KHA-CARI Update

Martin Gallagher
Chair, KHA-CARI Steering Committee
Overview

• Governance review
  – Response

• CARI reporting
  – Budgetary issues
  – Workplan

• KDIGO

• GRADE-ing evidence
CARI governance review 2009

• Terms of reference:
  1. Establish the standing of the body of work of the CARI Guidelines within the world literature of renal guidelines.
  2. Comment upon the relative value for money of this body of work (including the contribution of the volunteer workforce of guideline developers) in an international renal guidelines context.
  3. Comment upon the feasibility of the existing CARI Guidelines work being performed by other bodies (either local or international) to a similar or higher standard using historical funding levels.
  4. Suggest future areas for investment by CARI Guidelines to ensure ongoing relevance.
  5. In light of above recommendations, to comment upon appropriate funding levels and strategies by which secure and long term funding might be derived.
CARI governance review 2009

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  5. In light of above recommendations, to comment upon appropriate funding levels and strategies by which secure and long term funding might be derived.

Review summary:
The CARI guidelines & guideline group are well respected nationally and internationally.
CARI governance review 2009

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Review summary: “.... given the available resources CARI has completed a remarkable number of rigorously developed new guidelines and undertaken an associated program of research...”
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5. In light of above recommendations to comment upon appropriate funding levels and strategies by which secure and long term funding might be derived.

Review summary:
“It is very unlikely that any other guideline group, local or international, could undertake the program of existing CARI guidelines work within the current funding levels”
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Review summary:
‘...recommendations about improving governance, identifying clear strategic directions, improving business processes with a business plan with clear sets of deliverables, and linking with other groups, including those for identifying and gathering performance indicators.”
CARI governance review 2009

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Review summary:
“...needs to move to a more assured funding position and needs to be perceived to be independent of pharmaceutical company sponsorship. There should be a clear funding agreement between CARI and its governing body ...”
Aust guideline context

3 Clinical practice guidelines by key health area and federal and state government agency support

<table>
<thead>
<tr>
<th>Key health area</th>
<th>Funded or produced by government agencies (n = 167)</th>
<th>Not funded or produced by government agencies (n = 146)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Evidence-documented (n = 46)</td>
<td>Not evidence-documented (n = 121)</td>
</tr>
<tr>
<td>Asthma</td>
<td>2</td>
<td>9</td>
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<tr>
<td>Cancer</td>
<td>8</td>
<td>3</td>
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<tr>
<td>Cardiovascular disease</td>
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<td>1</td>
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<tr>
<td>Diabetes</td>
<td>5</td>
<td>0</td>
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<tr>
<td>Drugs and alcohol</td>
<td>5</td>
<td>27</td>
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<tr>
<td>Infectious diseases</td>
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<td>16</td>
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<tr>
<td>Injury</td>
<td>2</td>
<td>4</td>
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<tr>
<td>Mental health</td>
<td>7</td>
<td>9</td>
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<tr>
<td>Musculoskeletal disease</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Obesity</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Pregnancy and childbirth</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Renal disease</td>
<td>3</td>
<td>16</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
<td>41</td>
</tr>
</tbody>
</table>

Non-renal 30%
Renal 90%

Buchan et al, MJA 2010
Response

• Formal oversight by KHA Board
  – Continued links to ANZSN via DNT

• Guaranteed funding $250K per annum for 3yrs
  – Raised through pharma industry

• Ongoing attempts to secure further funding
  – Pharmaceutical industry
  – Government
  – NGO: KHNZ

