NICE National Institute for Health and Care Excellence

Research into practice – developing evidence-based guidelines

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What are clinical guidelines?

"Clinical practice guidelines are statements that include ***recommendations intended to optimize patient care*** that are informed by a ***systematic review of evidence*** and an ***assessment of the benefits and harms*** of alternative care options."

- Offer an evaluation of the quality of the relevant scientific literature and an assessment of the likely benefits and harms of a particular treatment.
- Enable healthcare providers to proceed accordingly, selecting the best care for a unique patient based on his or her preferences"
  - US Institute of Medicine 2011
    - http://www.iom.edu/Reports/2011/Clinical-Practice-Guidelines-We-Can-Trust/Report-Brief.aspx

How do we develop clinical guidelines?

1. Identifying and refining what is to be covered
2. Obtaining and assessing evidence in order to answer key clinical questions
   - Evidence reviews in the form of rapid systematic reviews addressing structured and focussed questions (PICO)

A technical process

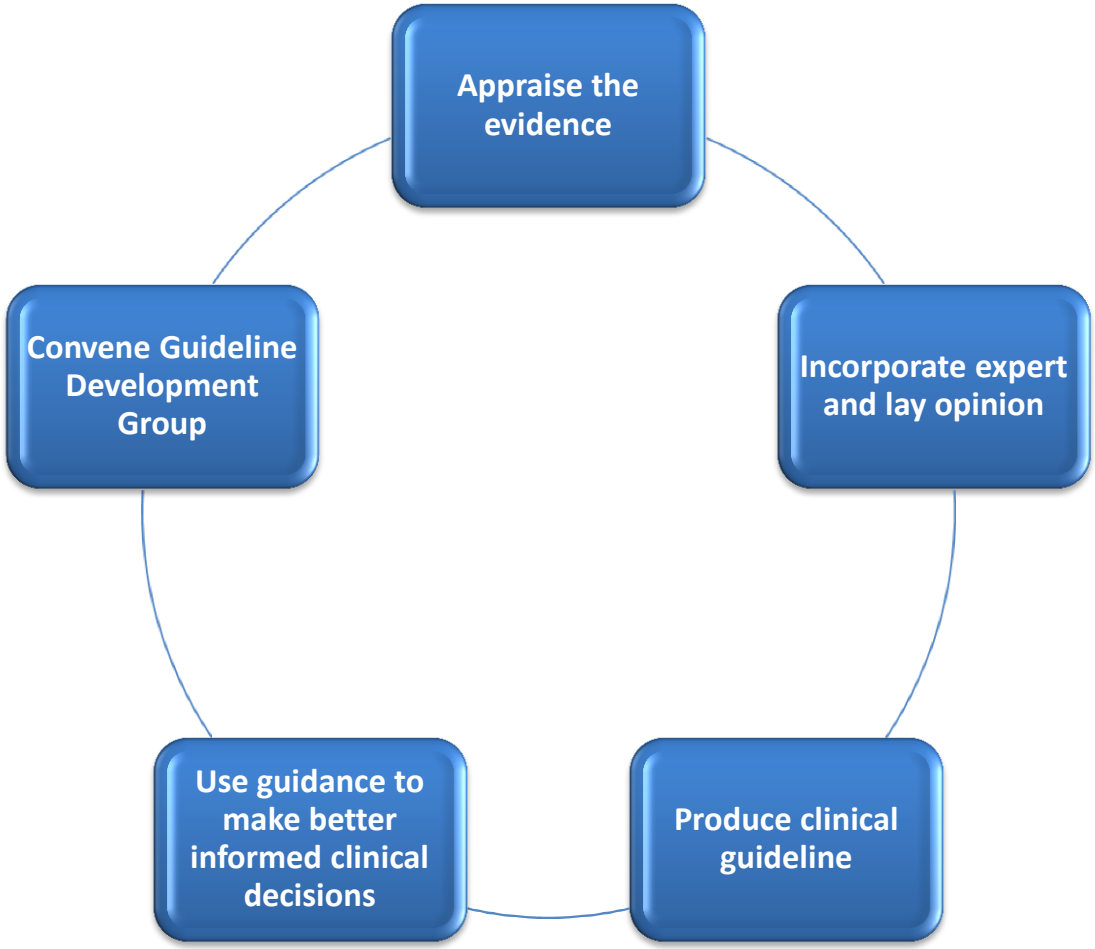
3. Convening and running guideline development groups
4. Translating the evidence into recommendations

A social process

5. Arranging external review of the guideline

Eccles M and Mason J. How to develop cost-conscious guidelines. Health Technol Assess 2001;5.

