Published in final edited form as:
Biol Psychiatry. 2010 February 1; 67(3): 255–262. doi:10.1016/j.biopsych.2009.08.040.

Antipsychotic Dose Equivalents and Dose-Years: A Standardized Method for Comparing Exposure to Different Drugs

Nancy C. Andreasen, **Marcus Pressler**, **Peg Nopoulos**, **Del Miller**, and **Beng-Choon Ho**
Mental Health-Clinical Research Center, Department of Psychiatry, Carver College of Medicine, University of Iowa Hospitals and Clinics, Iowa City, Iowa

Abstract

Background—A standardized quantitative method for comparing dosages of different drugs is a useful tool for designing clinical trials and for examining the effects of long-term medication side effects such as tardive dyskinesia. Such a method requires establishing dose equivalents. An expert consensus group has published charts of equivalent doses for various antipsychotic medications for first- and second-generation medications. These charts were used in this study.

Methods—Regression was used to compare each drug in the experts' charts to chlorpromazine and haloperidol and to create formulas for each relationship. The formulas were solved for chlorpromazine 100 mg and haloperidol 2 mg to derive new chlorpromazine and haloperidol equivalents. The formulas were incorporated into our definition of dose-years such that 100 mg/day of chlorpromazine equivalent or 2 mg/day of haloperidol equivalent taken for 1 year is equal to one dose-year.

Results—All comparisons to chlorpromazine and haloperidol were highly linear with R^2 values greater than .9. A power transformation further improved linearity.

Conclusions—By deriving a unique formula that converts doses to chlorpromazine or haloperidol equivalents, we can compare otherwise dissimilar drugs. These equivalents can be multiplied by the time an individual has been on a given dose to derive a cumulative value measured in dose-years in the form of (chlorpromazine equivalent in mg) × (time on dose measured in years). After each dose has been converted to dose-years, the results can be summed to provide a cumulative quantitative measure of lifetime exposure.

Selecting comparable doses of antipsychotic medications is an important challenge in the design of clinical trials. Ideally, studies that compare efficacy and side effects of two or more drugs should be based on some objective measure of the “best dose” so that drugs can be compared on a “level playing field.” This requires creating an empiric quantitative metric that can be used to make doses equivalent, and yet no such metric exists. Furthermore, because schizophrenia is usually a chronic illness, many patients are maintained on antipsychotic medications for long periods. A quantitative measure of the amount of medication exposure over long time durations is also useful to address a variety of other research questions, such as the relationship between long-term treatment and medication

Address correspondence to Nancy C. Andreasen, M.D., Ph.D., University of Iowa Health Care, Department of Psychiatry, Hawkins Drive, Iowa City, IA 52242-1057.

Competing Interests: Dr. Andreasen has received honoraria for a lecture from Eli Lilly and a lecture honorarium, an advisory board consulting fee, and research funding from Janssen-Cilag; Dr. Miller has received consulting fees from Organon Schering Plough and Otsuka Pharmaceuticals; Dr. Ho has received research funding from Janssen-Cilag. Drs. Nopoulos and Pressler reported no biomedical financial interests or potential conflicts of interest.

side effects (e.g., tardive dyskinesia). Previously, we developed a method to quantify cumulative antipsychotic drug exposure through calculation of dose-years (1 and 2). A dose-year is defined as the product of the dose of a particular antipsychotic (converted into equivalents of a "standard" medication such as chlorpromazine or haloperidol) and the time on that dose expressed in years. This concept is akin to "pack-years," in which lifetime exposure to smoking is calculated by multiplying the packs of cigarettes smoked per day by the years spent smoking.

The first step in meeting the dual goals of choosing comparable doses for clinical trials and measuring long-term drug exposure is to develop a method for determining dose equivalents. A traditional approach has been to use the concept of chlorpromazine equivalents. The earliest method for determining equivalents, developed by Davis, was based on double-blind studies reported in the literature that used chlorpromazine as the comparator; this method provided data about comparable doses chosen by clinicians to achieve a therapeutic effect and identified dose ratios in relation to 100 mg of chlorpromazine (3). Using this method, haloperidol, for example, was found to have a ratio of 1.6 (SEM .4). As "second-generation" or "atypical" antipsychotics became available, however, a need arose to determine chlorpromazine equivalents for these as well. Woods (4) developed equivalents for the newer antipsychotics using minimum effective dose data drawn from fixed-dose placebo-controlled trials conducted in drug development programs.

Defining equivalents on the basis of clinical trials has a variety of limitations, however. Most clinical trials recruit relatively chronic patients, and therefore they do not necessarily generalize more broadly to community or acute treatment settings. Furthermore, as Woods reported, only a few studies were available to derive most of his data; additionally, in most cases, the identified studies were early studies that might have reflected different dosing from what has become more common in current clinical practice.

