Combining GRADE, patient reported outcomes and costs in the NICE Lower Urinary Tract Symptoms (LUTS) Guideline

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RCGP Royal College of General Practitioners
Royal College of Nursing
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Background

- NICE Guideline on Lower Urinary Tract Symptoms (LUTS) (National Clinical Guideline Centre. (2010) The management of lower urinary tract symptoms in men. London: National Institute for Health and Clinical Excellence)
- Question: Alpha-blockers (AB) vs combination of AB+5-Alpha-Reductase Inhibitors (Combi)
- Trade-off between efficacy of intervention, side effects profile and costs

Economic perspective

- Cost-effectiveness as well as clinical effectiveness
- To be able to compare interventions across guidelines we use the same measure of effectiveness:

QALY (Quality-Adjusted Life-Year) = utility* time in state

Where utility is a quality of life value on a 0 – 1 scale based on public/patients preferences.

Estimating effectiveness in the model (1)

- No utility data in the RCTs included in the clinical review
- Main outcome was mean International Prostate Symptom Score (IPSS) on a scale from 0 (no symptoms) to 35 (worst symptom level)
- No formula converting IPSS to utilities

Estimating effectiveness in the model (2)

- Trueman and colleagues (1999) conducted a survey to collect utilities by symptoms severity in 1115 men in the UK:
  - Moderate LUTS = 0.78
  - No LUTS = 0.91
- If we know the proportion of patients with and without LUTS in both arms we can estimate utility in both arms and QALYs gained:

$$\text{QALYs per year} = \%_{noLUTS} * U_{noLUTS} + \%_{LUTS} * U_{LUTS}$$

Pragmatic approach

- We use a modified GRADE approach to evaluate clinical evidence quality
- This includes estimating the Minimally Important Difference (MID) to assess the imprecision of the evidence
- Based on a study on patient reported outcomes (Barry 1995) the Guideline Development Group (GDG) considered the MID for IPSS to be 3 points. The patient representatives and clinical experts thought this represented an important improvement.
- We made the assumption that important improvement = remission; likely overestimation of treatment effectiveness; we tested the important improvement assumption in a sensitivity analysis.

Using the MID to estimate transition probabilities

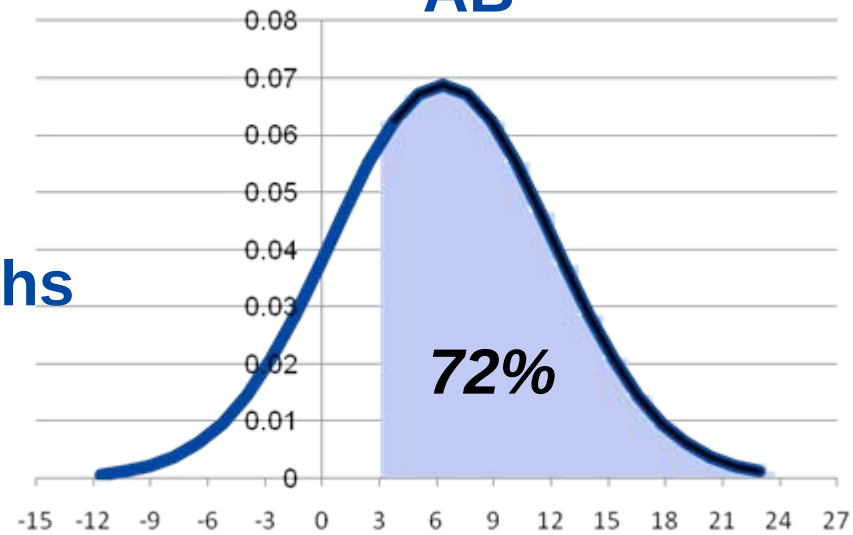
- From RCTs included in our meta-analysis we estimated the mean IPSS change from baseline to follow-up.
- Assuming a normal distribution around the mean IPSS change, we used the standard deviation (SD) to obtain the proportion of men who had at least a 3 point improvement in the AB arm and Combination arm.
- Assumption:
  - utility of patients with improvement ≥3 point = utility no LUTS;
  - utility of patients with an improvement <3 point = utility moderate LUTS.

