

Bias reduction with an adjustment for participants' intent to dropout of a randomized controlled clinical trial

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Background Attrition, which is virtually ubiquitous in randomized controlled clinical trials, introduces problems of increased bias and reduced statistical power. Although likelihood-based statistical models such as mixed-effects models can accommodate incomplete data, the assumption of ignorable attrition is usually required for valid inferences.

Purpose In an effort to make the ignorability assumption more plausible, we consider the value of one readily obtained covariate that has been recommended by others, asking participants to rate their *Intent to Attend* the next assessment session.

Methods Here we present a simulation study that compares the bias and coverage in mixed-effects outcome analyses that do and do not include *Intent to Attend* as a covariate.

Results For the simulation specifications that we examined, the results are promising in the sense of reduced bias and greater precision. Specifically, if the time-varying *Intent to Attend* variable is associated with attrition, outcome and treatment group, bias is substantially reduced by including it in the outcome analyses.

Limitations Analyses that are adjusted in this way will only yield unbiased estimates of efficacy if attrition is *ignorable* based on the self-rated intentions.

Conclusions Accounting for participants' *Intent to Attend* the next assessment session will reduce attrition bias under conditions examined here. The item adds little burden and can be used both for data analyses and to identify participants at risk of attrition. *Clinical Trials* 2007; 4: 540–547. <http://ctj.sagepub.com>

Introduction

The randomized clinical trial (RCT) is the preferred design for evaluation of the safety and efficacy of investigational agents in regulatory submissions. With randomized treatment assignment and a reasonable sample size, an RCT overcomes the problem of selection bias at baseline that is seen in observational studies. However, during the execution of the trial, some participants inevitably cease study participation prematurely. In fact, the right to drop out prior to protocol completion is one appealing factor for potential participants at the time of RCT recruitment. In psychopharmacology trials for example, the problem is nontrivial, with attrition rates typically

ranging from 25% to 50% or higher, depending on the indication [1]. Dropout generally complicates the statistical analysis in terms of potentially biased parameter estimates of the treatment effect, reduced statistical power, and degraded confidence intervals, and thereby may lead to false inferences.

Some general approaches to the analysis of incomplete RCT data include restricting analyses to subjects with complete data, imputation, and likelihood methods for analysis of incomplete data. For example, incomplete data from participants who dropout can be included in likelihood-based models such as mixed-effects analyses. However, valid likelihood-based inferences assume ignorable attrition. For this reason, there has been development of nonignorable methods that are

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based on factorization of the joint distributions of outcomes and nonresponse, such as pattern-mixture models and selection models [2,3]. Here we attempt to account for attrition in an arguably cost-effective, if not rather simplistic, manner. It is based on the recommendations of others [3–5] who, in the context of analytic approaches to informative missingness, suggested that one way to account for the dropout mechanism is to incorporate each subject's self-rating of the likelihood of attending the next scheduled RCT assessment session. This is clearly an uncomplicated approach which, if effective in reducing bias, would be well worth implementing.

The use of self-rated *Intent to Attend* as a predictor of attrition is consistent with the Theory of Reasoned Action [6,7] which asserts that an individual's actions are based on that individual's intention to perform those actions. If this variable proves to be associated with attrition as hypothesized, and it is included in the analyses of efficacy, the dropout mechanism could effectively be converted from nonignorable to ignorable. As a consequence, likelihood-based inferences from mixed-effects analyses of the incomplete data, for example, would then be valid if the other model assumptions are fulfilled [8].

Recently funded RCTs for mood and anxiety disorders include such an item in the protocol in an effort to reduce the bias that will stem from anticipated attrition. Eventually, the choice among predictors of attrition should be an empirical question and that answer will likely differ across indications and study designs. In lieu of such data, a simulation study is described below that evaluates the performance of models that include hypothetical information on self-rated *Intent to Attend* subsequent RCT assessment sessions. We acknowledge that the results of the simulation study are limited by the range of simulation specifications examined. The data analytic approach involves a two-stage strategy.

Stage 1: Accounting for the attrition mechanism. Consider a controlled clinical trial in which subjects are randomized to one of two groups, either the investigational agent or a comparator, and those randomized subjects will be assessed weekly for weeks $j=0$ to k . Each week $j-1$, for $j=1$ to k , the subject rates, $A_{i,j-1}$, his or her *Intent to Attend* the next scheduled assessment session. (Note that $A_{i,0}$ reflects the baseline rating.) Although this could be generalized to accommodate intermittent missingness, we assume that if subject i is missing outcome y_{ij} at week j , y_{ij} will be missing for all $j>j'$ (i.e., if a subject is missing outcome in week j , that subject will be missing all subsequent outcomes).

