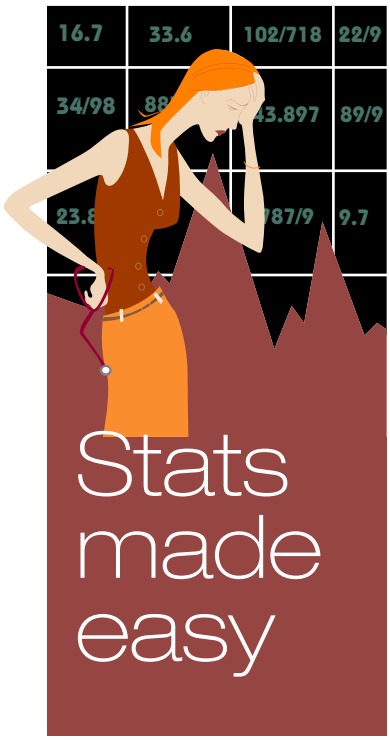
Applying systematic reviews



How useful are the results of trials in a systematic review when it comes to weighing up treatment choices for particular patients?

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The purpose of a systematic review is to summarise all the available evidence to assess the effect of a treatment. This is likely to include data from trials of different durations in different patient types, but the relative effect of treatment is nevertheless fairly consistent.

The first article in this series considered a systematic review that compared long-acting beta$_2$-agonists (LABA) with leukotriene receptor antagonists (LRTA) in chronic asthma, and the Forest plot summarising the trial results is shown again below.

The overall relative risk is 0.83, indicating a 17% relative risk reduction with the LABA. In practice, this data needs to be considered in relation to individual patients, and the absolute difference that the treatment makes will depend on the baseline risk of the patient.

Fewer patients will need to be treated for one to benefit in a group of asthmatics who have lots of exacerbations than for those who rarely suffer an exacerbation. This is demonstrated in the two smiley face diagrams opposite. The same relative risk of 0.83 has been applied to low-risk patients who suffer few exacerbations (baseline risk of 3%, Fish 2001) as to those who have more frequent exacerbations (baseline risk of 17%, Ilowite 2004).

These graphics are generated using Visual Rx, a free online calculator for NNT (www.nntonline.net). In each case, if all 100 patients are given LABA rather than LRTA, the green faces remain free from exacerbation and the red faces exacerbate anyway, and only the yellow faces become free from exacerbation due to the LABA.

There is a simple explanation for the higher risk of exacerbation in the Ilowite study: it lasted for 48 weeks, as opposed to just 12 weeks in the Fish study. So although NNT is useful in applying the results of trials and reviews to patients with different baseline risks, it is dangerous to use NNT to compare treatment effects between studies unless the baseline risks are the same.

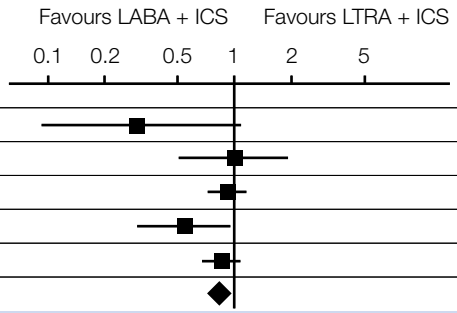
Question — can you work out, from the smiley face pictures, the risk difference for low-risk and high-risk patients who use LABA rather than LRTA?

Next month, I will look at study design.

Relative risk reduction

Meta-analysis of long-acting beta$_2$-agonists (LABA) versus leukotriene receptor antagonists (LTRA) as add-on therapy to inhaled corticosteroids (ICS) in chronic asthma

Study	Patients with ≥1 exacerbation needing corticosteroids [Total number in trial group]		Risk ratio [95% confidence interval]
	LABA + ICS	LTRA + ICS	
Nelson 2000	3 [222]	10 [225]	0.30 [0.08, 1.09]
Fish 2001	16 [476]	16 [472]	0.99 [0.50, 1.96]
Bjermer 2003	107 [743]	118 [747]	0.91 [0.72, 1.16]
Ringdal 2003	17 [404]	31 [401]	0.54 [0.31, 0.97]
Ilowite 2004	102 [718]	123 [734]	0.85 [0.67, 1.08]
		Pooled risk ratio:	0.83 [0.71, 0.97]