• New KHA representatives on CARI Steering Committee

• Name change:
  – KHA-CARI Guidelines

• Agreed work-plan
<table>
<thead>
<tr>
<th>YEAR</th>
<th>NEW GUIDELINES</th>
<th>GUIDELINE UPDATES</th>
<th>ADAPTED GUIDELINES (ADAPTE tool)</th>
<th>IMPLEMENTATION PROJECT</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>“Nutrition and Growth in Kidney Disease” (Jan 2011 – Nov 2011)</td>
<td></td>
<td>Conduct face to face meeting with units (Nov 2011)</td>
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<td></td>
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<td>Assessment of study results to commence (Apr 2012)</td>
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<td>Feedback results to participating units (May/Jun 2012)</td>
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<td></td>
<td>Commence writing Implementation phase paper (Jul 2012)</td>
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<td>2013</td>
<td>To be decided</td>
<td>“Prevention of Progression of Kidney Disease” (Jan 2013 – Nov 2013)</td>
<td>“Anemia in CKD” (Jun 2012 – Mar 2013)</td>
<td>To be decided</td>
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<td></td>
<td></td>
<td>“Bone Disease, Calcium &amp; Phosphate” (Jan 2013 – Nov 2013)</td>
<td>“Classification &amp; Management of CKD” (Jun 2012 – Mar 2013)</td>
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<td></td>
<td></td>
<td>“Biochemical &amp; Haematological Targets” (Jan 2013 – Nov 2013)</td>
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<td></td>
</tr>
<tr>
<td>Title</td>
<td>Topics Covered</td>
<td>Subtopics</td>
<td>Publication Date</td>
<td></td>
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<td>Chronic Kidney Disease</td>
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<td>1. (In development)</td>
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<td></td>
<td>2. Prevention of Progression of Kidney Disease</td>
<td>48</td>
<td>2. (Published April 2006 &amp; Feb 2007)</td>
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<td>5. Vitamin D, Calcimimetics and Phosphate Binders</td>
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<td>5. (Published April 2006)</td>
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<td></td>
<td>6. Urine Protein as Diagnostic Test</td>
<td>4</td>
<td>6. (Published October 2004)</td>
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<td></td>
<td>7. Evaluation of Renal Function</td>
<td>5</td>
<td>7. (Published October 2005)</td>
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<td></td>
<td>8. Kidney Stones</td>
<td>7</td>
<td>8. (Published Feb 2007)</td>
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<td>10. Renovascular Disease</td>
<td>6</td>
<td>10. (Published April 2010)</td>
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<td>11. Type 2 Diabetes: Kidney Disease</td>
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<td>11. (Published April 2010)</td>
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<td></td>
<td>12. Diagnosis and Treatment of Urinary Tract Infection in Children</td>
<td>9</td>
<td>12. (In development)</td>
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<td>Dialysis Guidelines</td>
<td>1. Acceptance onto Dialysis</td>
<td>13</td>
<td>1. (Published Oct 2005; April 2010)</td>
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<td>2. Biochemical and Haematological Targets</td>
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<td>2. (Published Mar 2000; April 2006; Aug 2008)</td>
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<td>Transplantation Guidelines</td>
<td>1. Deceased Kidney Donor Suitability</td>
<td>4</td>
<td>1. (Published Oct 2005)</td>
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<td></td>
<td>2. CMV Disease and Kidney Transplantation</td>
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<td>2. (Published Oct 2004)</td>
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<td></td>
<td>3. Calcineurin Inhibitors in Renal Transplantation</td>
<td>7</td>
<td>3. (Published Feb 2007)</td>
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<td>4. Recipient Assessment for Transplantation</td>
<td>7</td>
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<td></td>
<td>5. Living Kidney Donor</td>
<td>11</td>
<td>5. (Published April 2010)</td>
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<tr>
<td>Adaptations of KDIGO guidelines</td>
<td>1. CPG for the Care of Kidney Transplant Recipients</td>
<td>21</td>
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<tr>
<td></td>
<td>2. CPG for the Diagnosis, Evaluation, Prevention and Treatment of CKD Mineral and Bone Disorder</td>
<td>7</td>
<td>2. (In development)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. Acute Kidney Injury</td>
<td>7</td>
<td>3. (To commence)</td>
<td></td>
</tr>
</tbody>
</table>

In development | Being updated
KDIGO

• Kidney Disease: Improving Global Outcomes
  – International guidelines
  – Funded by NKF
  – Private company, incorporated in Belgium

• Increasing suite of guidelines
  – Hep C, Mineral bone disease, Transplant, AKI, Glomerulonephritis, blood pressure in CKD, anaemia in CKD

• Use of ADAPTE tool to apply to ANZ
  – Transplantation our first attempt
  – Probably ~2/3 the volume of work cf a new guideline

• Published commentary
  – Hep C
How does KDIGO relate to CARI?

• Frequent dialogue
  – Aust members of KDIGO Board
  – Attempts to synchronise work plans
• Lacks the engagement of the local workforce
• Imperatives may not reflect local needs/issues
  – Still very nephrologist focussed
• Implementation taskforce:
  – Difficult task on an international level

• KHA-CARI approach
  – Leverage the international investment as best we can
GRADE: What is it?

