DEBATE / *MÜNAZARA*

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Independent Researches are Important, Industry Supported Researches are not Safe

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In the formation of treatment guidelines and algorithms, one considers the evidence-base. Frequently, the most useful and applicable evidence comes from independent research rather than industry-sponsored research. Furthermore, the sponsors of industrial research often suppress the collection or release of important safety information. Safety, especially over the long term, is a very important consideration in the construction of algorithms for serious and chronic mental illness. I will illustrate this with examples from the research contributing to two of the algorithms of the Psychopharmacology Algorithm Project at the Harvard South Shore Program.

Schizophrenia: Meta-analyses have suggested that all antipsychotics are about equally effective, except for clozapine. These primarily industry-sponsored comparative studies often (90% of the time in one survey) do show differences because manufacturers pick comparators and choose doses that will enable their products to appear more favorable. However, when there are sufficient numbers of studies, these differences cancel when subjected to meta-analysis. Non-industry sponsored research, often observational studies, using outcome criteria such as all-cause discontinuation, and involving populations more representative of patients seen in typical practice, have produced different results. Risperidone, olanzapine, and first-generation antipsychotics seem more effective than others in these studies. These data have influenced their sequencing in our algorithm. Also, some industry-sponsored studies obscured important safety issues. The olanzapine manufacturer did not measure triglycerides in their large early studies even though it was known that clozapine, to which olanzapine is structurally related, produced significant weight and metabolic side effects. Later, independent research found markedly elevated triglycerides, which is understood to be connected with the insulin resistance induced by this agent. We have dropped olanzapine from our preferred recommendations for first-onset schizophrenia. Quetiapine prolongs QTc, but this was not made public for many years despite data collected in five major industry studies: only in 2011 did the U.S. Food and Drug Administration intervene and require a detailed warning and special procedures related to this effect. The company also discontinued a maintenance study showing poor outcome with quetiapine. Only in the last couple of years have meta-analyses revealed that quetiapine has the lowest or one of the lowest success rates in preventing future episodes of schizophrenia. For these safety and maintenance effectiveness reasons, we now do not recommend quetiapine as an initial treatment in our schizophrenia algorithm.

Depression: What is the first-line antidepressant? If we go by the industry-sponsored studies it would be the SSRIs. However, their sexual side effects can be disabling. The method of measuring sexual side effects in the development of all of these products has been to record side effects by non-specific patient report rather than by having specific questions about sexual functioning. This resulted in incidences of sexual side effects as low as 2% that misled patients and clinicians for years. Only later was the true incidence found to be much higher, up to 70% in some independent research. In our algorithms, we place bupropion among the first line antidepressants because of the lack of this side effect.

Key words: Independent researches, industry supported researches, safety, schizophrenia, depression

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