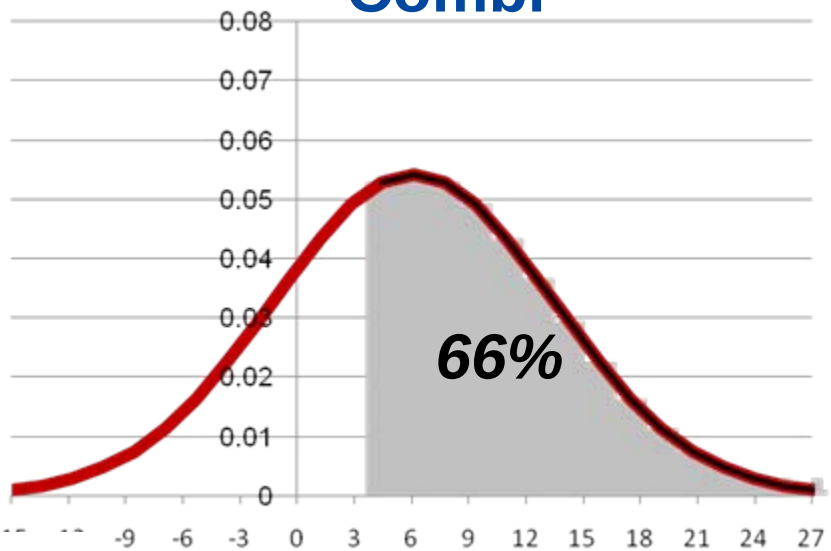
Proportion of men with symptoms remission

AB

Combi

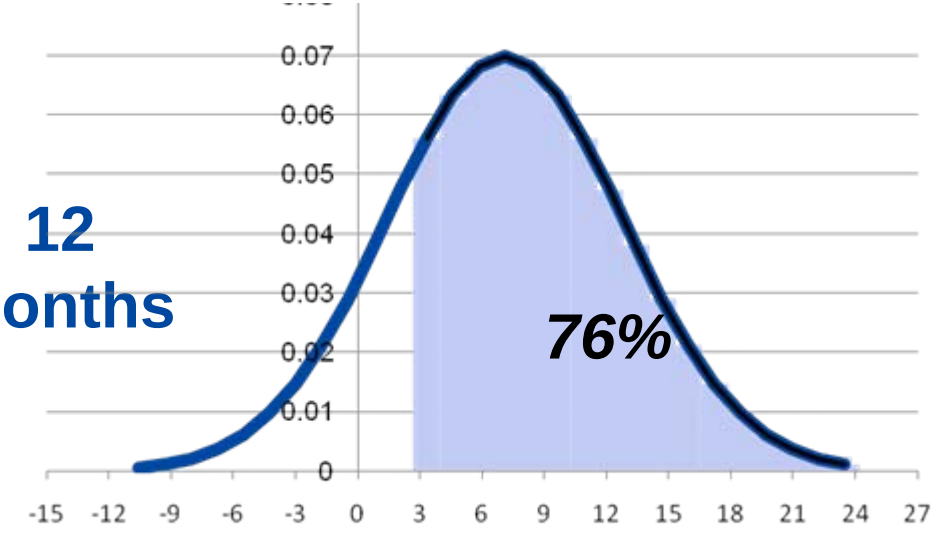
6 months

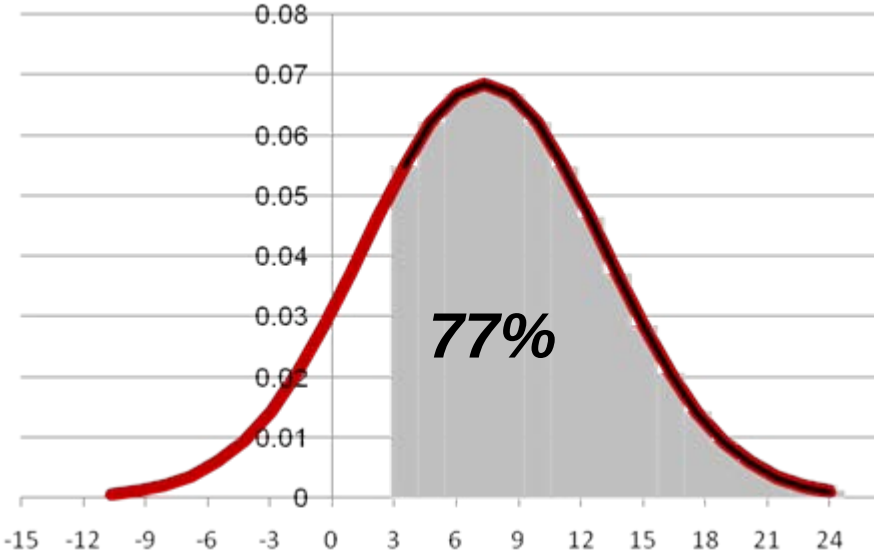




Mean IPSS change 6 months:	6.3 (SD 5.8)	6.1 (SD 7.4)
Mean IPSS change12 months:	7.1 (SD 5.7)	7.3 (SD 5.8)