Using expert clinical consensus concerning dose equivalence offers an alternative approach that may be more valid. In 2003, Kane *et al.* (5) conducted a survey of experts to address questions concerning "medication selection, dosing and dose equivalence, and the management of inadequate response, compliance problems, and relapse." Their survey included 60 questions and 994 options, which were sent to 50 national experts on pharmacologic treatment of psychotic disorders; 47 (94%) completed it. Guidelines derived from this survey were published as the "Expert Consensus Guideline Series. Optimizing Pharmacologic Treatment of Psychotic Disorders" (5). Guideline 5A consists of a table comparing several antipsychotic medication doses to their equivalent haloperidol doses. To determine these comparisons, mean and standard deviations of survey responses were used "to generate real-world doses rounded to currently available pill strengths." Guideline 5B used the same approach to define equivalent doses of risperidone. The authors noted that the responses "followed a very linear pattern" and proposed "it would probably be possible to use linear formulas to calculate dose equivalency."

Therefore, in developing an up-to-date and optimally accurate measure of dose equivalents and lifetime antipsychotic exposure expressed as dose years, we chose to use the charts from these guidelines. These doses were used to derive new chlorpromazine equivalency values for antipsychotic medications in our dose-year calculations. However, because many clinicians no longer use chlorpromazine and are unfamiliar with its dosing strategies, we also derived haloperidol equivalents. In addition, in the process we went further to develop a new and more direct way to calculate a standard drug comparator equivalency by using regression equations. This approach has several advantages that enhance validity. First, it is empirically and statistically based. Second, it is based on evaluations from 47 experts; this is a far larger number of evaluations than have been used in other efforts to identify dose

equivalents, and it therefore contributes maximal variance and enhances generalizability across diverse populations of patients, ranging from acute to chronic.

Methods and Materials

We used Guidelines 5A and 5B derived from the questionnaire in the Kane *et al.* survey (6). The authors stated regarding Guideline 5A "We asked the experts to write-in doses of conventional and atypical antipsychotics that they would consider equivalent to a range of haloperidol doses. We used the mean and standard deviations of their responses to generate real-world doses rounded to currently available pill strengths" (5). The same was done with Guideline 5B for risperidone. The charts from the experts' consensus were combined into a single table for use in regression analysis. Table 1 summarizes the means and standard deviations for the equivalency doses assigned by the experts to five dose ranges.

We used regression equations to derive values for chlorpromazine and haloperidol equivalents by treating dose equivalents as the dependent variable in the standard regression model. Expert doses were used as independent variables, permitting us to calculate regression coefficients and create formulas that could be used to convert specific drug doses to chlorpromazine or haloperidol equivalents. The formulas were then solved for chlorpromazine 100 mg to determine each drug's chlorpromazine equivalent in milligrams, using 100 mg of chlorpromazine as the comparator. Because many clinicians are no longer familiar with chlorpromazine or its dosage strategies, a similar calculation was performed using 2 mg of haloperidol as the standard comparator. The formulas derived from the regression equations were assessed for linearity using R^2. We also evaluated other approaches by comparing the linear results with logarithmic, polynomial, and power transformations.

The resulting chlorpromazine or haloperidol equivalents can then be used to calculate total cumulative antipsychotic exposure using the dose-year formula.

Results

The results of using linear regression to calculate dose equivalents are shown in Table 2. The formula that solves for the drug indicates the derived regression coefficients for the slope and the intercept. Our first step was to evaluate the linearity of our results by examining R^2. The formulas for calculating equivalent doses derived from using regression equations based on the Combined Expert Guidelines, as shown in Table 1, were found to be highly linear. R^2 values were close to 1 with values between .9282 (for ziprasidone) and .9972 (for haloperidol), indicating close correspondence between the equations generated and the actual data. The high R^2 values for linear formulas show that the experts' opinions regarding dose equivalency were highly linear.

However, we also noted that the intercepts of the linear equations were often larger than zero. This creates some conceptual problems and suggests a need to transform the data in some way. For example, the derived linear formula for ziprasidone has a y-intercept value of approximately 46, which implies that 46 mg of ziprasidone would be equivalent to 0 mg of chlorpromazine. Consequently, commonly available amounts such as 20 mg or 40 mg of ziprasidone would equate to negative values of chlorpromazine. Therefore, we concluded that the data needed to be transformed to achieve a more optimal solution. We examined three alternatives: logarithmic, polynomial, and power. The plots for these transformations for the six atypical medications are shown in Figure 1. We selected the best transformation based on both the plots and the R^2 values. We concluded that a power relationship (in the form of $y = mx^b$, wherein y is the dose of a given drug,×is the chlorpromazine dose, m is a

coefficient and *b* is the exponent) produced the best fit overall. One major advantage of using the power formulas over the linear formulas is the elimination of y-intercept values. For example, the derived power formula for ziprasidone would convert 20- and 40-mg doses to approximately 24 or 72 mg of chlorpromazine, respectively, rather than making them zero. Although some the linear R^2 values decreased in the power transformation (for olanzapine, risperidone, fluphenazine, trifluoperazine, and fluphenazine decanoate), these changes were slight. However, R^2 values for the least linear relationships (for aripiprazole and ziprasidone) had much higher R^2 values following power transformation. The remaining relationships (for clozapine, quetiapine, haloperidol, perphenazine, thioridazine, thiothixene, and haloperidol decanoate) also had positive, although modest, improvements. The overall gains of using the power formula outweighed the minor losses.

