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Psychiatric Diagnosis and Clinical Trial Completion Rates: Analysis of the FDA SBA Reports

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Completion rates may affect the safety and efficacy evaluations of psychotropics. We assessed completion rates in clinical trials evaluating psychotropics for five psychiatric disorders. We also examined differences in completion rates between psychotropics and placebo in each diagnostic category. We reviewed clinical data in the Food and Drug Administration summary basis of approval reports for 20 psychotropics evaluated for the treatment of depression, schizophrenia, obsessive compulsive disorder (OCD), generalized anxiety disorder (GAD), or panic disorder, consisting of 19 710 patients. Patients with OCD had the highest completion rates (78.0%), followed by patients with panic disorder (74.4%), GAD (69.2%), depression (64.7%) and schizophrenia (49.0%). Patients assigned to placebo had significantly lower completion rates in antipsychotic clinical trials. Patients assigned to psychotropics in OCD trials had significantly lower completion rates compared to the placebo group. A greater number of early terminations relating to a lack of efficacy was seen among patients assigned to placebo (17.4%) compared with patients assigned to psychotropics (12.2%). A greater number of early terminations relating to adverse events was seen among patients assigned to psychotropics (10.4%) compared with patients assigned to placebo (4.8%). Our findings suggest that psychiatric diagnosis and treatment assignment (placebo *vs* psychotropic) were associated with completion rates in clinical trials. These findings may help in the design of future psychopharmacology clinical trials.
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INTRODUCTION

Clinical trial completion rates affect safety and efficacy assessments (Mullins *et al*, 2005; Anderson and Tomenson, 1995; Baekeland and Lundwall, 1975; Pelagotti *et al*, 2004; Labelle *et al*, 1999). When patients terminate before the end of a trial or are lost for evaluations during a clinical trial, the result may be an inaccurate estimation of adverse effects or efficacy.

Thus, it is assumed that higher clinical trial completion rates lead to a more favorable outcome for psychotropics. Additionally, low completion rates may lead to results that have limited generalizability to larger samples of patients with the disorder (Kemmler *et al*, 2005). For example, results from an antidepressant clinical trial with an 85% completion rate may be considered more valid for all depressed patients compared with an antidepressant trial with only a 60% completion rate.

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A review of the literature indicates that the completion rate among antipsychotic clinical trials is roughly 47% (Arvanitis and Miller, 1997; Chouinard *et al*, 1993; Hamilton *et al*, 1998; Kane *et al*, 2002; Meltzer *et al*, 2004; Potkin *et al*, 2003), 54.5% for obsessive compulsive disorder (OCD) trials (Greist *et al*, 1995; Koran *et al*, 2002; Montgomery *et al*, 1993), 59.1% for antidepressant trials (Claghorn *et al*, 1992; Cohn and Wilcox, 1985; Dunbar *et al*, 1991; Dunbar *et al*, 1993; Fabre *et al*, 1995; Feighner and Boyer, 1989; Fontaine *et al*, 1994; Lineberry *et al*, 1990; Lydiard *et al*, 1997; Mendels *et al*, 1995; Reimherr *et al*, 1990; Kiev, 1992; Rickels *et al*, 1992; Shrivastava *et al*, 1992; Smith and Glaudin, 1992), 62.1% for generalized anxiety disorder (GAD) trials (Enkelmann, 1991; Gelenberg *et al*, 2000; Liebowitz *et al*, 2002; Rickels *et al*, 2000; Stein *et al*, 1998), and 64.7% in panic disorder trials (Andersch *et al*, 1991; Ballenger *et al*, 1998; Lecrubier *et al*, 1997; Lecrubier and Judge, 1997; Londborg *et al*, 1998; Pollack *et al*, 1998; Rapaport *et al*, 2001). These published reports represent a heterogeneous sample that is nonetheless composed exclusively of published data; publication bias is therefore a concern when considering these results.