Stages of development



Evidence reviews – NICE approach

- Define a series of review questions
  - Based on the scope
- Develop review protocols
  - Population
  - Intervention
  - Comparator where appropriate
  - Outcomes
  - Other parameters
    - Study design or study methods
    - Dates…

Evidence reviews – NICE approach

- Type of evidence needs to ‘match’ the question being asked
  - RCTS not always ‘best’ design
  - But they can provide most robust evidence for effectiveness
  - Careful consideration of the question
  - Careful consideration of the evidence
    - Technical
    - Contextual, clinical, experiential interpretation

Evidence reviews – NICE approach

- Regardless of question
  - Need to consider internal validity
  - And external validity
- Process of quality assessment
- Process of synthesis
- Process of interpretation
- All different skills, different processes
- All vital

Evidence reviews – NICE approach

- Considers cost effectiveness as well as clinical effectiveness
- Assesses the evidence where possible using GRADE
  - GRADE is a system developed by an international working group for rating the quality of evidence across outcomes in systematic reviews and guidelines
  - GRADE rates the quality of evidence for a particular outcome across studies and does not rate the quality of individual studies

http://www.gradeworkinggroup.org/index.htm

GRADE

- The following are assessed for the evidence found for each 'critical' and each 'important' outcome from a systematic review:
  - *study limitations* (risk of bias)
    assessing the 'internal validity' of the evidence
  - *inconsistency*
    assessing heterogeneity or variability in the estimates of treatment effect across studies
  - *indirectness*
    assessing the degree of differences between the population, intervention, comparator for the intervention and outcome of interest
  - *imprecision* (random error)
    assessing the extent to which confidence in the effect estimate is adequate to support a particular decision
  - *publication bias*
    assessing the degree of selective publication of studies

GRADE – definitions of quality

- Quality of evidence is classified as high, moderate, low or very low
  - 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

Developing guideline recommendations – key principles

- Transparency
  - Need to show how the Guideline Development Group moved from the evidence to the recommendations
  - “Evidence to Recommendations” section
- “Strength” of a guideline recommendation
  - Takes into account the quality of the evidence
  - Strong versus weak (conditional) recommendations

Strength of recommendations - strong

- GRADE definition
  Based on the available evidence, if clinicians are very certain that benefits do, or do not, outweigh risks and burdens they will make a strong recommendation
  - Short-term aspirin reduces the relative risk of death after myocardial infarction by approximately 25%.
  - Aspirin has minimal side effects and very low cost.
  - People's values and preferences are such that virtually all patients suffering a myocardial infarction would, if they understood the choice they were making, opt to receive aspirin.
  - Clinicians can thus offer a strong recommendation for aspirin administration in this setting.

Strength of recommendations - weak

- GRADE definition
  Based on the available evidence, if clinicians believe that benefits and risks and burdens are finely balanced, or appreciable uncertainty exists about the magnitude of benefits and risks, they must offer a weak recommendation.
  In addition, clinicians are becoming increasingly aware of the importance of patient values and preferences in clinical decision making. When, across the range of patient values, fully informed patients are liable to make different choices, guideline panels should offer weak recommendations.

Strength of recommendations - weak

- Consider a 40 year-old man who has suffered an idiopathic deep venous thrombosis and has been taking adjusted dose warfarin for one year.
- If the patient continues on standard-intensity warfarin his risk of recurrent DVT will be reduced by approximately 10% per year.
- The inevitable burdens of the treatment include taking a warfarin pill daily, keeping dietary intake of vitamin K constant, monitoring the intensity of anticoagulation with blood tests, and living with the increased risk of both minor and major bleeding.
- Some patients who are very averse to a recurrent DVT may consider the down sides of taking warfarin well worth it. Others are likely to consider the benefit not worth the risks and inconvenience.

http://www.gradeworkinggroup.org/FAQ/

What needs to be considered when discussing the evidence?

- Relative value placed on the outcomes considered
  - Health outcomes
    - Mortality/morbidity/disability/quality of life
  - Intermediate or surrogate health outcomes
    - For example, BP, cholesterol, HBA1c targets
- Trade-off between benefits and harms
  - Qualitative
    - “the evidence of a reduction in mortality outweighed a small increase in side effects”
  - Quantitative
    - using a decision model

What needs to be considered when discussing the evidence?

- Trade-off between net health benefits and resource use
  - if there are net health benefits from an intervention, there should be an explanation of how the implications of resource use were considered in determining cost effectiveness
    - informal
    - formal (health economic modelling)
- Quality of the evidence
  - how the presence of potential biases and uncertainty in the clinical and economic evidence has influenced the recommendation, and why

Research into practice

- NICE guidelines are based on ‘best available’ evidence
  - dependent on the question
- Different research answers different questions
- Different research has different strengths and limitations
- NICE guidelines take these into account when developing recommendations