The new power formulas for each individual drug, and the chlorpromazine and haloperidol equivalents that are calculated from them, are shown in Table 3. These can be entered into the dose-year formula to calculate cumulative drug exposure.

$$\text{Dose Years}=\left((\text{DOSE mg/day})\frac{100\text{mg CPZ}}{\text{CPZ equivalent}}\right)\times\left((\text{Days On Drug Dose})\frac{1\text{year}}{365.25\text{days}}\right)\times\left(\frac{1\text{Dose Year}}{(100\text{mg CPZ/day})^{*}1\text{year}}\right)$$

Equation 1 DOSE is equal to the dose of a given drug. CPZ represents chlorpromazine. CPZ equivalent represents the amount of a given drug equivalent to CPZ 100 mg. DaysOnDrugDose represents the number of days an individual has been on a particular dose of a given drug. The last large parenthetical expression represents the definition of one dose-year as equivalent to taking CPZ 100 mg daily for one year. 365.25 days/year is used to account for leap-years.

Discussion

Using Dose Equivalents to Determine Values of Comparator Doses in Clinical Trials

An important benefit of deriving an empiric measure of dose equivalents is the ability to compare doses in clinical trials. For example, selection of appropriate doses was an important issue in the influential Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) trial (7). The designers chose to use dose ranges recommended by each of the manufacturers, average doses prescribed in the United States at the time, and knowledge of clinical practice patterns; additionally a relatively low dose was chosen for perphenazine to minimize extrapyramidal side effects. The availability of empirically derived comparator doses based on expert consensus permits us to evaluate dosage choices from a quantitative perspective. Table 4 summarizes the mean modal doses for the five medications studied in the trial, permitting an objective comparison of dosage choices. Using the chlorpromazine-derived dose equivalents, the rank order from high to low runs as follows: olanzapine, quetiapine, perphenazine, risperidone, and ziprasidone. Using the haloperidol equivalents, the rank of perphenazine drops and the order becomes olanzapine, quetiapine, risperidone, perphenazine, and ziprasidone. The table also shows the values that would be derived using the Woods equivalents for the atypicals and the Davis (3) value for perphenazine; these change the order again, with quetiapine ranking at the top.

Dose-Years

Our previously established dose-year equation can now be modified to incorporate the chlorpromazine or haloperidol equivalents using values based on the power formulas described above. For example, a patient diagnosed with schizophrenia might have been on haloperidol 2 mg nightly for 60 days, then 5 mg nightly for 120 days, then risperidone 3 mg

nightly for 180 days. Calculating the dose-years for each medication change and summing the values shows that the patient has so far been exposed to 1.47 dose-years. However, this patient's exposure could also be reported as 1.26 “typical” dose-years and .21 “atypical” dose-years. Separating “typical” dose-years from “atypical” dose-years may be useful, considering the differing mechanisms of action between these classes of drugs (e.g., the serotonin 5-HT2A blockade among atypical antipsychotics). With these values separated one can investigate the differential effects of each class. For example, Corson *et al.* (8) found that typical neuroleptics increased basal ganglia volume over a 2-year period, whereas atypicals did not. If so desired, the formula could also be broken down into specific drugs, so that dose-year exposure to (for example), olanzapine, haloperidol, and risperidone could be calculated.

Much of the research, and many of the recommendations, regarding dose and dose-equivalence are based on efficacy data from clinical drug trials (3, 4 and 9). However, the results from the experts' consensus provided detailed information about dose-equivalents at many levels (low dose, medium dose, high dose), allowing a comprehensive view of dosage equivalents over a wide range. By incorporating their results through the regression formulas, the dose-year method can be more focused on dosage-range equivalents, as opposed to dosage equivalence based on the average therapeutic dose. The dose-year can be used as a parameter for many purposes, such as correlations with long-term side effects or changes in brain structure or function.

Comparison with Previous Dose Equivalence Coefficients

One way to evaluate the clinical validity of the empiric dose equivalents is to compare them with ones previously suggested from clinical trial data. The more that estimates derived in different ways are in agreement, the more likely they are to be valid. The derived chlorpromazine equivalents for the newer atypical antipsychotic medications were similar to those reported by Woods (4) in many respects, especially for aripiprazole (6.42 mg and 7.5 mg, respectively), olanzapine (4.75 mg and 5 mg, respectively), and ziprasidone (50.5 mg and 60 mg, respectively). However, our results diverged from Woods's with regard to quetiapine: whereas we calculated an equivalency of 142 mg, Woods reported an equivalence of 75 mg. This discrepancy may be explained in part by the early studies Woods used to determine the quetiapine equivalency, which do not reflect the high-dose treatment that has become more common (10 and 11). The experts' consensus may reflect this trend in current practice. Woods' chlorpromazine equivalent was based primarily on the placebo-controlled fixed-dose study by Arvinitis *et al.* (12), which found a minimum effective dose of 150 mg. Our chlorpromazine equivalent, by contrast, may be more in line with the findings of a placebo-controlled study by Small *et al.* (13) that used flexible dosing. Davis and Chen used both studies in their meta-analysis when creating a dose response curve for quetiapine, but the Small study suggested a near-maximal response at a dose 100 mg higher than in the Arvinitis study. They compared the studies and speculated in their Web supplement (3 and 9) why they had different outcomes but ultimately concluded it was unclear and would require further studies to determine which was more representative of a true dose– response curve.