Recently, a large federally funded clinical trial (CATIE, Lieberman *et al*, 2005) assessing the efficacy of five

antipsychotic agents was published using completion rates as the primary outcome variable. Besides using this novel primary dependent variable, these researchers chose not to focus on other efficacy measures such as the Brief Psychiatric Rating Scale or the Positive and Negative Syndrome Scale. These investigators did not include a placebo control group, making the study similar to a non-inferiority design rather than a superiority design.

This study failed to detect any significant differences among the five antipsychotics evaluated. Such a finding is not surprising. Trials using a design such as non-inferiority are prone to type II errors, because it is extremely difficult to power the trials to find significant differences (Leon, 2000). Furthermore, caution is warranted because the investigators could not evaluate completion rates in a placebo group using their design. This is of importance because efficacy measures and completion rates may or may not be closely related. Even more important, patients may terminate prematurely from psychopharmacology trials for different reasons when assigned to psychotropics and placebo.

Because of the ambiguous results of the CATIE trial and general lack of specificity of completion rates based on a current literature review, we assessed the underlying assumptions of completion rates as an outcome measure. Specifically, we assessed whether clinical trial design factors (Khan *et al*, 2004, 2005; Khan and Schwartz, 2005) such as psychiatric diagnosis, assignment to psychotropics *vs* placebo, duration of the clinical trial, dosing schedules, and number of treatment arms are associated with psychotropic clinical trial completion rates. We noted previously that placebo response and drug–placebo differences were significantly associated with psychiatric diagnosis (Khan *et al*, 2005). Hence, we suspect that completion rates may also be related to psychiatric diagnosis.

We hypothesized that both patient characteristics (psychiatric diagnosis) and clinical trial features (treatment assignment, duration of the clinical trial, dosing schedule, and number of treatment arms) may be related to completion rates. This hypothesis is based on previous observations that have linked these variables with well-accepted measures of clinical trial outcomes (Khan *et al*, 2003a, b, 2004, 2005).

METHODS

The US Food and Drug Administration (FDA) staff generates Summary Basis of Approval (SBA) reports on every new drug and indication for each New Drug Application (NDA). The FDA staff including physicians, chemists, pharmacologists, toxicologists, and clinical pharmacists review different aspects of the NDA and compile the data into a SBA report containing pre-clinical and clinical data reviews (in abbreviated form) on patients voluntarily participating in the respective clinical trials. The senior physician signs off on the completed report and then incorporates portions of the information into product labeling. This information is sent to the Department of Freedom of Information for public availability.

Sections of the SBA reports commonly include recommendations for approvability, an overview of the clinical program, efficacy data, safety findings, dosing recommendations, and information for use in special populations. The efficacy section details pivotal trials used to evaluate the superiority of the investigational medication over placebo or an established comparator. This section contains information such as the number of patients participating in the trials and the number of patients who complete the clinical trial. The safety section does not contain completion rates for the clinical trials, although sections may report on patient drop-outs based on the evaluated cause. However, these data do not match the data reported in the efficacy section, severely limiting their usefulness.

We obtained FDA SBA reports for each NDA of clinical trial data for the following psychotropics approved in the United States between 1985 and 2004: antidepressants: bupropion SR, citalopram, duloxetine, escitalopram, fluoxetine, mirtazapine, nefazodone, paroxetine, sertraline, venlafaxine, venlafaxine ER; antipsychotics: aripiprazole, olanzapine, quetiapine, risperidone, ziprasidone; panic agents: clonazepam, paroxetine, sertraline; OCD agents: clomipramine, fluoxetine, fluvoxamine, paroxetine, sertraline; GAD agents: buspirone, venlafaxine.

We recorded the completion rates for the 19 710 patients participating in FDA phase II and phase III clinical trials evaluating psychotropic medications for five psychiatric disorders—depression, schizophrenia, anxiety, panic disorder, OCD, and GAD. In Table 1, we list all trials evaluated for each psychotropic and specify the diagnosis studied for all psychotropics that have multiple indications. The trial number, length of trial, dosing schedule (fixed *vs* flexible dosing), number of treatment arms, number of patients randomized to either placebo or an active medication (investigational medication or active comparator), and the number of patients who completed are listed for each study.