Stage 2: Efficacy analyses. A mixed-effects linear regression model [9] is then used to compare the relative efficacy of treatment on weekly assessments of a normally distributed outcome, y_{ij} , a measure of illness severity for subject i ($i=1, \dots, N$) at time j ($j=1, \dots, k$).

Simulation Study

The performance of the adjustment for time-varying *Intent to Attend* was evaluated in a simulation study, which involved separate data generation and data analytic models for each of two stages: the Outcome model and the Attrition model. A factorial design for the simulation study involved two variables from the Attrition model and one variable from the Outcome Model (described below).

Complete outcome data

The continuous outcome, y_{ij} , is based on a standard mixed model:

$$y_{ij} = \beta_0 + \beta_G G_i + \beta_T T_j + \beta_{GT} G_i T_j + \beta_A A_{i,j-1} + v_i + \varepsilon_{ij} \quad (1.1)$$

where β_0 is the intercept, β_G is the coefficient for treatment group G_i ($G_i=0$ for comparator; $G_i=1$ for investigational agent), T_j represents time and was coded 0, 1, ..., $k-1$, and β_T is the slope for time. The treatment by time interaction, $G_i T_j$, represents the treatment group difference in slopes over time (β_{GT}). $A_{i,j-1}$ represents the time-varying *Intent to Dropout* before the next assessment session, session j . In the simulation study $A_{i,j-1}$, v_i , the subject-specific random intercept and ε_{ij} , the error term, were all generated as standard normal variables, namely, distributed as $N(0,1)$.

The outcome model data were generated by varying the association of the intent variable, $A_{i,j-1}$, with outcome, expressed as a slope:

$$\beta_A = 0, 0.25, 0.50.$$

Other aspects of the outcome model were specified with the following constants:

$$\begin{aligned} \text{Effects of time and group: } \beta_0 &= 0; \beta_T = 0.05; \\ \beta_G &= 0; \beta_{GT} = 0.15. \end{aligned}$$

The correlation among any pair of repeated measures of outcome, y_{ij} with $y_{i'j}$, for every j and j' , $\rho_y = 0.50$.

Nonresponse mechanism

To motivate the attrition model, we use the notion of the threshold concept [10]. A latent dropout score, d_{ij} , for subject i at time j , is based on the following model:

$$d_{ij} = \alpha_0 + \alpha_T T_j + \alpha_G G_i + \alpha_{GT} G_i T_j + \alpha_A A_{i,j-1} + \alpha_{MAR} y_{i,j-1} + \alpha_{MNAR} y_{ij} + \varepsilon_{ij}^* \tag{1.2}$$

where α_0 is the intercept term, α_T is the slope for the time effect (T_j), α_G is the slope for treatment group (G_i), α_{GT} is the slope for the group by time interaction term ($G_i T_j$), α_A is the slope for *Intent to Dropout* ($A_{i,j-1}$), and the residual term, ε_{ij}^* , follows a standard logistic distribution. Two terms are used to account for the association of latent dropout, d_{ij} , with outcome, with coefficients that correspond to two missingness mechanisms from the Rubin hierarchy [11], Missing at Random (MAR) and Missing Not at Random (MNAR). Specifically, α_{MAR} and α_{MNAR} represent the strength of the association of latent dropout, d_{ij} , with $y_{i,j-1}$ and y_{ij} , respectively. That is, MAR is operating, if d_{ij} is a function of prior outcome $y_{i,j-1}$; whereas, MNAR is operating if dropout at time j , d_{ij} , is a function of contemporaneous outcome $y_{i,j}$. To highlight the distinction between arbitrary (or intermittent) missingness and attrition, Diggle and Kenward [12] referred to MAR and MNAR mechanisms as ‘random dropout’ and ‘non-ignorable dropout’, respectively.