12 months

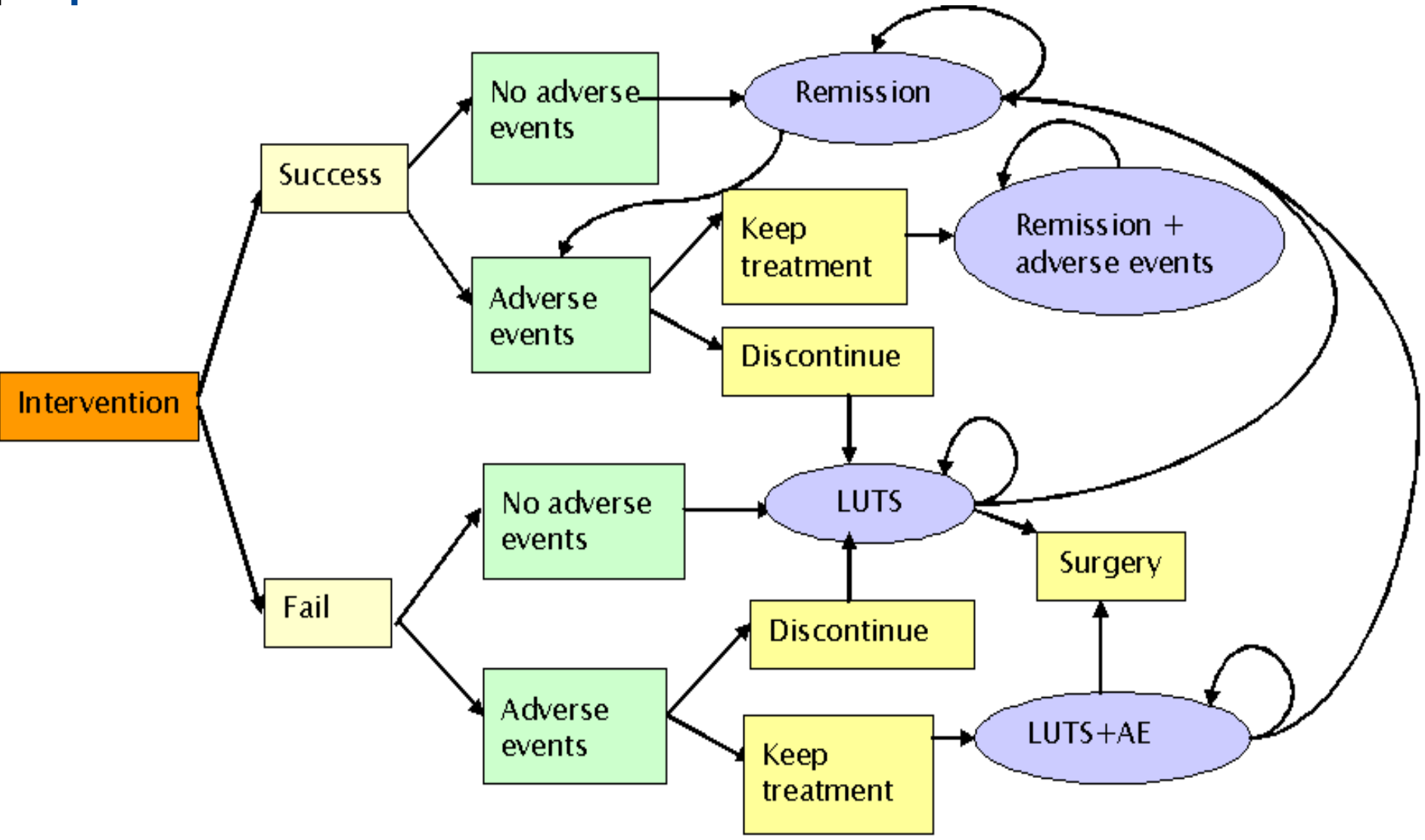




Other model inputs

- Cost of treatment:
  - lifelong treatment if successful;
  - if unsuccessful discontinuation after one year; additional cost of GP visits; some will have surgery (expensive).
- Effectiveness of treatment is stable after one year (from conclusions of our clinical review)
- Incidence of adverse events (AE):
  - AB: 21.4%
  - Combi: 27.0%
- Different adverse events profile in the two arms: dizziness more common in AB arm, sexual side-effects more common in Combi arm. Disutilities and costs.