In Table 2, we present the percentage of completers for all patients assigned to either placebo or active medication in each diagnostic category. We rank-ordered (lowest to highest) the diagnostic categories based on the percentage of completers.

Using χ^2 analysis, we conducted several tests. First, we determined whether significant differences in completion rates existed between participants in antidepressant, antipsychotic, anti-anxiety, panic disorder, OCD, and GAD clinical trials. For this first analysis, we assessed completion rates regardless of treatment assignment (psychotropic *vs* placebo). To determine whether treatment assignment influenced completion rates, we examined whether completion rates differed for patients assigned to an active medication across the psychiatric disorders.

Next, we analyzed differences among patients assigned to the placebo arm in the various clinical trials. We then evaluated whether completion rates in the psychotropic group differed significantly from the placebo group in each diagnostic category. Additionally, we evaluated whether trends existed in completion rates based on the number of treatment arms, dosing schedule (fixed *vs* flexible), and length of trial in weeks.

In Table 3, we present the number of patients discontinuing for lack of efficacy, adverse events, and other reasons for both the psychotropic and the placebo groups in each of the five psychiatric diagnosis categories. Using χ^2 analysis, we compared psychotropic and placebo for each of the

Table 1 Demographic Information for All Studies Obtained in the FDA SBA Reports

						Placebo		Psychotropics	
Psychotropic	**Trial no.**	**Disorder**	**Length**	**Dosing**	**Arms**	***N***	**Completers**	***N***	**Completers**
Aripiprazole	93202	Schizophrenia	4	Flex	3	35	12	68	41
	94202	Schizophrenia	4	Fix	5	64	29	243	147
	97201	Schizophrenia	4	Fix	4	106	58	308	190
	97202	Schizophrenia	4	Fix	4	103	52	301	190
	138001	Schizophrenia	6	Fix	4	108	30	312	112
Bupropion	203	Depression	8	Fix	2	121	61	120	67
	205	Depression	8	Fix	3	124	85	239	145
	212	Depression	8	Fix	2	154	106	150	103
Buspirone	1012	GAD	4	Flex	3	38	25	79	59
	2044	GAD	3	Flex	3	20	20	40	39
	764	GAD	4	Flex	3	20	18	40	36
	995	GAD	4	Flex	3	56	41	107	78
	994	GAD	4	Flex	3	67	33	136	90
	996	GAD	4	Flex	3	29	18	61	35
Citalopram	85A	Depression	4	Flex	2	91	51	89	48
	86141	Depression	6	Flex	2	51	38	98	64
	89303	Depression	6	Fix	3	66	46	134	100
	91206	Depression	6	Fix	4	129	88	390	262
Clomipramine	59	OCD	10	Flex	2	121	108	118	102
	61	OCD	10	Flex	2	139	127	142	128
Clonazepam	NZ14197D	Panic	9	Fix	6	69	51	335	242
	NZ14275B	Panic	6	Flex	2	216	161	222	181
Duloxetine	HMAQa	Depression	8	Flex	3	70	46	103	67
	HMAQb	Depression	8	Flex	3	75	44	119	80
	HMATa	Depression	8	Fix	4	90	62	264	181
	HMATb	Depression	8	Fix	4	89	52	264	157
	HMBHa	Depression	8	Fix	2	122	86	123	80
	HMBHb	Depression	8	Fix	2	139	90	128	78
Escitalopram	99001	Depression	8	Fix	2	189	160	191	160
	99003	Depression	8	Flex	3	164	139	317	298
	MD-01	Depression	8	Fix	3	122	91	244	188
	MD-02	Depression	8	Flex	3	127	105	248	195
Fluoxetine	E079	OCD	8	Fix	4	57	42	160	119
	HCEP 1	OCD	13	Fix	4	89	76	266	205
	19	Depression	5	Flex	2	25	14	22	11
	25	Depression	5	Flex	2	24	14	18	10
	27	Depression	6	Flex	3	59	22	61	31
	62	Depression	6	Fix	3	104	64	415	256
Fluvoxamine	5529	OCD	10	Flex	2	80	76	80	64
	5534	OCD	10	Flex	2	80	64	80	59

