

Martin M. Katz: Onset of antidepressant effect

Donald F. Klein's response to Martin M. Katz's reply to Carlos Morra's comment

Dr. Morey and I both had trouble with Marty's response to my reply to Carlos Morra's comment in that the tables were insufficiently labeled. The section following is a copy of the tables and Marty's description.

Below are the 2X2 Tables for the active drugs, the placebo and the chi square results. The rows are number of "early improvements" (>20%), the columns are number of recovered (>50%) at outcome.

I. Active Drugs

		Depressed mood-retardation		
		Early Improvement (EI) Recovered (>50% Ham-D decrease)		
		No		Yes
	15	2		17 chi square=18.5
	8	25		33 p<0.0001
	23	27		50

Using this as an example, if we transcribe and label which row represents >20%. Say it is Row 1. Since we know that there will be a positive correlation between greater than 20% and greater than 50% this infers that column 1 is greater than 50%.

	C1	C2
Row 1	15	2
Row 2	8	25

PPV is Positive Predictive Value, i.e., of those predicted to be positive, the proportion that is

actually positive.

	>50%	<= 50%	
>20%	15	2	PPV= 15/ (15+2) =.88
<=20%	8	25	

Reasonable - but 17 were predicted to do well and 27 did-a marked under prediction however if we had guessed. Looks that Row 1 is <=20% it would be sensible to reverse the column labels to preserve the predicted positive correlation

<=50%	> 50%	PPV= 25/ (25+8) = .76
<=20%	15	2
>20%	8	25 Recovery rate 27/50=.54

The difference in PPVs is enough to indicate that Marty's directions are ambiguous, as Dr. Morey also found. Note 33 are predicted to do well but only 27 did, an over prediction. This approximates Marty's statement that, "It was further demonstrated in these studies that this amount of 'early improvement', i.e., >20% decrease, was clinically significant in that it could predict that 70% of patients showing this early improvement would go on to respond at 6 or 8 weeks to the experimental treatment". So the second table is probably the correct one. However, it is unclear to me how this over-prediction means that it is clinically significant. Further, there is no contrast with placebo either in the: paper by Katz MM, Berman N, Bowden CL, Frazer A., or here.

II. Placebo Treatment Group

	Hamilton Rating Scale		
	EI Recovered		
	No	Yes	
3	10	13	chi-square=0.102
1	5	6	p<0.75

4

15

19

Taken literally, this seems to indicate that 15/19 recovered on placebo. Dr. Morey puzzles over this, “The Katz et al. (2004) article indicates a 30% response rate for placebo (presumably 6 of 20 patients), yet the 2x2 table in Dr. Katz’s response indicates that 15 of 19 patients recovered. Again, it appears that rows and columns were switched, and doing a transposition provides the reported results suggesting 6 patients responding to placebo over the course of the trial.” This seems reasonable Col 2 should be 1 5. To preserve the chi-square the Table looks like: So 6/19 recovered

	<=50%	> 50%	
<=20%	10	5	Recovery rate 6/19= .32
>20%	3	1	

	Drug	Placebo
Rec	27	6
Nrec	25	13

Contrasting the two recovery rates available, chi-square = 2.3, which is far from significant and casts doubt on any “finding”.

Other major problems This table is referred to as active drug. The results somehow combine the 24 in Paroxetine study with the 26 in DMI study. No justification is given for this. Since Paroxetine was picked as a serotonergic agent and DMI as a Noradrenergic agent, the combination is really strange. This table is not what we asked for which was the individual studies.

I thank Marty for providing the placebo data as used in the calculations by Dr. Morey. That this non-significant 6 week contrast is held to justify a much shorter trial escapes me.

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