

TABLE 1. Computed Doses of Antipsychotics at 600 and 1,000 mg Chlorpromazine Equivalents From Consensus and Calculation Methods

Drug (mg)	600 mg Chlorpromazine Equivalents				1,000 mg Chlorpromazine Equivalents				Dosing		
	Consensus		Calculation		Consensus		Calculation		Highest Dose	Recommended Range ^a	
	Kane ^b	Gardner ^c	Woods ^d	Andreasen ^e	Kane ^b	Gardner ^c	Woods ^d	Andreasen ^e	Kane ^b	Gardner ^f	
Risperidone	6.6	6	12	7.9	11.7	10.0	20.0	13.2	10.5	8.5 (1.0)	2–8
Olanzapine	24.0	20	30	28.5	33.3	33.3	50.1	47.5	40.0	30 (0)	10–20
Quetiapine	720.0	750	450	852.0	1,000.0	1,250.0	751.5	1,420.0	950.0	1,000 (162)	300–750
Ziprasidone	168.0	160	360	303.0	200.0	266.7	601.2	505.0	180.0	200 (40)	80–160
Aripiprazole	24.0	30	45	38.5	33.3	50.0	75.2	64.2	30.0	30 (0)	10–30
Haloperidol	12.0	10	12	11.0	22.2	16.7	20.0	18.4	25.0	20 (4.0)	6–20

^a Recommended dose range for treatment of an acute episode (3).

^b Doses obtained and approximated from haloperidol, 10 mg for 600 mg of chlorpromazine equivalents and 20 mg for 1,000 mg of chlorpromazine equivalents, from guideline 5A of Kane et al. (4).

^c Doses computed from dose equivalency ratio versus chlorpromazine (5).

^d Doses calculated from table provided in Woods (6).

^e Doses calculated from power transformation for chlorpromazine equivalent (7).

^f Median (interquartile range) maximum doses (5).

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Metformin and Alzheimer's Disease Risk

TO THE EDITOR: In the September issue of the *Journal*, Jarskog et al. (1) report and Correll et al. (2) discuss a 4-month trial of metformin that concluded “metformin was modestly effective in reducing ... risk factors for cardiovascular disease” and “represents a safe ... option for patients who are motivated to lose weight.” That study spanned 4 months, but the treatment of cardiovascular risk factors may continue indefinitely. Imfeld et al. (3) reported that long-term metformin use (over 60 prescriptions or more than 7 years) but not use of other antidiabetic medications such as sulfonylureas,

thiazolidinediones, or insulin was associated with a small increased risk of developing Alzheimer's disease (adjusted odds ratio, 1.71).

I would be grateful if Jarskog et al. and Correll et al. would compare the benefit they anticipate from reducing cardiovascular risk factors with metformin in psychiatric, non-diabetic patients to the risk of increased Alzheimer's disease from metformin.

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Response to Rosenfeld

TO THE EDITOR: We appreciate Dr. Rosenfeld bringing attention to a recent report by Imfeld et al. (1) suggesting that long-term metformin use may increase the risk for Alzheimer's disease in elderly patients with diabetes mellitus. In fact, a number of clinical and preclinical reports within the past 5

years have provided conflicting data on the relationship between Alzheimer's disease and metformin. In neuronal cell cultures, metformin can increase production of β -amyloid peptides via transcriptional upregulation of β -secretase activity (2). However, in a mouse model of type 2 diabetes, metformin treatment was associated with a reduction in phosphorylated tau and total tau proteins, primary components of neurofibrillary tangles (3). Imfeld et al. observed a modest increase in risk for Alzheimer's disease (adjusted odds ratio=1.71, 95% confidence interval [CI]=1.12–2.60) in 7,086 individuals age 65 years and older with diabetes (mean age, 80.7 years) and long-term metformin use (1). In contrast, a prospective cohort study of 127,209 individuals age 50 years and older without dementia, followed over an 8-year period, found that type 2 diabetes was associated with a more than twofold greater risk of dementia and that metformin reduced this risk by about 25% (4). Taken together, these data indicate the need for further research to better understand the potential relationship between metformin and Alzheimer's disease. Currently, the available data do not support indefinite use of metformin for weight loss in overweight patients with schizophrenia given that the longest studies have lasted 24 weeks. However, because of excess mortality due to cardiovascular disease in schizophrenia, metformin may have a long-term role because of its ability to reduce cardiometabolic risk factors. Longer studies that include an assessment of both cardiometabolic risk factors and cognitive functioning can help

further address the long-term risks and benefits of metformin use in overweight patients with schizophrenia.

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Correction

In the March 2011 article "Overactive Error-Related Brain Activity as a Candidate Endophenotype for Obsessive-Compulsive Disorder: Evidence From Unaffected First-Degree Relatives" by Anja Riesel, Dipl.-Psych., et al. (*Am J Psychiatry* 2011; 168:317–324. doi:10.1176/appi.ajp.2010.10030416), the scaling of the y axes in part A of Figure 2 should have been inverted. In event-related potential research, negative is usually printed upwards so for Figure 2A, –5 should have been depicted upwards. In the online version, the scaling of the y axes has been corrected.