Table 1 Continued

						Placebo		Pscyhotropics	
Psychotropic	**Trial no.**	**Disorder**	**Length**	**Dosing**	**Arms**	***N***	**Completers**	***N***	**Completers**
Mirtazapine	003-002	Depression	6	Flex	2	44	19	44	26
	003-003	Depression	6	Flex	2	45	24	45	27
	003-008	Depression	6	Fix	4	28	17	88	30
	003-020/3220	Depression	6	Flex	3	39	24	81	48
	003-021/3220	Depression	6	Flex	3	48	21	93	49
	003-022/3220	Depression	6	Flex	3	50	36	99	77
	003-023/3220	Depression	6	Flex	3	39	34	97	69
	003-024/3220	Depression	6	Flex	3	48	27	99	65
	84023	Depression	6	Flex	2	54	30	59	37
	85027	Depression	5	Flex	2	66	48	64	51
Nefazadone	03AOA-003	Depression	6	Fix	4	45	24	135	94
	CN104-002	Depression	6	Flex	3	57	38	112	98
	CN104-005	Depression	8	Flex	3	91	61	169	112
	CN104-006	Depression	8	Flex	3	78	50	159	87
Olanzapine	HGAD	Schizophrenia	6	Fix	5	68	25	267	125
	HGAP	Schizophrenia	6	Fix	3	50	10	102	31
Paroxetine	108	Panic	12	Flex	2	60	52	60	55
	120	Panic	10	Fix	4	69	46	209	142
	187	Panic	12	Flex	3	123	81	244	180
	223	Panic	10	Flex	3	68	50	154	108
	116	OCD	12	Fix	4	89	74	260	207
	118	OCD	12	Flex	3	75	86	157	106
	136	OCD	12	Flex	3	99	60	305	216
	01-001	Depression	6	Flex	2	24	NR	24	NR
	02-001	Depression	6	Flex	2	53	37	51	38
	02-002	Depression	6	Flex	2	34	22	36	25
	02-003	Depression	6	Flex	2	33	14	33	21
	02-004	Depression	4	Flex	2	40	20	38	22
	03-001	Depression	4	Flex	3	38	20	80	39
	03-002	Depression	4	Flex	3	40	14	80	42
	03-003	Depression	4	Flex	3	42	22	82	40
	03-004	Depression	4	Flex	3	40	18	80	36
	03-005	Depression	6	Flex	3	42	31	77	57
	03-006	Depression	6	Flex	3	37	7	78	33
Quetiapine	0006	Schizophrenia	6	Flex	2	55	23	54	28
	0008	Schizophrenia	6	Flex	3	96	41	190	88
	0013	Schizophrenia	6	Fix	7	51	17	310	135
Risperidone	201	Schizophrenia	6	Flex	3	54	16	106	51
	204	Schizophrenia	8	Fix	6	88	26	435	228
Sertraline	103	Depression	6	Fix	4	91	46	278	145
	104	Depression	8	Flex	3	150	94	298	184
	315	Depression	8	Flex	3	86	41	178	96

Table 1 Continued

Psychotropic	Trial no.	Disorder	Length	Dosing	Arms	Placebo		Pscyhotropics	
						N	Completers	*N*	Completers
	237/248	OCD	8	Flex	2	44	36	43	40
	371/372	OCD	12	Fix	4	84	60	240	176
	529	Panic	12	Fix	4	44	31	127	82
	546	Panic	12	Flex	2	79	56	85	61
	629	Panic	10	Flex	2	87	73	79	60
	630	Panic	10	Flex	2	88	72	88	71
Venlafaxine ER	600B2-210	GAD	8	Fix	4	97	78	273	190
	600B2-214	GAD	8	Fix	4	104	68	301	188
	208	Depression	12	Flex	3	91	43	166	88
	209	Depression	8	Flex	2	100	51	91	60
	367	Depression	8	Fix	4	82	53	241	209
Venlafaxine	600A-203	Depression	6	Fix	4	92	48	231	125
	600A-206	Depression	4	Flex	2	47	23	46	36
	600A-301	Depression	6	Flex	3	78	47	135	72
	600A-302	Depression	6	Flex	3	75	44	138	89
	600A-303	Depression	6	Flex	3	79	50	142	79
	600A-313	Depression	6	Fix	3	75	54	149	119
Ziprasidone	104	Schizophrenia	4	Fix	4	50	27	150	76
	106	Schizophrenia	4	Fix	3	48	24	91	52
	114	Schizophrenia	6	Fix	3	92	45	210	112
	115	Schizophrenia	6	Fix	5	83	27	250	137

