future research. While it is also true that assumptions concerning proportional hazards may not be met for this study, given the intersection of survival curves in Figure 2, this can sometimes be addressed by breaking the curves into shorter time frames. We would like to request that the authors provide, if possible, hazard ratios or another measure of effect size for their reported outcomes, especially the time to first suicide attempt (since examining suicidal behavior alone, rather than outcomes including prophylactic hospitalizations, has previously been a more sensitive measure for detecting differences in suicidal behavior among medications [2]).

In addition, the authors powered their study for a 1:5 difference in suicidality and argue that even a 1:2 difference might be clinically important. However, I would argue that even a 20% difference in suicide or suicidal behavior risks between psychiatric agents—if reliably demonstrated—may prove clinically significant. A 20% difference was the target for the International Suicide Prevention Trial study (2), and it remains relevant today. While Oquendo et al. are right to address concerns of overdose toxicity, thus far the Baldessarini et al. (3) meta-analysis points to decreases in suicide deaths as well as suicidal behavior in lithium recipients and a decreasing ratio of suicides to suicide attempts. These patterns seem the opposite of what we would expect if overdose toxicity clearly outweighed the possible clinical and behavioral benefits of lithium.

Clearly the important field of psychiatric medication and suicide risk warrants continued investigation; further detail about the results (e.g., hazard ratios) from Oquendo and colleagues' valuable trial would be an important step.

References

1. Oquendo MA, Galfalvy HC, Currier D, Grunebaum MF, Sher L, Sullivan GM, Burke AK, Harkavy-Friedman J, Sublette ME, Parsey RV, Mann JJ: Treatment of suicide attempters with bipolar disorder: a randomized clinical trial comparing lithium and valproate in the prevention of suicidal behavior. Am J Psychiatry 2011; 168:1050–1056
2. Meltzer HY, Alphs L, Green AI, Altamura AC, Anand R, Bertoldi A, Bourgeois M, Chouinard G, Islam MZ, Kane J, Krishnan R, Lindenmayer JP, Potkin S, International Suicide Prevention Trial Study Group: Clozapine treatment for suicidality in schizophrenia: International Suicide Prevention Trial (InterSePT). Arch Gen Psychiatry 2003; 60:82–91
3. Baldessarini RJ, Tondo L, Davis P, Pompili M, Goodwin FK, Hennen J: Decreased risk of suicides and attempts during long-term lithium treatment: a meta-analytic review. Bipolar Disord 2006; 8:625–639

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Differential Lithium Efficacy in Reducing Suicidal Behaviors Compared With Suicidal Thoughts

To the Editor: We applaud the extensive effort and recognize the ethically challenging nature of designing and conducting the randomized clinical trial comparing lithium and valproate in the treatment of suicidal behavior (1) reported in the October 2011 issue of the *Journal*. Such studies are desperately needed to identify pharmacological treatment approaches that reduce suicide. The report by Oquendo et al. (1) should further encourage such experimental approaches. However, our concern is that the article's conclusions could discourage clinicians from prescribing lithium for at-risk bipolar patients.

Lithium therapy has been associated with a reduction in the risk of suicidal behavior, defined as a suicide attempt or completion (2). However, there exists limited evidence to suggest that planning for a suicide, a subtype of suicidal ideation, is attenuated by lithium therapy. In a recent consensus statement, experts argued that combining suicidal thinking and behavior should not be a standard endpoint for randomized controlled trials (3), and ideation per se does not have a well-documented biological basis. Oquendo et al. emphasize that they calculated power to detect a relative risk of 5 or greater, which compares favorably with the relative risks associated previously with not taking lithium versus taking lithium (relative risk=4.91, 95% CI=3.82–6.31) (2). However, sufficient power is only derived from including individuals with a plan for a suicidal act. Can the authors provide a power analysis only for suicidal behavior as an outcome, and discuss conclusions based on the outcome of that analysis?

A current hypothesis about the biological mechanism of lithium action in preventing suicide—consistent with available evidence—is that lithium does not reduce suicidal thoughts, but it reduces acting on such thoughts by decreasing impulsivity, aggression, or decision-making deficits, which are well-defined endophenotypes intermediate to suicidal behaviors (4). It is possible that lithium could have the greatest effect in preventing suicidal acts in patients who have a plan for suicide and that by intervening, as per the experimental design, the therapeutic effects of lithium would not be observed. We recognize that the experimental options were limited by ethical concerns that the authors were unmistakably correct to follow, but that does not reduce the rationale for considering that such a mechanism may be important.