Comparison with the Davis equivalents for the older antipsychotics is also informative. In general, the two methods are surprisingly close, despite the differing ways in which they were derived. In some cases, the expert-derived equivalents are higher (1.76 vs. 1.2 for fluphenazine, 1.84 vs. 1.6 for haloperidol, 5.09 vs. 2.8 for trifluoperazine) and in other cases lower (6.90 vs. 8.9 for perphenazine, 87.3 vs. 95.3 for thioridazine, 4.91 vs. 5.2 for thiothixene). However, apart from trifluoperazine, they are close, suggesting that the expert-derived values are likely to be reasonably accurate.

Evaluating Accuracy by Using Positron Emission Tomography (PET) and In Vitro Data

Can we evaluate the validity of the conversion factors using data from either PET studies or receptor binding profiles obtained in vitro? PET studies of receptor binding, principally evaluating D2 receptor binding using C (11) raclopride, have substantially expanded our knowledge about how to balance dose ranges to maximize efficacy and minimize side effects (14, 15, 16 and 17). It is difficult to extrapolate from this work to equivalency coefficients, however, because most of this work examines only one aspect of pharmacologic efficacy— ability to block dopamine type 2 receptors—whereas most of the newer medications are believed to exert their therapeutic effects through pharmacologic profiles that affect other receptors as well, particularly serotonin 5HT2A receptors. An examination of the Ki for D2 receptors indicates the nature of the problem: clozapine, 134; olanzapine, 63; quetiapine, 122; risperidone, 1.1; ziprasidone, 2.7 (18). (The lower the Ki, the higher the affinity.) If these alone were used to calculate a conversion coefficient or recommend dosing strategies, results would be very different from clinical practice; risperidone, which binds most tightly, does not have a per-dose potency 60 times greater than that of olanzapine, as one might infer using Ki only. Examining the Ki for the 5-HT2A receptor, or a combination such as the D2/5HT2A ratio, makes it clear that these cannot be easily converted to a dose equivalency coefficient; the respective Ki for each of these medications is 3.7, 2.5, 135, .2, and three for the 5-HT2A receptor, and the ratio is 17, 2, .9, 5.5, and .9. Although ziprasidone and quetiapine have identical ratios, few would propose that they be prescribed in equal doses. Despite the appeal of being able to base conversion equivalents on pharmacologic rather than clinical data, at present we do not have methods for summarizing it in a way that would capture all the complexities of multiple receptor types with different drug affinities.

Limitations

Although the conversion coefficients have the benefit of being empirically derived and based on expert clinician consensus, as well as often being similar to the previous Davis and Woods values, this does not necessarily prove their validity. When they are used to calculate cumulative doses over long periods, if small errors are present in the initial conversion factor, these could additively produce increasingly greater errors as the time periods grow longer. This may be especially problematic for those medications that have the greatest disagreements between Woods/Davis estimates and our quantitative estimates, such as quetiapine. Furthermore, as the quetiapine example indicates, a conversion based on expert consensus may be subject to vogues and vary over time, creating a need for reassessment of the equivalencies from time to time. Finally, although it is advantageous to have both chlorpromazine and haloperidol equivalents, we have no data that will indicate which is more valid. In the absence of evidence indicating superiority of one over the other; however, we recommend the use of haloperidol equivalents because of greater clinical familiarity with haloperidol.

Another limitation is that the dose-year formula only provides a summary of cumulative exposure. For example, it cannot address the possible interactive effects of polypharmacy; the effect of combining two medications, such as clozapine and haloperidol may not be simply additive, but the dose-year method has no way of taking this into account. It also does not take into account the fact that variability in overall intensity might have different effects, in terms of both efficacy and side effects. Although it might be reasonable, for example, to assume that haloperidol taken 4 mg/day for 5 years is probably equivalent to taking 5 mg/day for 4 years, could haloperidol taken 20 mg/day for a year be equivalent to taking 2 mg/day for 10 years? Therefore, inferences about specific time periods must be made with caution.