Table 2 Completion Rates during Clinical Trials Evaluating Psychotropics for the Treatment of Five Psychiatric Disorders

Clinical trials	# of Trials	Active compounds			Placebo		
		N	# of Completers	%	*N*	# of Completers	%
Schizophrenia	16	3483	1800	51.7*	1145	470	41.0*
Depression	58	8164	5320	65.2	4213	2684	63.7
GAD	8	1037	715	68.9	431	301	69.8
Panic	10	1433	1063	74.2	824	617	74.9
OCD	11	1936	1483	76.6*	993	801	80.7*

*Significant difference ($p \leqslant 0.05$) between drug and placebo.

diagnosis categories to determine whether significant differences were present in terms of the number of patients terminating prematurely due to lack of efficacy, terminating due to adverse events, and terminating for other reasons.

Last, we compared the completion rates obtained from this study with rates obtained from a sample found in the literature. We utilized χ^2 analysis to compare the differences between the disorders, and also between the active drugs and placebo groups.

RESULTS

Using χ^2 analysis, we found an overall significant difference ($\chi^2 = 826.301$, df $= 4$, $p \leqslant 0.000$) in completion rates among diagnostic categories, regardless of treatment assignment (psychotropic and placebo). As shown in Table 2, we report the highest completion rates among those patients participating in OCD trials (78%), followed by panic disorder trials (74.4%), GAD trials (69.2%), antidepressant trials (64.7%) and antipsychotic trials (49%).

Table 3 Comparison of Drug *vs* Placebo in Terms of Number Terminating Due to Lack of Efficacy, Number Terminating Due to Adverse Events, and Number Terminating for Other Reasons for Each of the Five Psychiatric Diagnoses Examined

Trial	Drug	%	Placebo	%	*p*
Section A: Number of psychiatric patients terminating early due to lack of efficacy					
Depression	514/7602	6.8	584/4052	14.4	0.000
Schizophrenia	800/1683	23.0	403/1151	35.0	0.000
GAD	21/574	3.7	15/201	7.5	0.027
OCD	37/1011	3.7	42/569	7.4	0.000
Panic Disorder	22/557	3.9	47/285	16.5	0.000
Total	1394/11 427	12.2	1091/6258	17.4	0.000
Section B: Number of psychiatric patients terminating early due to adverse events					
Depression	895/7602	11.8	183/4052	4.5	0.000
Schizophrenia	200/3483	5.7	66/1151	5.7	NS*
GAD	114/574	19.9	17/201	8.5	0.000
OCD	91/1011	9.0	14/569	2.5	0.000
Panic disorder	72/557	12.9	18/285	6.3	0.003
Total	1372/13 227	10.4	298/6258	4.8	0.000
Section C: Number of psychiatric patients terminating early due to loss of follow-up or other reasons					
Depression	1234/7602	16.2	711/4052	17.5	NS
Schizophrenia	759/3483	21.8	220/1151	19.1	NS
GAD	61/574	10.6	23/201	11.4	NS
OCD	94/1011	9.3	46/569	8.1	NS
Panic disorder	40/557	7.2	22/285	7.7	NS
Total	2188/13 227	16.5	1022/6258	16.3	NS

*$p > 0.05$.

As expected, the differences in completion rates among diagnostic categories remained significant when we examined the rates separately for those patients receiving a psychotropic ($\chi^2 = 443.761$, df = 4, $p \leqslant 0.000$) and those patients assigned to placebo ($\chi^2 = 430.683$, df = 4, $p \leqslant 0.000$).