Smiley face comparison

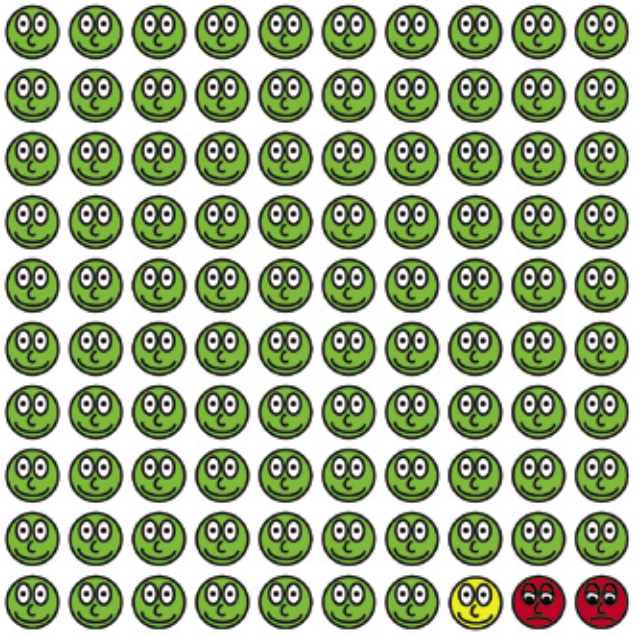
Effect of giving LABA rather than LRTA in low- and high-risk patients

Low-risk patients

With treatment

NNT:
197

95% confidence interval:
115–1112



Key

Good outcome

Bad outcome

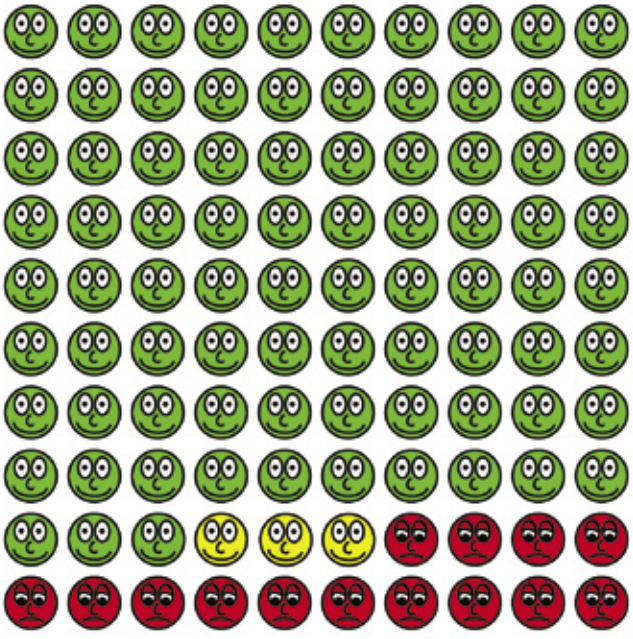
Better with treatment

High-risk patients

With treatment

NNT:
35

95% confidence interval:
21–197



"In each case, if all 100 patients are given LABA rather than LRTA, the green faces remain free from exacerbation and the red faces exacerbate anyway, and only the yellow faces become free from exacerbation due to the LABA"

REFERENCE

Ram FSF, Cates CJ, Ducharme FM. *Long-acting beta$_2$-agonists versus antileukotrienes as add-on therapy to inhaled corticosteroids for chronic asthma* (Cochrane review). Chichester: John Wiley & Sons, 2005 (available at www.tinyurl.com/e32rx).

ANSWER

The risk difference is the inverse of the NNT, so 1/197 = 0.05% for low-risk patients and 1/35 = 3% for high-risk ones.