According to the threshold concept, subject i ’s binary dropout event, D_{ij} , is deemed to have occurred ($D_{ij}=1$) at time j when $d_{ij}>0$. y_{ij} is missing at that time point and all subsequent timepoints, but it is observed at all prior time points. Because the errors for latent dropout, d_{ij} , follow a standard logistic distribution, the binary attrition model can be expressed as a logit for the observed dropout D_{ij} , where each coefficient, α , is a $\ln(\text{odds ratio})$.

$$\ln\left(\frac{D_{ij}}{1-D_{ij}}\right) = \alpha_0 + \alpha_T T_j + \alpha_G G_i + \alpha_{GT} G_i T_j + \alpha_A A_{i,j-1} + \alpha_{MAR} y_{i,j-1} + \alpha_{MNAR} y_{ij} \tag{1.3}$$

We believe that in practice the item should be worded in a positive manner, i.e., *Intent to Attend* and not *Intent to Dropout*. However, in order that specified odds ratios in the subsequent description of the simulation study represent *elevated* risk of attrition, we refer to *Intent to Dropout*. In fact, the sign of the α ’s in the models described here will indicate that we are treating $A_{i,j-1}$ as *Intent to Dropout* and not *Intent to Attend*.

The following specifications regarding attrition varied for purposes of data generation:

Correlation of *Intent to Dropout*, $A_{i,j-1}$, with group, G_i : $\rho_{AG} = 0.25, 0.50$.

Missingness mechanism: either $e^{\alpha_{MAR}} = 1.5$ and $e^{\alpha_{MNAR}} = 1.0$; or $e^{\alpha_{MAR}} = 1.0$ and $e^{\alpha_{MNAR}} = 1.5$.

The attrition process was specified with the following additional parameter values that did not vary:

Association of *Intent to Dropout*, $A_{i,j-1}$, with Attrition, D_{ij} : $e^{\alpha_A} = 1.5$.

Association of time and group with dropout, expressed as odds ratios: $e^{\alpha_T} = 1.1$, $e^{\alpha_G} = 0.69$; $e^{\alpha_{GT}} = 1.2$.

Attrition model intercept term, $\alpha_0 = 0.05$.

Average correlation among repeated measures of the time-varying *Intent to Dropout*, A_{ij} with $A_{ij'}$, for every j and j' , $\rho_A = 0.20$.

The simulated data sets included 100 subjects randomized to each group, with a maximum of 6 repeated observations over time. For each combination of the simulation specifications, 1000 data sets were simulated and analyzed. FORTRAN programs were written to generate the simulated data and to consolidate summary information from the analyses. In generating the simulated data, a linear congruential generator due to Schrage [13] was used to yield uniform random numbers. The uniform random numbers were then transformed to standard normal deviates using the polar method [14]. Once a data set was generated, the MIXREG program [15] was used for analysis.

Data analytic model: outcome

A random-intercept linear regression model examined efficacy, as specified in (1.1). This model accounts for the time-varying *Intent to Dropout* by including the term, $A_{i,j-1}$. To examine the impact of model misspecification, a more naïve model that excluded $A_{i,j-1}$ was also fitted. The primary focus is on the added value of including *Intent to Dropout*, $A_{i,j-1}$, as a covariate. Therefore, we analyzed each data set in two ways, one that included $A_{i,j-1}$ in the data analytic outcome model and one that omitted it. This allowed an assessment of the benefit of including the *Intent* term, $A_{i,j-1}$.

Evaluation criteria

The models were compared on several criteria including bias (the absolute value of the difference between the specified treatment effect and the

parameter estimate), standardized bias (ratio of bias to the empirically estimated standard deviation of the parameter estimate), root mean square error (RMSE: e.g., $\sqrt{E_G(\hat{G} - G)^2}$), bias reduction (proportion of bias in an unadjusted model that is reduced with the adjustment for *Intent to Dropout*), and 95% probability coverage (the proportion of the estimated 95% confidence intervals that include the specified treatment effect). Retention rates were also tracked. Tables that present results highlight (in bold) values that exceed noteworthy thresholds: probability coverage less than 90% and, as recommended by Demirtas [16], absolute standardized bias greater than 0.40.

Simulation Study Results

MAR models

The MAR models were specified in such a way that the prior outcome is associated with attrition, but the contemporaneous outcome was not (i.e., $e^{\alpha_{\text{MAR}}} = 1.5$ and $e^{\alpha_{\text{MNAR}}} = 1.0$). Retention rates never exceeded 68% (Table 1), which is characteristic of that seen in RCTs for antidepressants, but were as low as 47%, which is not unusual in trials of antipsychotics [1]. By design the retention rates varied across treatment groups. Retention decreased with increases in the association of *Intent to Dropout* with group, ρ_{AG} , and *Intent to Dropout* on outcome, β_A .