To evaluate the impact of treatment assignment on completion rates, we analyzed differences in rates between the active compound and placebo groups for the five diagnostic categories using χ^2 analysis. During antipsychotic clinical trials, those patients assigned to placebo (41.0%) had a significantly lower completion rate compared to those patients assigned to an antipsychotic (51.8%), $\chi^2 = 38.974$, df = 1, $p \leqslant 0.000$. When we examined OCD trials, we noted that the completion rates were statistically higher among the placebo group (80.7%) compared with the psychotropic group (76.6%), $\chi^2 = 6.311$, df = 1, $p = 0.0119$.

For the three remaining diagnostic categories—depression (63.7% placebo, 65.2% psychotropic), GAD (69.8% placebo, 68.9% psychotropic), and panic disorder (74.9% placebo, 74.2% psychotropic)—the differences in rates between psychotropics and placebo did not reach statistical significance.

Table 3 shows the results of χ^2 analyses comparing medication and placebo for each of the five diagnostic categories based on the number of patients terminating due to lack of efficacy (Section A), adverse events (Section B), and loss to follow-up or other reasons (Section C). Not surprisingly, for each of the five diagnostic categories, significantly more patients in the placebo group terminated due to lack of efficacy compared to the psychotropic group. Similarly, for every psychiatric diagnosis except schizophrenia, significantly more patients in the psychotropic group terminated due to adverse effects compared with the placebo group. For the schizophrenia sample, an equal percentage (5.7%) of patients terminated due to adverse events. No significant differences were found between medication and placebo regarding the number of patients terminating due to loss to follow up and other reasons.

Finally, we used χ^2 analysis to examine differences by diagnostic category in completion rates based on number of treatment arms, dosing schedule (fixed *vs* flexible), and length of trials in weeks. For all three variables we could not establish any pattern in completion rates for all five diagnostic categories. In other words, completion rates did not significantly increase or decrease in increments with additional treatment arms or length of trial, nor did one diagnostic category favor one dosing schedule over another. The only exception occurred in antipsychotic clinical trials.

The percentage of patients completing 6-week antipsychotic trials (35.6%) was significantly lower ($\chi^2 = 20.73$, df = 1, $p = 0.000$) than the percentage of patients completing 4-week trials (49.8%).

DISCUSSION

The aim of our study was to assess whether patient characteristics such as psychiatric diagnosis and clinical trial features such as treatment assignment, duration of the clinical trial, dosing schedule, and number of treatment arms may be related to completion rates. Although clinical trial design features such as the duration of the clinical trial, dosing schedule, and number of treatment arms had little relationship to completion rates, both psychiatric diagnosis and treatment assignment (psychotropic *vs* placebo) showed a significant relationship to clinical trial completion rates.

Overall, patients participating in antipsychotic clinical trials had the lowest completion rate (49.0%), whereas patients participating in OCD clinical trials had the highest completion rates (78.0%). Completion rates varied between 64.7 and 74.4% for patients with major depression, GAD, and panic disorder during the respective clinical trials.

We found significant differences in overall completion rates between patients treated with a psychotropic and those treated with placebo during antipsychotic and OCD clinical trials. We also found significantly higher completion rates among patients treated with an antipsychotic compared with those treated with placebo. On the other hand, patients assigned to placebo had a higher rate of completion than did patients receiving an OCD agent.

Interestingly, treatment assignment did not play a significant role in completion rates for antidepressant, GAD, or panic disorder clinical trials. In other words, patients in these trials assigned to either a psychotropic or a placebo had similar completion rates.

These results have specific implications for future psychopharmacology clinical trials. First, it is erroneous to assume that completion rates are similar among patients with various psychiatric diagnoses. Second, it is unclear whether completion rates can be significantly changed among psychopharmacology clinical trials as they are currently designed and conducted. For example, it would be impractical and unethical to consider whether completion rates can be significantly increased among patients with schizophrenia in antipsychotic trials where lack of efficacy is the primary reason for discontinuation regardless of treatment assignment. However, with the discovery of a much more effective treatment(s), this pattern may change.