References

1. Oquendo MA, Galfalvy HC, Currier D, Grunebaum MF, Sher L, Sullivan GM, Burke AK, Harkavy-Friedman J, Sublette ME, Parsey RV, Mann JJ: Treatment of suicide attempters with bipolar disorder: a randomized clinical trial comparing lithium and valproate in the prevention of suicidal behavior. Am J Psychiatry 2011; 168:1050–1056
2. Baldessarini RJ, Tondo L, Davis P, Pompili M, Goodwin FK, Hennen J: Decreased risk of suicides and attempts during long-term lithium treatment: a meta-analytic review. Bipolar Disord 2006; 8:625–639
3. Meyer RE, Salzman C, Youngstrom EA, Clayton PJ, Goodwin FK, Mann JJ, Alphs LD, Broich K, Goodman WK, Greden JF, Meltzer HY, Normand SL, Posner K, Shaffer D, Oquendo MA, Stanley B, Trivedi MH, Turecki G, Beasley CM Jr, Beautrais AL, Bridge JA, Brown GK, Revicki DA, Ryan ND, Sheehan DV: Suicidality and risk of suicide: definition, drug safety concerns, and a necessary target for drug development: a consensus statement. J Clin Psychiatry 2010; 71:e1–e21
4. Kovacsics CE, Gottesman II, Gould TD: Lithium's antisuicidal efficacy: elucidation of neurobiological targets using endophenotype strategies. Annu Rev Pharmacol Toxicol 2009; 49:175–198

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Response to Letters

TO THE EDITOR: We thank Dr. Smith and Dr. Gould et al. for their interest in our study. The importance of conducting a power calculation based on suicide attempts instead of suicidal ideation with plans is a point well taken. Because the power calculator originally used for the article appears to have been removed from the Johns Hopkins web site, we identified a different power calculator and double-checked it with our in-house power calculation script. With N=94 and 50% dropout, and an attempt rate of 13% for lithium, the minimum hazard ratio for valproate detectable with 80% power is around 3.2. Based on these same assumptions for suicide events, the hazard ratio would be 2.2. In other words, based on these new calculations, it appears that the study was better powered than originally stated in the article. Note that these calculations 1) are based on the proportional hazards regression analysis and 2) assume exponential times to event or attempt, neither of which applies to this data set. We are currently working on a power calculator for the log-rank test based on resampling.

We concur with Dr. Smith that even a 20% effect size would be of great clinical utility. This would be especially true in the context of a randomized controlled trial, in which one can obviate problems such as confounding by indication (doctors shying away from giving lithium to those patients at risk for overdose), sample bias (many lithium clinic data come from samples with a mean age over 40, possibly excluding the high-risk patients who may have already died from suicide), and key clinical variables (routine monitoring of blood levels maximizes both patient adherence to treatment and the likelihood of therapeutic levels of medication). It is our opinion that subdividing the hazard curves into smaller intervals would be a stretch of the data, especially given that the curves cross each other more than once, casting doubt that observed variations in the position of the curves with regard to each other are caused by the pharmacologic properties of the drugs.

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Corrections

Table 4 in the article "Behavioral Health Insurance Parity: Does Oregon's Experience Presage the National Experience With the Mental Health Parity and Addiction Equity Act?" by K. John McConnell, Ph.D., et al. (published online September 2, 2011) contained an error in the last row, "Pooled plans A, B, C, D (N=100,328)." With respect to the 95% confidence interval in the difference-in-difference probability of using mental health and substance abuse services, the 95% CI should have read –0.79 to –0.11.

This error was corrected for the article's print appearance in the January 2012 issue and for its online posting as part of that issue.

At the time the article "Risk of Death From Accidental Overdose Associated With Psychiatric and Substance Use Disorders," by Amy S.B. Bohnert et al., was published online on September 28, 2011, Tables 1 and 2 contained several errors in hazard ratios and confidence intervals, some of which were repeated in the abstract and in the Results section. The errors in Table 1 were in the percentage of all patients in the 60–69 age group (the correct number is 19.8) and in the confidence interval for the 70–79 age group (the correct range is 0.16–0.28). The errors in Table 2 are highlighted below.

These errors were corrected for the article's print appearance in the January 2012 issue and for its online posting as part of that issue. None of the errors affected the study findings.

TABLE 2. Adjusted Models of the Association of Psychiatric Diagnoses With Any Accidental Overdose Death, Medication-Related Accidental Overdose Death, and Alcohol/Illegal Drug-Related Accidental Overdose Death Among Veterans Health Administration Patients[a]

	Any Accidental Overdose Death		Medication-Related Accidental Overdose Death		Alcohol/Illegal Drug-Related Accidental Overdose Death	
Diagnosis	Hazard Ratio	95% CI	Hazard Ratio	95% CI	Hazard Ratio	95% CI
Any substance use disorder	4.84**	4.41–5.30	4.19**	3.81–4.61	5.92**	5.03–6.97
Alcohol use disorders	3.73**	3.42–4.07	3.34**	3.01–3.71	4.05**	3.46–4.74
Drug use disorders	5.57**	5.04–6.15	4.67**	4.21–5.19	7.36**	6.08–8.91
Cannabis use disorders	**2.86****	**2.55–3.19**	2.39**	2.08–2.74	3.63**	2.85–4.65
Stimulant use disorders	**3.95****	**3.57–4.37**	2.72**	2.37–3.13	7.03**	5.79–8.55
Opioid use disorders	**8.78****	**7.73–9.96**	7.37**	6.24–8.70	9.29**	7.34–11.76
Other drug use disorders	**5.16****	**4.69–5.67**	4.56**	4.14–5.03	5.84**	4.93–6.91