Bias and coverage

As expected there is virtually no bias in the MAR models in which *Intent* is not related to outcome ($\beta_A = 0$) and minimal bias in all models where group and *Intent* are uncorrelated ($\rho_{AG} = 0$). Yet, despite the MAR mechanism, if the *Intent* covariate was not included in the outcome model, bias increases as ρ_{AG} and β_A increase. Notably, the bias that is seen is in the parameter estimate for the main effect of group (which represents the group difference when time equals 0), not for the estimate of the group by time interaction (Table 1). Standardized bias ranges from 56.66 to 109.59 for $\rho_{AG} > 0$ with $\beta_A = 0.25$; and from 112.43 to 217.42 with $\beta_A = 0.50$. However, if the *Intent* covariate is included in outcome analyses of those models, 50% to 99% of that bias is removed and standardized bias < 5.0 . (Due to space constraints the tables do not present results for the time effect, β_T .) RMSE paralleled standardized bias, with increases when the *Intent* covariate was

omitted from outcome analyses. The models with coverage < 0.90 were the same as those with the greatest bias, models with both $\rho_{AG} \neq 0$ and $\beta_A \neq 0$. In contrast, probability coverage exceeded 91% in all models that included the *Intent* covariate.

MNAR models

The MNAR simulated models were specified such that the outcome measure is associated with contemporaneous attrition (i.e., $e^{\alpha_{\text{MAR}}} = 1.0$ and $e^{\alpha_{\text{MNAR}}} = 1.5$). Retention in the MNAR models is slightly lower than in models with MAR attrition. Retention rates range from 44 to 68% (Table 2).

Bias and coverage

Overall the bias in the MNAR models was greater than in the MAR models and again was typically greater for the parameter estimate of the main effect of group than for the group by time interaction (Table 2). When the *Intent* covariate was not included in the outcome model, bias increased with the association of *Intent* on outcome, β_A , and, within a level of β_A , bias increased as the correlation of group and *Intent* increased. Specifically, in the outcome analyses that did not include the *Intent* covariate, the bias in parameter estimates for the null main effect of group ($\beta_G = 0$) ranges from about 0.02 to 0.21 (for $\beta_A = 0.25$) and from about 0.03 to 0.40 (for $\beta_A = 0.50$). A substantial proportion of that bias, however, was removed by including the *Intent* covariate in the outcome analyses, ranging from 3 to 89% of the bias removed (for $\beta_A = 0.25$) and from 32% to 96% (for $\beta_A = 0.5$). This pattern is also seen for standardized bias and RMSE. Inclusion of the *Intent* covariate in the outcome analyses consistently reduced standardized bias and RMSE for both β_G and β_{GT} , but of a much greater magnitude for the former. Coverage around β_G was inversely related to the two parameters specifying associations with *Intent*, ρ_{AG} and β_A . Coverage was adversely affected when the *Intent* covariate was not included in the outcome analyses.

Discussion

The value of incorporating a self-rated assessment of *Intent to Attend* into outcome analyses of an RCT has been considered. The simulation study

Table 1 Comparison of the performance of models that account for and fail to account for Intent to Dropout: MAR=1.5