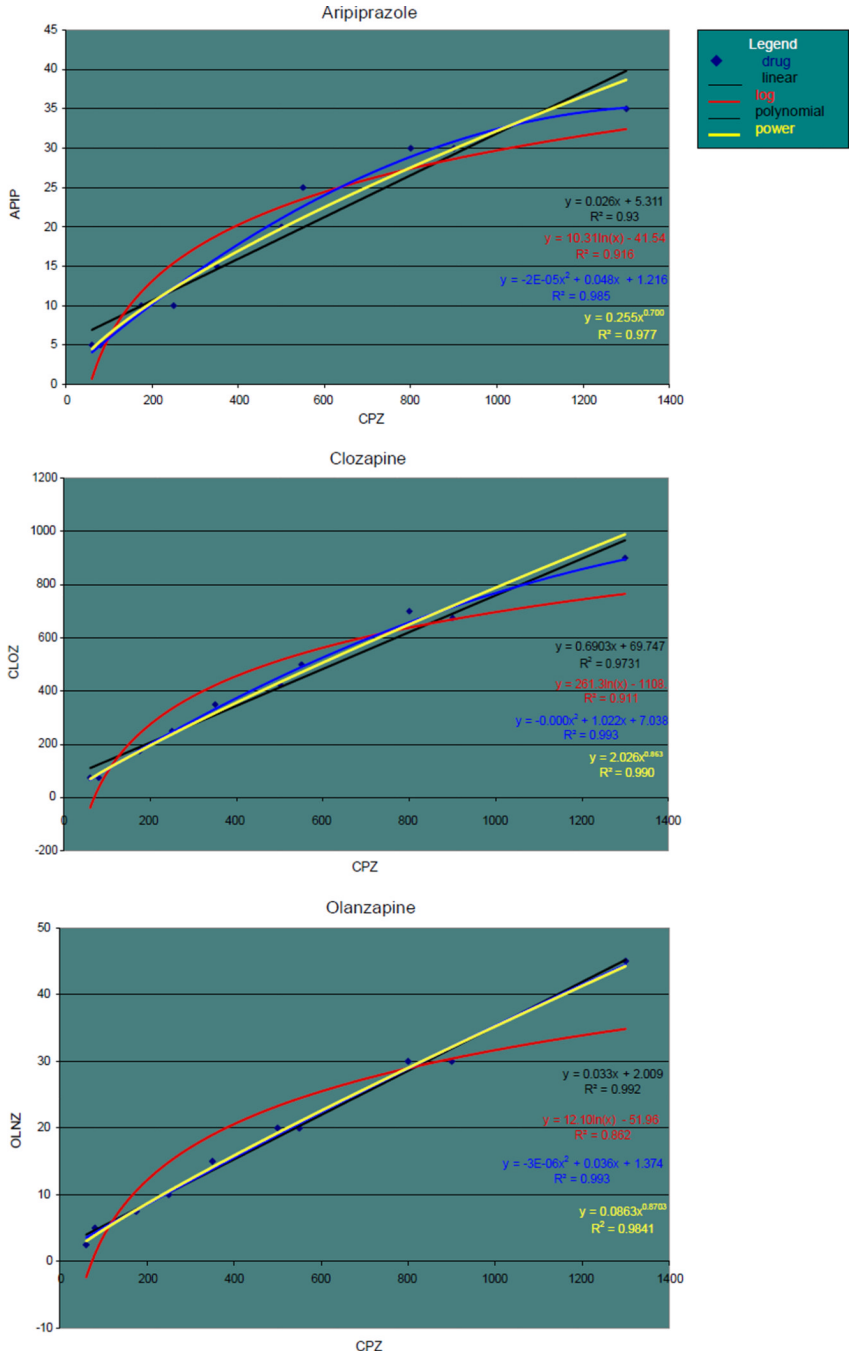
Acknowledgments

This study was performed at the University of Iowa, Iowa City, under the following support from the National Institute of Mental Health : Grant Nos. MH31593, MH40856, MH19113, and MHCRC43271.

References

1. Andreasen NC, Flaum M, Arndt S. The comprehensive assessment of symptoms and history (CASH). An instrument for assessing diagnosis and psychopathology. Arch Gen Psychiatry. 1992; 49:615–623. [PubMed: 1637251]
2. Miller DD, Flaum M, Nopoulos P, Arndt S, Andreasen NC. The concept of dose years: A reliable method for calculating lifetime psychotropic drug exposure. Schizophr Res. 1995; 15:159.
3. Davis JM. Dose equivalence of the antipsychotic drugs. J Psychiatr Res. 1974; 11:65–69. [PubMed: 4156792]
4. Woods SW. Chlorpromazine equivalent doses for the newer atypical antipsychotics. J Clin Psychiatry. 2003; 64:663–667. [PubMed: 12823080]
5. Kane JM, Leucht S, Carpenter D, Docherty JP. The expert consensus guideline series. Optimizing pharmacologic treatment of psychotic disorders. Introduction: Methods, commentary, and summary. J Clin Psychiatry. 2003; 64(suppl 12):5–19. [PubMed: 14640142]
6. Kane JM, Leucht S, Carpenter D, Docherty JP. The expert consensus guideline series. Optimizing pharmacologic treatment of psychotic disorders. J Clin Psychiatry. 2003; 64(suppl 12):2–97. Quiz 98—100. [PubMed: 14640143]
7. Lieberman JA, Stroup TS, McEvoy JP, Swartz MS, Rosenheck RA, Perkins DO, et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. N Engl J Med. 2005; 353:1209–1223. [PubMed: 16172203]
8. Corson PW, Nopoulos P, Miller DD, Arndt S, Andreasen NC. Change in basal ganglia volume over 2 years in patients with schizophrenia: Typical versus atypical neuroleptics. AmJ Psychiatry. 1999; 156:1200–1204. [PubMed: 10450260]
9. Davis JM, Chen N. Dose response and dose equivalence of antipsychotics. J Clin Psychopharmacol. 2004; 24:192–208. [PubMed: 15206667]
