Should guidelines or individual care be utilized by specialists?

Robert A. Wise, M.D.
Johns Hopkins University
AAAAAI February 24, 2013
“Are these just guidelines, or are they actual new policies”
Question:

Should guidelines or individual care be utilized by specialists?
Answer

Yes, of course
Clinical Guidelines - Strengths

• Compendium of evidence-based medicine
  – Literature Review
  – Assess Quality of data
  – Define areas of uncertainty or ignorance

• Expert opinion
  – Consensus of experts
  – Strength of recommendation
Expert Opinion

“I don't always know what I'm talking about but I know I'm right.”
--Muhammad Ali
Former World Heavyweight Boxing Champion
Consensus

“A consensus means that everyone agrees to say collectively what no one believes individually”

Abba Eban
Israeli Foreign Affairs Minister
United Nations Ambassador
Expert Opinion: NAEPP Guidelines for treatment of GERD in asthma

“Even in the absence of suggestive GERD symptoms, consider evaluation for GERD in patients who have poorly controlled asthma, especially with nighttime symptoms.... Treatment includes: ... using proton pump inhibitor medication.”

Guidelines for the Diagnosis and Management of Asthma (EPR-3) 2007. NIH, NHLBI. August 2007. NIH publication no. 08-4051.
Study of Acid Reflux in Asthma SARA Trial
Episodes of poor asthma control

- Placebo (n = 193)
- Esomeprazole (n = 200)

- **EPAC 1**
  - Placebo: p = 0.72
  - Esomeprazole: p = 0.72

- **EPAC 2**
  - Placebo: p = 0.80
  - Esomeprazole: p = 0.80

Note: The p-values indicate the statistical significance of the differences between the groups.
…this committee suggests the following combined therapy (corticosteroid and either azathioprine or cyclophosphamide) … Given the poor prognosis for patients with IPF, many experts have recommended that treatment be initiated in all patients with IPF who do not have contraindications to therapy.
Panther study – stopped early because of excess deaths in treatment group


Treatment = 8 deaths
Placebo = 1 death
Clinical Guidelines – The Dark Side

• Methodology varies widely in scope of literature review, interpretation of strength of evidence, and process of consensus development
• Some recommendations, by their nature, are arbitrary
• Selection of experts weighted toward academia rather than practitioners
• Conflicts of interest both financial and intellectual
“Are you just pissing and moaning or can you verify what you’re saying with data”
Evidence-Based Medicine
Hierarchy of evidence 1

1. Randomized Controlled Clinical Trials
2. Controlled Observational Studies
3. Uncontrolled Observational Studies
4. Case Series
5. Case Reports / Anecdotes
6. Biological Evidence

Modified from: Dept Health Human Services [www.AHRQ.gov](http://www.AHRQ.gov)
Adult Preventive Services Task Force
Hierarchy of Evidence 2

1. **Systematic reviews and meta-analyses**
2. **Randomized controlled trials with definitive results**
3. **Randomized controlled trials with non-definitive results**
4. Cohort studies
5. Case-control studies
6. Cross sectional surveys
7. Case reports.

Greenhalgh, T. 1997. How to read a paper: getting your bearings (deciding what the paper is about. BMJ 1997; 315: 243.)

Hierarchy of evidence 3

1. N-of-1 randomized trial.
2. Systematic reviews of randomized trials.
4. Systematic reviews of observational studies.
5. Single observational studies.
6. Physiological studies.
7. Unsystematic observations.

Generalizability of Clinical Trials

General Population Survey of 3500 adults
749 people tested for current asthma
179 with current asthma (Dx and PFT variability)

Assessed against eligibility criteria for 17 major trials cited in GINA guidelines.

On average, only 4% of pts with asthma were eligible
(Median 6%, range 0-36%)
RCT Evidence is often lacking
Conclusions As with many interventions intended to prevent ill health, the effectiveness of parachutes has not been subjected to rigorous evaluation by using randomised controlled trials. Advocates of evidence based medicine have criticised the adoption of interventions evaluated by using only observational data. We think that everyone might benefit if the most radical protagonists of evidence based medicine organised and participated in a double blind, randomised, placebo controlled, crossover trial of the parachute.
Not all guidelines are consistent: Early Use of Antibiotics in Sepsis

- Surviving Sepsis Campaign (SSC)
  - 2004 Recommendation: Early use of antibiotics
    - Grade E (level IV or V evidence -- nonrandomized, historical controls, uncontrolled studies, expert opinion, lowest level of evidence)
  - 2008 Recommendation: Early use of antibiotics
    - 1B (if shock is present) and 1D (if shock is absent)
      (Strong recommendations – 3 new observational studies but no trials)

GRADE systematic approach to clinical guidelines

• Systematic collection of evidence
• The quality of evidence across studies for each important outcome
• Which outcomes are critical to a decision
• The overall quality of evidence across these critical outcomes
• The balance between benefits and harms
• The strength of recommendations.