Intent covariate in outcome model	ρ_{AG}	Retention		Main effect: $\beta_G = 0$					Interaction: $\beta_{GT} = 0.15$				
		Group 1	Group 2	Coverage	Bias	Percent bias reduction	Std. bias	RMSE	Coverage	Bias	Percent bias reduction	Std. bias	RMSE
Intent on outcome: $\beta_A = 0$													
Yes	0	0.63	0.55	0.93	0.004	*	2.20	0.190	0.96	0.000	*	1.12	0.039
No				0.92	0.004		2.34	0.191	0.96	0.001		1.64	0.039
Yes	0.25	0.65	0.52	0.93	0.001	*	0.75	0.192	0.96	0.000	*	0.78	0.039
No				0.93	0.001		0.62	0.190	0.96	0.001		1.82	0.039
Yes	0.5	0.67	0.50	0.93	0.000	*	-0.02	0.195	0.96	0.000	*	0.04	0.039
No				0.93	0.001		-0.50	0.190	0.96	0.000		0.87	0.039
Intent on outcome: $\beta_A = 0.25$													
Yes	0	0.63	0.55	0.95	0.003	54.6	1.90	0.178	0.94	0.002	*	-4.93	0.041
No				0.95	0.007		4.12	0.181	0.94	0.004		-9.06	0.043
Yes	0.25	0.66	0.52	0.95	0.001	98.8	-0.68	0.179	0.95	0.002	*	-4.59	0.041
No				0.92	0.102		56.66	0.207	0.94	0.004		-8.54	0.043
Yes	0.5	0.69	0.49	0.95	0.005	97.5	-2.73	0.182	0.94	0.002	*	-4.58	0.041
No				0.83	0.197		109.59	0.267	0.94	0.003		-8.05	0.043
Intent on Outcome: $\beta_A = 0.50$													
Yes	0	0.63	0.54	0.96	0.008	43.1	4.47	0.175	0.96	0.001	*	-1.39	0.040
No				0.96	0.014		7.48	0.185	0.95	0.005		-12.33	0.044
Yes	0.25	0.66	0.51	0.96	0.004	98.1	2.23	0.177	0.96	0.001	*	-1.25	0.040
No				0.82	0.207		112.43	0.276	0.95	0.005		-11.37	0.044
Yes	0.5	0.69	0.47	0.96	0.002	99.6	0.91	0.181	0.95	0.001	*	-2.03	0.041
No				0.44	0.399		217.42	0.439	0.95	0.004		-10.16	0.044

Notes: β_G is the main effect of group and β_{GT} is the interaction of group by time on outcome. β_A is the slope of Intent on outcome; ρ_{AG} is the correlation between Intent and Group. Coverage is bolded when <0.90 and standardized bias (std. bias) is bolded if its absolute value is ≥ 40 . *Bias reduction is not presented when bias in the unadjusted model is ≤ 0.005 .

Table 2 Comparison of the performance of models that account for and fail to account for Intent to Dropout: MINAR = 1.5

Intent covariate in outcome model	ρ_{AG}	Retention			Main effect: $\beta_C = 0$					Interaction: $\beta_{GT} = 0.15$				
		Group 1	Group 2	Group 2	Coverage	Bias	Percent bias reduction	Std. bias	RMSE	Coverage	Bias	Percent bias reduction	Std. bias	RMSE
Intent on outcome: $\beta_A = 0$														
Yes	0	0.63	0.53	0.94	0.012	0.9	6.19	0.191	0.94	0.009	-0.6	-23.43	0.041	
No				0.93	0.012		6.22	0.192	0.94	0.009		-22.94	0.042	
Yes	0.25	0.65	0.50	0.94	0.011 *	*	5.85	0.191	0.94	0.011	-2.8	-27.59	0.042	
No				0.94	0.005		2.54	0.191	0.94	0.011		-26.59	0.042	
Yes	0.5	0.67	0.48	0.94	0.010 *	*	5.34	0.194	0.94	0.013	-0.3	-32.37	0.042	
No				0.94	0.000		-0.09	0.190	0.94	0.013		-32.15	0.043	
Intent on outcome: $\beta_A = 0.25$														
Yes	0	0.62	0.52	0.95	0.024	3.0	13.15	0.186	0.95	0.011	5.1	-27.10	0.042	
No				0.94	0.025		13.41	0.188	0.94	0.012		-27.65	0.044	
Yes	0.25	0.65	0.49	0.94	0.024	79.3	13.14	0.187	0.94	0.013	8.4	-32.26	0.043	
No				0.89	0.118		63.09	0.221	0.93	0.014		-33.91	0.045	
Yes	0.5	0.68	0.46	0.94	0.024	88.6	12.68	0.190	0.93	0.015	11.4	-37.65	0.044	
No				0.77	0.209		111.95	0.280	0.93	0.017		-41.11	0.046	
Intent on outcome: $\beta_A = 0.50$														
Yes	0	0.61	0.51	0.95	0.020	32.1	11.15	0.178	0.94	0.009	38.3	-21.86	0.042	
No				0.95	0.029		15.78	0.186	0.94	0.015		-33.63	0.046	
Yes	0.25	0.64	0.47	0.95	0.018	91.6	10.25	0.178	0.94	0.012	38.0	-27.77	0.043	
No				0.79	0.216		117.58	0.283	0.93	0.019		-42.42	0.048	
Yes	0.5	0.68	0.44	0.95	0.016	95.9	9.03	0.182	0.94	0.014	33.2	-33.60	0.044	
No				0.43	0.402		218.63	0.443	0.94	0.021		-49.11	0.048	

Notes: β_G is the main effect of group and β_{GT} is the interaction of group by time on outcome.