Third, the reasons for early termination rates among psychiatric patients are different among patients assigned to placebo than for patients assigned to psychotropics. The cause of early termination among patients assigned to placebo was much more related to lack of efficacy rather than to adverse events. On the other hand, early termination due to adverse events was higher among patients assigned to psychotropics compared to patients assigned to placebo. Unexpectedly, in these trials rates of early termination from antipsychotic clinical trials for adverse events were similar among patients assigned to the psychotropic compared with those assigned to placebo.

Fourth, the patterns of completion rates are not synonymous with patterns related to primary efficacy measures among these psychopharmacology clinical trials based on our earlier analysis (Khan *et al*, 2005, see Figure 1). Specifically, the psychotropic–placebo differences were greatest in trials evaluating antipsychotics and OCD agents. The assumption that the larger effect sizes could be due to the higher number of patients completing trials does not bear out when completion rates are evaluated for these two disorders.

In other words, a larger effect size for a psychotropic agent does not imply that completion rates were high among these trials. The antipsychotic and OCD trials with the largest effect sizes had either the lowest or the highest completion rates. Paradoxically, among antidepressant and anxiolytics, the completion rates and effect sizes were intermediary. These data reinforce the concern about generalizability of many psychopharmacology trials (Kemmler *et al*, 2005) from a single or a small sample of trials.

Last, these data suggest caution in interpreting results from trials such as CATIE because it is evident that completion rates are confounded by several factors. Furthermore, the lack of a placebo control group in such a trial design is problematic. Specifically, the therapeutic index of a majority of psychopharmacology agents is low, meaning the risk–benefit ratio is small, particularly in disorders such as schizophrenia and OCD. Using conventional efficacy measures, the symptom reduction among patients with schizophrenia is approximately 12–15% from baseline and with placebo the symptom reduction is 1–5% (Khan *et al*, 2005). Thus, to detect differences across a group of approved antipsychotics using completion rates as a surrogate efficacy measure would require power in the range of several thousand patients per treatment arm (Leon, 2000).

We were surprised that the completion rates among the clinical trials reported in the FDA SBA reports were significantly higher than the rates in published reports. This was especially true for the OCD clinical trials. Published reports indicated completion rates of 54.5% (Greist *et al*, 1995; Koran *et al*, 2002; Montgomery *et al*, 1993), whereas the SBA reports indicated completion rates of 78% during OCD trials. This is a substantial difference in reported completion rates. However, the discrepancies are most likely due to the nature of published reports. The SBA reports include trials with both positive and negative outcomes in trials. Published reports typically include only positive outcomes.

Our findings are directly contrary to what would be expected given the supposition that completion rates should be an indicator of positive trial outcome, in which case the more positively biased published reports would have been expected to show higher rates of completion. Again, this observation undermines the assumption of completion rates as a valid indicator of trial outcome. The only exception was the antipsychotic clinical trials, in which the rates in the SBA reports did not significantly differ from the published reports (Arvanitis and Miller, 1997; Chouinard *et al*, 1993; Hamilton *et al*, 1998; Kane *et al*, 2002; Meltzer *et al*, 2004; Potkin *et al*, 2003).

In conclusion, using FDA SBA reports, we found that study completion rates among patients participating in psychopharmacology clinical trials were significantly associated with the psychiatric diagnosis of the patients. A significant difference was found between completion rates among psychiatric patients assigned to placebo compared with patients assigned to psychotropics in trials evaluating antipsychotic and OCD agents. Furthermore, the reason for terminating early was related to treatment assignment. Significantly more psychiatric patients terminated early when assigned to placebo compared with psychotropics for lack of efficacy, and significantly more psychiatric patients terminated early when assigned to psychotropics compared with placebo for adverse events. These findings suggest that completion rates are not synonymous with efficacy measures, based on earlier analysis of these clinical trials (Khan *et al*, 2005). Last, these findings suggest caution in using completion rates as a substitute for conventional efficacy measures.

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