http://www.gradeworkinggroup.org/
GRADE – Quality of Evidence

• Randomized trial = high
• Observational study = low
• Any other evidence = very low


http://www.gradeworkinggroup.org/
GRADE – Strength of Evidence

- **High** = Further research is very unlikely to change our confidence in the estimate of effect.
- **Moderate** = Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- **Low** = Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
- **Very low** = Any estimate of effect is very uncertain.


http://www.gradeworkinggroup.org/
GRADE – Strength of Recommendation (Strong vs. Weak)

• Balance between benefits and harms
• Quality of the evidence
• Translation of the evidence into specific circumstances
• Certainty of the baseline risk
• Costs
• Resource utilization


http://www.gradeworkinggroup.org/
Illustration of GRADE recommendations – Obesity in Asthma

• Weight loss by diet and exercise
  – Strong recommendation with low quality evidence

• Weight loss by bariatric surgery
  – Weak recommendation with low quality evidence

Adeniyi FB, Young T. Weight loss interventions for chronic asthma. Cochrane Database Syst Rev. 2012 Jul 11
Concerns about the GRADE system

- Requires value judgments that may or may not be explicit
- Has not been externally validated
- Poor agreement on rating among experts (Kappa = 0.27)
- Separation of strength of recommendation from evidentiary basis for recommendation is not logical nor feasible

Sometimes obvious things are not so obvious when put into practice
Education and self-care in COPD

Ideally, educational messages should be incorporated into all aspects of care for COPD ... Education should be tailored to the needs and environment of the individual patient...

The topics that seem most appropriate for an education program include the following: smoking cessation; basic information about COPD and pathophysiology of the disease, general approach to therapy and specific aspects of medical treatment, self-management skills, strategies to help minimize dyspnea, advice about when to seek help, self-management, and decision making during exacerbations...

GOLD COPD guidelines 2007
COPD Education and Self-Care VA Trial

• 4 – 90 minute group training sessions
• Educational and reference materials
• Individualized action plan
• Monthly calls from care manager x 3, then 3 month calls
• 24 hour access to care manager
A Comprehensive Care Management Program to Prevent Chronic Obstructive Pulmonary Disease Hospitalizations: A Randomized, Controlled Trial


**Hospitalizations**

- Usual care
- CCMP

**Deaths**

- Usual care
- CCMP

Participants at risk, n

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Guidelines often do not take other guidelines into account
Effect of Overlapping Guideline Treatment for Common Conditions

• Hypothetical typical patient:
  79 year old woman with 5 chronic conditions of moderate severity: Asthma/COPD, HTN, DM, Osteoporosis, Osteoarthritis

• Generated an aggregate treatment regimen
  – explicit instructions
  – once a day dosing
  – generic
  – synergies between CPGs
  – least adverse effects / interactions

• Cost to patient
<table>
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<tr>
<th>Time</th>
<th>Medications</th>
<th>Non-pharmacologic Therapy</th>
<th>All Day</th>
<th>Periodic</th>
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<tr>
<td>7 AM</td>
<td>Tiotropium / ICS LABA I Alendronate 70mg weekly</td>
<td>Check feet</td>
<td>Joint protection</td>
<td>Pneumonia vaccine, Yearly influenza vaccine</td>
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<tr>
<td></td>
<td></td>
<td>Sit upright 30 min.</td>
<td>Energy conservation</td>
<td>All provider visits: Evaluate Self-monitoring blood glucose, foot exam and BP</td>
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<td></td>
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<td>Check blood sugar</td>
<td>Exercise (non-weight bearing if severe foot disease, weight bearing for osteoporosis)</td>
<td>Quarterly HbA1c, biannual LFTs</td>
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<tr>
<td>8 AM</td>
<td>Eat Breakfast</td>
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<td>Muscle strengthening exercises, Aerobic Exercise ROM exercises</td>
<td>Yearly creatinine, electrolytes, microalbuminuria, cholesterol</td>
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<tr>
<td></td>
<td>HCTZ 12.5 mg</td>
<td>2.4gm Na, 90mm K, Adequate Mg, ↓ cholesterol &amp; saturated fat, medical nutrition therapy for diabetes, DASH</td>
<td>Avoid environmental exposures that might exacerbate asthma</td>
<td>Referrals: Pulmonary rehabilitation</td>
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<tr>
<td></td>
<td>Lisinopril 40mg</td>
<td></td>
<td>Wear appropriate footwear</td>
<td>Physical Therapy</td>
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<td></td>
<td>Glyburide 10 mg</td>
<td></td>
<td>Albuterol MDI prn</td>
<td>DEXA scan every 2 years</td>
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<td>ECASA 81 mg</td>
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<td>Limit Alcohol</td>
<td>Yearly eye exam</td>
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<td>Metformin 850mg</td>
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<td>Maintain normal body weight</td>
<td>Medical nutrition therapy</td>
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<td>Naproxen 250mg</td>
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<td>Patient Education: High-risk foot conditions, foot care, foot wear</td>
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<td>Omeprazole 20mg</td>
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<td>Osteoarthritis</td>
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<td>Calcium + Vit D 500mg</td>
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<td></td>
<td>MDI medication and delivery system training</td>
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<td>12 PM</td>
<td>Eat Lunch</td>
<td>Diet as above</td>
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<td>Diabetes Mellitus</td>
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<td></td>
<td>Prn Nebulizer / MDI</td>
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<tr>
<td>5 PM</td>
<td>Eat Dinner</td>
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<td>Metformin 850mg</td>
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<td>ICS - LABA</td>
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<tr>
<td>11 PM</td>
<td>Prn Nebulizer / MDI</td>
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Fortunately, there are now guidelines for how to individualize guidelines
Considerations in Individualized Care (other than –omics)

