*IN BOX:*

*Archimedes* seeks to assist practising clinicians by providing “evidence-based” answers to common questions that are not at the forefront of research but are at the core of practice (format adapted from BestBETS published in the *Emergency* *Medicine Journal*). A full description of the format is available online at http://bit.ly/ArchiTemplate.

Readers wishing to submit their own questions—with best evidence answers—are encouraged to review those already proposed at www.bestbets.org. If your question still hasn’t been answered, feel free to submit your summary according to the instructions for authors at http://bit.ly/ArchiInstructions

## [What about mixedupness?](http://blogs.bmj.com/adc/2015/03/27/what-about-mixedupness/)

The subject of heterogeneity (mixed~up~ness) in systematic reviews is tricky. A bit like ‘[significance](http://blogs.bmj.com/adc/2013/06/26/statsminiblog-significance-tests-step-one/)‘ you can think about it as both a clinical and statistical concept, and in the same way, you can get results that aren’t always concordant. (Remember the idea of a drug that, for 99.999% sure, reduces your systolic blood pressure by 0.01 mmHg. It’s a statistical association that’s unlikely to be due to chance, but is clinically irrelevant.) The same questions need to be asked of heterogeneity within studies as you do of ‘significance’.

Ask first: are the clinically different, and any attempt to add them up is daft, or are they similar enough to try to combine? Then, if they make sense, you should look at if the results look like they are similar, or different, and perhaps have a look at the [statistical measures of heterogeneity](http://blogs.bmj.com/adc/2011/03/27/its-how-mixed-up-meta-analysis-models-step-one/) (which in this setting means “more different than you’d expect by chance”).

But a quick “hold on” before the answer arrives too simply.

What does ‘clinically too mixed up mean’? Remember, the differences between the studies, to make them too heterogenous, should mean that we expect the treatment to actually have a truely different effect in the different study groups.

Then if you can explain why they could be different, and why you might be expecting to need to do something different with those groups of patients, you can quite reasonably say that any sort of lumping is the wrong thing to do and you’ll ignore any meta-analytic results that emerge. Because it might not be statistically heterogenous, but it’s clinically too mixed up to make sense.

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