Model structure



Results – base case analysis

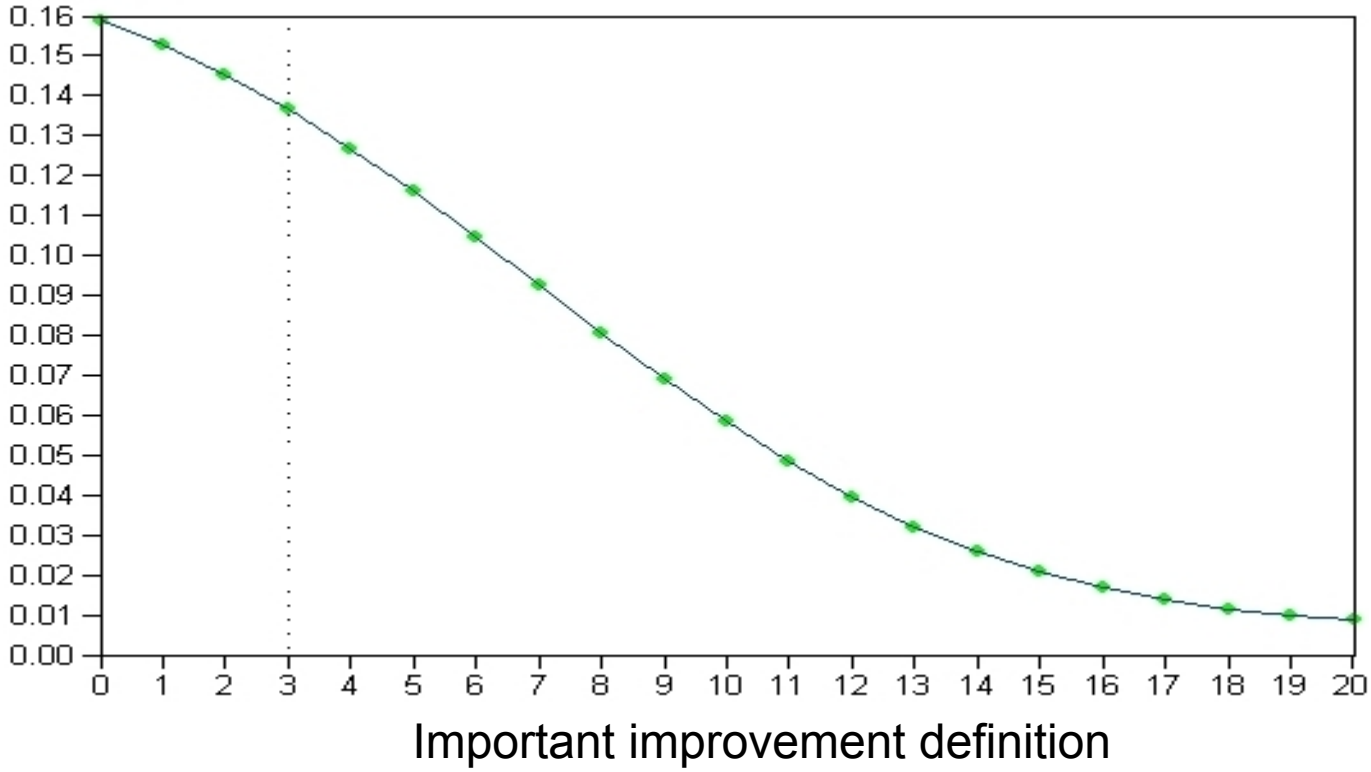
	Mean cost (£)	QALYs
Alpha-blockers	3,824	12.4347
Combination	6,411	12.4276

Combination is dominated – fewer QALYs but increased cost.

Combination may be slightly more effective at reducing symptoms in the long term. However, it is less effective in the short-term and is associated with more adverse events.

Sensitivity analysis on important improvement

Incremental net health benefit of AB vs Combi at £20k/QALY threshold



When the definition of the MID was varied from 0 to 20, the incremental net health benefit of AB was always positive.

Discussion and conclusions

- In the absence of direct evidence we estimated the difference in utilities using the MID calculated for GRADE.
- Approximate method using continuous data to estimate categorical data. Is MID meaningful and does it correlate with utilities?
- Issue if results were sensitive to the definition of important improvement.
- However in this case study the results in terms of cost-effectiveness were not sensitive to this.
- Collaboration between clinical reviewers, health economists and patients' representatives is helpful in deciding whether changes in health outcomes are large enough to justify the cost.