- Demographics
- Co-morbidities
- Drug interactions
- Patient preference
- Financial considerations
- Insurance coverage
- Disease characteristics
- History of response to treatment
Take Home Message

• Adherence to guideline care is good for comparing patterns of care between populations of patients.
• Adherence to guideline care should be tailored for individual patients.
“While the individual man is an insoluble puzzle, in the aggregate he becomes a mathematical certainty. You can, for example, never foretell what any one man will be up to, but you can say with precision what an average number will be up to. Individuals vary, but percentages remain constant. So says the statistician.”
How do doctor’s think?
Medical Decision-Making – Do you really think like this?

Flow chart of asthma treatment (Adapted from: British Guidelines on the Management of Asthma, British Thoracic Society April 2004)

Frances Viney, Specialist Respiratory Pharmacist March 2005

1. Commencing treatment: Start at the step most appropriate to the initial severity

2. Before stepping up treatment: Assess compliance and inhaler technique. Try to eliminate provoking trigger factors

3. Stepping down treatment: if stable, consider decreasing inhaled steroid dose by 25-50% every 3 months

4. Rescue courses of prednisolone may be needed at any time and at any step. Dose: adult prednisolone 40-50mg om, for at least 5 days. Child: prednisolone 1-2mg per kg om (or 2-5years 20mg om, over 5 years 30-40mg om)

1. Diagnosis of symptomatic asthma

2. Short acting B2 agonist when required
   - No more than 3 doses/week

3. Consider decreasing total dose of steroid to once a day (if in product licence)

4. Well controlled

5. Continue

6. Response?
   - Yes
   - Partial
   - None

7. Continue LABA plus Beclometasone DP-CFC or equivalent
   - Adult: 300mcg bd
   - Child: 200mcg bd

8. Lab test control

9. Stop LABA Beclometasone DP-CFC or equivalent
   - Adult: 400mcg bd
   - Child: 200mcg bd

10. Add Leukotriene receptor antagonist or Theophyllines or (adult only) MR salbutamol

11. Increase beclometasone DP-CFC or equivalent to: adults: 1000mcg bd; child (5-12yrs): 800mcg bd

12. Consider adding 4th drug (1 month trial):
   - Leukotriene receptor antagonists
   - Theophyllines
   - (adult only): MR salbutamol

13. Refer to respiratory specialist

14. Other preventer (2nd line: less effective):
   - Nedocromil
   - Sodium cromoglicate
   - Leukotriene receptor antagonists
   - Theophyllines

15. NOT APPROPRIATE

16. Stop LABA Beclometasone DP-CFC or equivalent

17. Add leukotriene receptor antagonist

18. Age?
   - 0-2yrs
   - 2-5yrs

19. Refer to respiratory specialist

20. Desired outcome steps 1 to 3:
   - Minimal chronic symptoms
   - Minimal exacerbations
   - Minimal need for reliever bronchodilators
   - No limits on activities including exercise
   - Circadian variation in peak expiratory flow <20%
   - PEF >80% of predicted or best
   - Minimal adverse effects from medication

21. Add regular oral steroids
   - Monitoring: incl: blood pressure, blood glucose, bone densitometry

22. Consider referring to respiratory specialist

23. Refer to respiratory specialist

24. Desired outcome steps 4 and 5:
   - Least possible symptoms
   - Least possible need for reliever bronchodilators
   - Least possible limitation of activity
   - Best PEF
   - Least adverse medication effects

25. Rescue course of prednisolone may be needed at any time and at any step.

Dose: adult prednisolone 40-50mg om, for at least 5 days.
Child: prednisolone 1-2mg per kg om (or 2-5yrs 20mg om, over 5 yrs 30-40mg om)
Professional Autonomy

"I'm a doctor—I can add 'ectomy' to any word I choose."

I'm a doctor, I can add "ectomy" to any word I choose
Human intelligence = Rapid pattern recognition + prediction
Thank you