- GRADE = Grading of Recommendations, Assessment, Development, and Evaluation

- Set up in 2000 - developed by a group of international guideline developers

- GRADE Working Group
  - Methodologists and guideline developers

- www.gradeworkinggroup.org/
GRADE Uptake

- UpToDate
- British Medical Journal
- ACP
- BMJ Clinical Evidence
- Society of Vascular Surgery
- European Respiratory Society
- Society of Critical Care Medicine
- American College of Chest Physicians
- EBM Guidelines Finland
- Infectious Disease Society of America
- National Institute for Clinical Excellence
- Agency for Health Care Research and Quality
- Swedish National Board of Health and Welfare
- Canadian Agency for Drugs and Technology in Health
- Ontario MOH Medical Advisory Secretariat
- Agencia sanitaria regionale, Bologna
- The German Agency for Quality in Medicine
- Evidence-based Nursing Sudtirol, Alt Aida
- Norwegian Knowledge Centre for the Health Services
- University of Pennsylvania Health System Center for Evidence-Based Practice
- Journal of Infection in Developing Countries
- Japanese Society of Oral and Maxillofacial Radiology
- World Health Organization
- American Thoracic Society
- Cochrane Collaboration
- Polish Institute for EBM
- Society of Pediatric Endocrinology
- American Endocrine Society
- Surviving sepsis campaign
- European Soc of Thoracic Surgeons
- Allergic Rhinitis in Asthma Guidelines

Meanwhile, back on planet Quack-o....
Why?

• To help resolve confusion
  – various different systems of rating evidence and recommendations exist.
    • Guyatt’s User’s Guide; USPSTF; Oxford Centre for EBM; ICSI; SIGN; NHMRC; NZGG

• Various problems:
  – Many designed around need for RCTs: may not be possible
  – Some don’t take account of the “overall” picture of evidence
  – Fail to judge strength of evidence and applicability to the population
  – Users misinterpret the strength as reflecting importance
    • Rather than strength of supporting evidence.
Key advantages

• Separation:
  – Quality of evidence
    • extent to which one can be confident that an estimate of effect is correct
  – Strength of recommendation
    • extent to which one can be confident that adherence to the recommendation will do more good than harm

• Explicit rules for upgrading/downgrading evidence

• Clarity regarding recommendations (and what they mean)
  – Includes explicit judgement around values/trade-offs/costs

• International uptake
  – KDIGO in nephrology
Rate the quality of evidence for each outcome, across studies
RCTs start high, observational studies start low
(-)
Study limitations
Imprecision
Inconsistency of results
Indirectness of evidence
Publication bias likely

(+)
Large magnitude of effect
Dose response
Plausible confounders would ↓ effect when an effect is present or ↑ effect if effect is absent

Final rating of quality for each outcome: high, moderate, low, or very low

Rate overall quality of evidence
(lowest quality among critical outcomes)

Decide on the direction (for/against) and grade strength (strong/weak*) of the recommendation considering:
- Quality of the evidence
- Balance of desirable/undesirable outcomes
- Values and preferences

Decide if any revision of direction or strength is necessary considering: Resource use

*also labeled “conditional” or “discretionary”
What to know before you start?

Writers/reviewers need to understand the process

   Be aware that it may be more work than previously

Need to specify all outcomes before starting

Need to develop a hierarchy of pt outcomes
   Critical vs non-critical

Fig 1 Hierarchy of outcomes according to importance to patients to assess effect of phosphate lowering drugs in patients with renal failure and hyperphosphataemia
Little or no evidence?

• Will mean “low” or “very low” quality evidence
• There may be situations where it is given a “strong” recommendation
  – Where consequence of not using treatment is high (risk of harm, cost)
    • Eg: gadolinium in patients with CKD
      – Data low quality
      – Severe complication
      – Strong recommendation not to use it
  – Equivalence of two treatments, big differences in cost
• Doesn’t stop guideline writers including ‘expert opinion’
CARI

• Planning for all guidelines using the GRADE evidence methodology

• NHMRC
  – Additional levels of evidence grading
  – Components: evidence base, consistency, clinical impact, generalisability, applicability
  – Requirement to use GRADE
    • For NHMRC endorsement
    • For inclusion on Aust govt. g
    • When money flows......
Summary

• Lots of change over the last 2 years
  – High standing of KHA-CARI reinforced
  – New governance arrangements in place
  – Balance of work:resources our biggest challenge

• Evolution of methods:
  – ADAPTE tool
  – GRADE evidence guidelines
Acknowledgements

• CARI Steering Committee
  – Executive group: Rowan Walker, Jonathan Craig, Tim Matthew
• Guideline convenors and writers
  – Members of ANZSN, esp DNT sub-committee
• CARI Office
  – Denise Campbell
  – Others: Martin Howell, Pamela Lopez-Varga, Michelle Irving
• Kidney Health Australia
• Pharmaceutical supporters
  – Amgen Australia
  – Janssen-Cilag Pty Ltd
  – Genzyme Corporation
  – Roche Products Pty Ltd
  – Shire Australia Pty Ltd
  – Novartis Pharmaceuticals Australia Pty Ltd
  – Baxter Healthcare Pty Ltd