10. Keck P Jr, Buffenstein A, Ferguson J, Feighner J, Jaffe W, Harrigan EP, et al. Ziprasidone 40 and 120 mg/day in the acute exacerbation of schizophrenia and schizoaffective disorder: A 4-week placebo-controlled trial. Psychopharmacology. 1998; 140:173–184. [PubMed: 9860108]
11. Mamo D, Kapur S, Shammi CM, Papatheodorou G, Mann S, Therrien F, et al. A PET study of dopamine D2 and serotonin 5-HT2 receptor occupancy in patients with schizophrenia treated with therapeutic doses of ziprasidone. Am J Psychiatry. 2004; 161:818–825. [PubMed: 15121646]
12. Arvanitis LA, Miller BG. Multiple fixed doses of “Seroquel” (quetiapine) in patients with acute exacerbation of schizophrenia: A comparison with haloperidol and placebo. The Seroquel Trial 13 Study Group. Biol Psychiatry. 1997; 42:233–246. [PubMed: 9270900]
13. Small JG, Hirsch SR, Arvanitis LA, Miller BG, Link CG. Quetiapine in patients with schizophrenia. A high- and low-dose double-blind comparison with placebo. Seroquel Study Group. Arch Gen Psychiatry. 1997; 54:549–557. [PubMed: 9193196]
14. Farde L, Nordstrom AL, Wiesel FA, Pauli S, Halldin C, Sedvall G. Positron emission tomographic analysis of central D1 and D2 dopamine receptor occupancy in patients treated with classical neuroleptics and clozapine. Relation to extrapyramidal side effects. Arch Gen Psychiatry. 1992; 49:538–544. [PubMed: 1352677]
15. Farde L, Wiesel FA, Halldin C, Sedvall G. Central D2-dopamine receptor occupancy in schizophrenic patients treated with antipsychotic drugs. Arch Gen Psychiatry. 1988; 45:71–76. [PubMed: 2892477]
16. Tauscher J, Hussain T, Agid O, Verhoeff NP, Wilson AA, Houle S, et al. Equivalent occupancy of dopamine D1 and D2 receptors with clozapine: Differentiation from other atypical antipsychotics. Am J Psychiatry. 2004; 161:1620–1625. [PubMed: 15337652]
17. Tauscher J, Kapur S. Choosing the right dose of antipsychotics in schizophrenia: Lessons from neuroimaging studies. CNSDrugs. 2001; 15:671–678.

