
<td>1</td>
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<tr>
<td>F/U ≥ 6 months</td>
<td></td>
<td></td>
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<tr>
<td>Calcium supplementation</td>
<td></td>
<td></td>
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<td>F/U ≥ 6 months</td>
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<td></td>
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<tr>
<td>Bisphosphonates, calcitonin, estrogen, progesterone, SERMs, intermittent PTH</td>
<td>Treatment vs placebo/active control</td>
<td>3 Bisphosphonates</td>
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<tr>
<td>F/U ≥ 6 months</td>
<td></td>
<td></td>
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<tr>
<td>Diet</td>
<td>Dietary phosphate restriction vs standard diet (must quantify phosphate intake)</td>
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<tr>
<td>CKD stages 3-5, 5D, or 1-5T</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCTs⁹</td>
<td>N ≥ 10 per arm</td>
<td>0</td>
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<tr>
<td>F/U ≥ 1 month for biochemical ≥ 6 months for bone outcomes</td>
<td></td>
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</tbody>
</table>
The KDIGO approach: topics not related to treatments

<table>
<thead>
<tr>
<th>Topic</th>
<th>Question</th>
<th>Screening criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural history of bone and CVD abnormalities</td>
<td>What is the natural history of bone abnormalities, and vascular and valvular calcification in CKD, after transplantation and after PTx?</td>
<td>CKD stages 3-5D and T Prospective, longitudinal F/U ≥ 6 months N ≥ 50 Predictors: bone biopsy; DXA; qCT; Vascular/Valvular calcification by echo, EBCT, MSCT, qCT, carotid IMT, aortic X-ray Outcomes: change in predictor over time, with or without interim transplantation or PTx</td>
</tr>
<tr>
<td>Evaluation of biochemical markers</td>
<td>What is the association between calcium, phosphorus, CaXP and PTH, and (a) morbidity and mortality, (b) bone abnormalities (histology, DXA, qCT), and (c) vascular and valvular calcification? How do these vary by CKD stage?</td>
<td>CKD stages 3-5D and T Prospective, longitudinal F/U ≥ 6 months N ≥ 100, for bone biopsy N ≥ 20 Predictors: serum calcium (ionized, correct, total), serum phosphorus, CaXP, second, third generation or ratio PTH Outcomes: mortality, bone outcomes, CVD outcomes</td>
</tr>
<tr>
<td>Evaluation of bone imaging tests, including plain radiographs, qCT, and quantitative US</td>
<td>What is the association between additional biomarkers of bone turnover, and (a) morbidity and mortality, (b) bone abnormalities, and (c) vascular and valvular calcification?</td>
<td>CKD stages 3-5D and T naïve to treatment with vitamin D Prospective, longitudinal F/U ≥ 6 months N ≥ 100, for bone biopsy N ≥ 20 Predictors: total alkaline phosphatase, bone-specific alkaline phosphatase, TRAP, OC, OPG, C-terminal cross links Outcomes: mortality, bone outcomes, CVD outcomes</td>
</tr>
<tr>
<td>Evaluation of bone imaging tests, including plain radiographs, qCT, and quantitative US</td>
<td>What is the association between vitamin D (25(OH)D and 1,25(OH)_{2}D), and (a) morbidity and mortality, (b) bone abnormalities, and (c) vascular and valvular calcification in individuals not treated with vitamin D replacement?</td>
<td>CKD stages 3-5D and T, naïve to treatment with vitamin D Prospective, longitudinal F/U ≥ 6 months N ≥ 100, for bone biopsy N ≥ 20 Predictors: vitamin D, 25(OH)D for all, 1,25 (OH)_{2} D for non-dialysis Outcomes: mortality, bone outcomes, CVD outcomes</td>
</tr>
<tr>
<td>Evaluation of bone imaging tests, including plain radiographs, qCT, and quantitative US</td>
<td>How do bone biopsy and DXA, and other bone imaging tests, including plain radiographs, qCT, and quantitative US predict (a) clinical outcomes and (b) surrogate outcomes for bone and CVD?</td>
<td>CKD stages 3-5D and T Prospective, longitudinal F/U ≥ 1 year, ≥ 6 months for transplant N ≥ 50, for bone biopsy N ≥ 20 Predictors: bone biopsy, DXA, DXA in combination with biochemical markers, change in DXA over 1 year, bone imaging by qCT (spine, wrist), qUS (heel) Outcomes: mortality, bone outcomes, CVD outcomes</td>
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Overview of selective update (1)

• Select the questions that the CPG will address
  – are any new questions needed?