18. Seeman P. Atypical antipsychotics: Mechanism of action. Focus. 2004; 2:48–58.



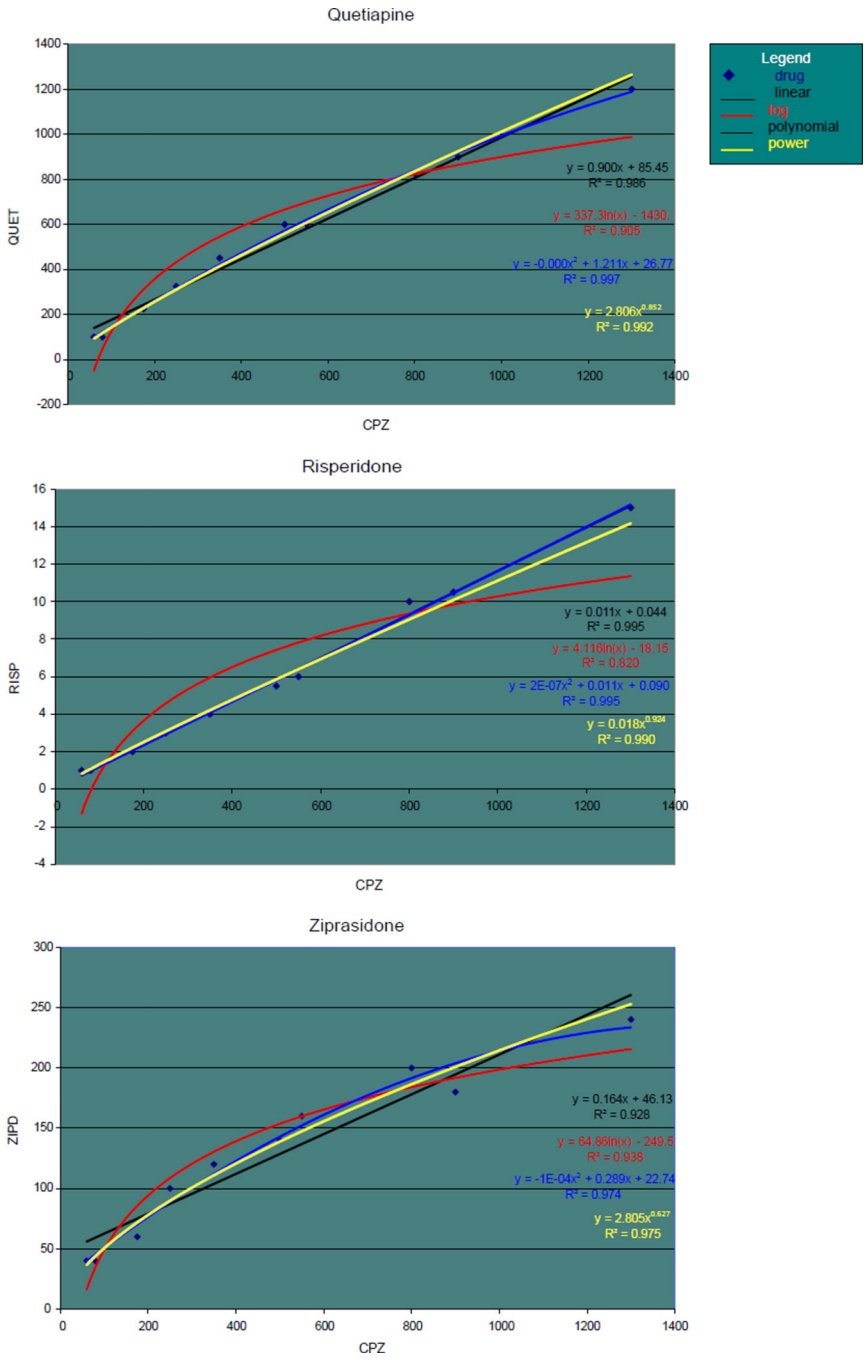


Figure 1.
Plots for transformation of regression equation. Black indicates linear; ref, log; blue, polynomial; yellow, power.

Table 1

Combined Experts' Guidelines 5A and 5B for Dose Equivalencies

	Equivalent Doses, Combined Guidelines 5A and 5B[a]									
	Haloperidol (mg)					**Risperidone (mg)**				
	1 (SD)	**5 (SD)**	**10 (SD)**	**20 (SD)**	**30 (SD)**	**1 (SD)**	**2 (SD)**	**4 (SD)**	**6 (SD)**	**10 (SD)**
Atypical Antipsychotics										
Aripiprazole	5 (2.7)	10 (3.8)	20 (7.9)	30 (14.5)	35 (11.6)	5 (1.8)	10 (2.6)	15 (5.4)	25 (5.5)	30 (7.6)
Clozapine	75 (37.9)	250 (80.0)	425 (134.9)	675 (153.7)	900 (196.5)	75 (35.4)	175 (60.3)	350 (90.1)	500 (109.5)	700 (148.6)
Olanzapine	2.5 (1.6)	10 (3.6)	20 (5.1)	30 (11.7)	45 (19.4)	5 (1.8)	7.5 (2.7)	15 (3.4)	20 (4.8)	30 (6.6)
Quetiapine	100 (66.6)	325 (118.7)	600 (185.1)	900 (336.6)	1200 (520.4)	100 (39.8)	225 (73.3)	450 (144.7)	600 (148.1)	825 (187.2)
Risperidone	1 (.4)	3 (1.0)	5.5 (1.8)	11 (4.1)	15 (5.2)	1 (NA)	2 (NA)	4 (NA)	6 (NA)	10 (NA)
Ziprasidone	40 (24.6)	100 (35.2)	140 (41.4)	180 (51.7)	240 (91.8)	40 (18.2)	60 (25.9)	120 (34.2)	160 (42.7)	200 (55.4)
Typical Antipsychotics										
Chlorpromazine	60 (29.6)	250 (64.9)	500 (123.4)	900 (213.3)	1300 (369.5)	80 (25.5)	175 (53.6)	350 (136.6)	550 (169.9)	800 (249.1)
Fluphenazine	1 (.2)	5 (.3)	10 (.8)	20 (1.7)	30 (2.7)	1 (1.2)	5 (2.3)	7.5 (4.2)	13 (4.8)	15 (7.3)
Haloperidol	1 (NA)	5 (NA)	10 (NA)	20 (NA)	30 (NA)	1.5 (.5)	3.5 (1.2)	7.5 (2.6)	12 (4.3)	17 (6.7)
Perphenazine	4 (1.9)	16 (6.5)	32 (13.0)	64 (20.8)	88 (29.9)	6 (2.0)	12 (6.3)	24 (12.5)	40 (16.8)	54 (19.2)
Thioridazine	50 (26.7)	200 (55.7)	450 (135.0)	750 (207.5)	1,000 (365.2)	75 (32.1)	150 (64.2)	300 (131.2)	475 (154.9)	650 (186.2)
Thiothixene	3 (1.5)	12 (5.4)	25 (10.7)	40 (17.4)	60 (24.5)	4 (1.4)	8 (4.1)	17 (8.1)	25 (11.5)	35 (12.4)
Trifluoperazine	3 (1.4)	12 (5.3)	25 (10.3)	40 (21.4)	55 (19.9)	4 (2.1)	10 (4.1)	15 (6.8)	25 (9.5)	35 (14.2)
Fluphenazine decanoate[b] (mg/2–3 wk)	6.3 (3.0)	13 (7.3)	25 (13.2)	50 (25.8)	75 (39.5)	6.25 (3.4)	13 (5.9)	25 (11.1)	38 (20.7)	50 (40.9)
Haloperidol decanoate[b] (mg/4 wk)	25 (22.7)	100 (43.0)	150 (62.4)	250 (77.5)	300 (109.9)	25 (14.5)	50 (27.0)	100 (50.2)	150 (73.5)	225 (89.8)

[a] Per the Experts' Consensus, "We asked the experts to write-in doses of conventional and atypical antipsychotics that they would consider equivalent to a range of haloperidol doses. We used the mean and standard deviations of their responses to generate real-world doses rounded to currently available pill strengths" (3). The same method was used to determine risperidone dose equivalencies in Guideline 5B. Data were taken from the tables presented in Guidelines 5A and 5B. SDs were taken from Survey Results, Tables 7 and 8 (pp. 58–59).

[b] For fluphenazine decanoate and haloperidol decanoate, the experts were asked to indicate the dosage they consider equivalent to that dose of oral haloperidol or oral risperidone being given daily on an ongoing basis.

Table 2

Linear Formulas, R^2 Values, and Chlorpromazine Equivalents for Each Antipsychotic Medication

Drug	Linear Formula (Solving for Drug)	R^2	Chlorpromazine Equivalent (mg)
Atypicals			
Aripiprazole	y = 0.0266x[a] + 5.311	0.9946	7.971
Clozapine	y = 0.6903x + 69.747	0.9731	138.777
Olanzapine	y = 0.0332x + 2.0093	0.9925	5.3293
Quetiapine	y = 0.9004x + 85.459	0.9867	175.499
Risperidone	y = 0.0116x + .0446	0.9956	1.2046
Ziprasidone	y = 0.1649x + 46.134	0.9282	62.624
Typicals			
Fluphenazine	y = .0225x - .4531	0.9847	1.7969
Haloperidol	y = .0230x - .7359	0.9971	1.5641
Perphenazine	y = .0686x - .0374	0.9972	6.8226
Thioridazine	y = 0.7817x + 21.873	0.9946	100.043
Thiothixene	y = 0.0450x + .5519	0.9969	5.0519
Trifluoperazine	y = 0.0420x + 1.5443	0.9951	5.7443
Fluphenazine decanoate (mg/2–3 wk)	y = 0.0562x + 2.1125	0.9812	7.7325
Haloperidol decanoate (mg/4 wk)	y = 0.2354x + 20.615	0.9724	44.155

[a]Chlorpromazine is represented by "x" in the above formulas, such that chlorpromazine 100 mg would yield the equivalents in the far-right column.

Table 3

Formulas for Calculating Dosage Equivalents Using Regression with Power Transformation, and Chlorpromazine and Haloperidol Equivalents Based on Them

	Formulas and Equivalents			
Medications	**Formula[a] (x = CPZ)**	**Chlorpromazine Equivalent (mg)**	**Formula[b] (x = Haloperidol)**	**Haloperidol Equivalent (mg)**
Atypical Antipsychotics				
Aripiprazole	$y = 0.255x^{0.700}$ [d]	6.42	$y = 4.343x^{0.645}$ [d]	6.79
Clozapine	$y = 2.027x^{0.863}$ [f]	108	$y = 66.58x^{0.796}$ [e]	115.61
Olanzapine	$y = 0.086x^{0.870}$ [e]	4.75	$y = 2.900x^{0.805}$ [e]	5.07
Quetiapine	$y = 2.806x^{0.852}$ [f]	142	$y = 88.16x^{0.786}$ [e]	151.97
Risperidone	$y = 0.019x^{0.924}$ [f]	1.32	$y = 0.790x^{0.851}$ [e]	1.43
Ziprasidone	$y = 2.805x^{0.628}$ [d]	50.5	$y = 35.59x^{0.578}$ [d]	53.13
Typical Antipsychotics				
Chlorpromazine	$y = x$	100	$y = 56.98x^{0.923}$ [f]	108.04
Fluphenazine	$y = 0.011x^{1.112}$ [d]	1.76	$y = 0.940x^{1.028}$ [d]	1.92
Haloperidol	$y = 0.013x^{1.082}$ [f]	1.84	$y = x$	2
Perphenazine	$y = 0.071x^{0.994}$ [f]	6.9	$y = 3.937x^{0.919}$ [f]	7.44
Thioridazine	$y = 0.989x^{0.973}$ [f]	87.3	$y = 50.51x^{0.898}$ [f]	94.14
Thiothixene	$y = 0.057x^{0.967}$ [f]	4.91	$y = 2.852x^{0.892}$ [f]	5.29
Trifluoperazine	$y = 0.066x^{0.939}$ [f]	5.09	$y = 3.001x^{0.866}$ [f]	5.47
Fluphenazine decanoate (mg/2–3 wk)	$y = 0.163^{x0.843}$ [c]	7.91	$y = 4.921x^{0.778}$ [c]	8.44
Haloperidol decanoate (mg/4 wk)	$y = 0.635x^{0.872}$ [d]	35.3	$y = 21.662x^{0.803}$ [d]	37.8

[a] Chloropromazine is represented by "x" in this column, such that CPZ 100 mg would yield the equivalents in the next column over to the right.

[b] Haloperidol is represented by "x" in this column, such that haloperidol 2 mg would yield the equivalents in the next column over to the right.

[c] $R^2 > .96$.

[d] $R^2 > .97$.

[e] $R^2 > .98$.

[f] $R^2 > .99$.

Table 4

Clinical Antipsychotic Trials of Intervention Effectiveness Doses:[a] Effects of Dose Equivalent Conversions

Drug Mean Dose	Derived CPZ Equivalent Dose	Derived Haloperidol Equivalent Dose	Woods/Davis CPZ Equivalent Dose
Olanzapine 20.1	421.05	7.89	400
Perphenazine 20.8	301.45	5.59	233
Quetiapine 543.4	382.39	7.65	724
Risperidone 3.9	295.45	5.91	233
Ziprasidone 112.8	223.37	4.25	188

CPZ, chlorpromazine

[a] All doses are in milligrams.