• Reuse prior questions if possible
  – reduces work of framing, searching, writing
  – makes knowledge translation (KT) easier

• Execute new searches
  – identify questions where there is new evidence
Overview of selective update (2)

• Review existing recommendations in light of new data

• Draft recommendations to address new questions

• Decide on KT implications
Existing CPG or SR can sometimes be used to speed up the literature search

Identifying literature for an update

Key questions and recommendations to be updated

Is there an up-to-date CPG that addresses the issue satisfactorily?²

No

Search for systematic reviews from the date of the original CPG search onwards.⁴

Search for original studies from the last search date of the identified systematic reviews.⁵

Yes

Assess whether to adopt, adapt or use as a source³

Redesign original search strategies:
1. Define descriptors and terms in titles and abstracts of main systematic reviews and clinical trials.
2. Combine with methodological design filters (high-specificity version).
3. Check for any developments in descriptors of interest and methodological filters.
4. Search onwards from the complete year in which the original CPG was completed.

Spanish MOH CPG manual
It’s important to highlight new or revised recommendations in CPG

Recommendations for the Basque Health Service

18 Clinical Practice Guideline on Hypertension (2007 update)

When AMPA is used to follow up hypertensive patients, a three-day minimum BP self-monitoring schedule is recommended, with three measurements every 12 hours in the week prior to consultation.

When AMPA is used in suspected white coat hypertension, figures equal to or greater than 145/95 mmHg diagnose a patient as hypertensive, while lower figures require MAPA.

Follow-up of white coat hypertension should include non-pharmacological measures and regular evaluation of cardiovascular risk and risk of involvement of target organs.

[Translated from Spanish]
Goals of the current meeting

• Review and identify which recommendation statements need updating based on evidence published since 2008 (or 2007?)

• Provide rationale for updating or not

• Goal is NOT to draft new recommendations or reappraise specific quality level of evidence for each recommendation. Rather, the goal is provide a suggested roadmap for future Work Group to follow
Suggestion 1: each group should answer the following questions about each recommendation

1. Are there important and relevant new data?
   if no → no changes needed (unless to address implementability issues or changes in values placed on outcomes or available resources)
   if yes → proceed to next question
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   **relevant new data** = data about the treatment of humans + low risk of bias

   i.e.  good quality RCTs or extremely strong, consistent observational data
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definitely not: experimental or animal studies

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not: weak RCTs, single observational studies, observational data with small effects
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   - if yes → proceed to next question

2. Do the data suggest that the recommendation might/should change?
   - if no → revised CPG would simply cite new studies
   - if yes → proceed to next question
3. What are the factors that one should consider when deciding whether to revise or not?

- Change in magnitude or direction of net benefit/harm of Rx
- Change in quality of evidence
- Availability of new interventions, strategies or techniques
- Changes in any of the above for specific populations:
  - e.g. elderly, pediatric, transplant, non-dialysis vs. dialysis/Tx, etc
Suggestion 2: each group to consider whether additional recommendations are needed

• What new topics should the updating Work Group consider?

• To assist the literature search, can the new question(s) be specified in PICOD format (Population, Intervention, Comparator, Outcome, Duration/Design)?
Suggestion 3: Final considerations

- Despite progress made since 2009, what are the existing controversial questions and how can future research or improved trial design better resolve them?
Breakout session #1

Answer the questions established by each WG

Is there any new evidence in adults, elderly, transplant recipients and children about:

- What are the best ways to measure calcium or phosphorus status, or how frequently should this be measured? (recommendations 3.1.1, 3.1.2, 3.1.5, 5.1 and 5.2). Factors to consider:
  - albumin binding: tCa vs iCa vs cCa
  - variation: intraindividual (diurnal), therapy (dialysis)-induced, inter-assay
  - diagnostic properties (Sn, Sp, PPV, NPV)
  - availability/cost
  - balance vs excretion vs serum levels
  - consider for G3-G5a, HD/PD and CKD-T separately

- What is the target range for serum phosphorus or calcium (recommendations 4.1.1 and 4.1.2)? Factors to consider:
  - different ranges for G3-G5a, HD/PD and Tx?
  - are there other clinical characteristics that should affect the target range?
Breakout session #2

Answer the more specific questions below for each recommendation:

- Change in magnitude or direction of net benefit/harm of Rx
- Change in quality of evidence
- Availability of new interventions, strategies or techniques
- Changes in any of the above for specific populations:
  - e.g. elderly, pediatric, transplant, non-dialysis vs. dialysis/Tx, etc

should this recommendation be revised?
Discussion

KDIGO