β_A is the slope of Intent on outcome; ρ_{AG} is the correlation between Intent and Group.

Coverage is bolded when <0.90 and standardized bias (std. bias) is bolded if its absolute value is ≥ 40 .

*Bias reduction is not presented when bias in the unadjusted model is ≤ 0.005 .

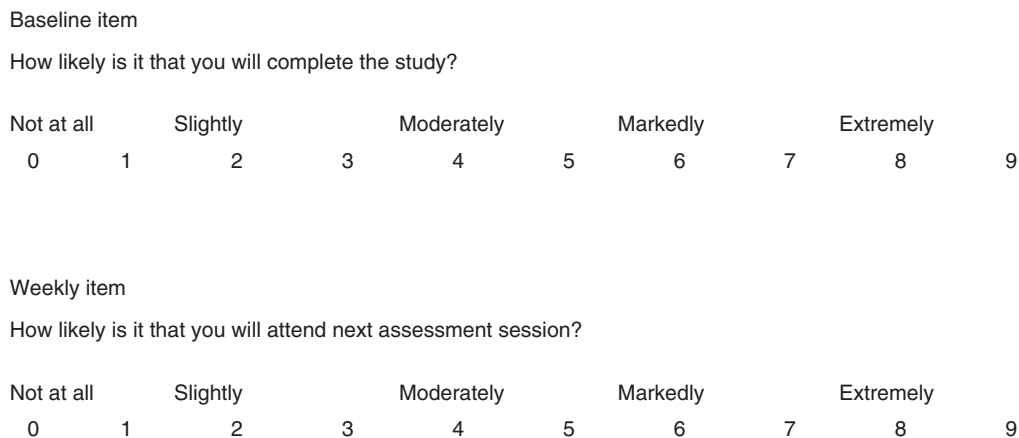


Figure 1 Examples of Rating of a study participant's *Intent to Attend*

evaluated the performance of mixed-effects linear regression analyses of repeated measures of outcome while accounting for attrition with this self-rating. The results showed that if *Intent* is related to attrition, outcome and treatment group, model performance is greatly improved with the adjustment. At the same time, if *Intent* is not related to outcome and treatment group, its inclusion does not adversely affect model performance. Furthermore, the results illustrate that even if attrition is related to an observed outcome (i.e., MAR), an omitted covariate can result in biased estimates of efficacy.

Consider the applicability of this adjustment strategy for outcome analyses in an RCT. The mixed-effects framework allows analyses to include all available observations and, most appealing in the face of attrition, a varying number of post-baseline observations per subject. However, for valid inferences with mixed-models, ignorable attrition is assumed. Strategies for accounting for nonignorable attrition include the pattern-mixture model and the selection model [2,3]. In addition, we have shown here that under certain conditions inclusion of time-varying *Intent to Attend* in outcome analyses can aid in fulfilling the ignorable attrition assumption. This strategy accounts for the attrition mechanism to the extent that the self-rating is both related to the participant's *Intent* and, in turn, associated with attrition. At minimum, the *Intent to Attend* covariate could serve as a component of sensitivity analyses. Although the analysis mode was chosen to be the mixed-effects model, the proposed approach may be beneficial under other analysis methods such as inverse probability weighting on the grounds that including causes or correlates of missingness and/or outcomes in the analysis has potential to reduce the bias that incurs due to nonresponse.

The simulation study examined a time-varying *Intent to Dropout* as a standard normal variable. Perhaps the examples of *Intent to Attend* items presented in Figure 1 would be more practical for the applied setting. This includes separate items for baseline and each subsequent assessment time and the response choices are presented on an ordinal scale. The *Intent to Attend* item adds minimal burden to the demands of either the RCT participants or the investigators. Furthermore, if the response to the question suggests that attrition is imminent, a blinded assessor could query into the specific motivation for early termination. If it involves transportation costs, scheduling difficulties, or other aspects of the trial implementation that can be reasonably adapted to the needs of a participant, efforts to prevent attrition may well be implemented. Although such action might attenuate the magnitude of association of the *Intent to Attend* item with attrition, it could serve to reduce attrition and thereby diminish the attrition bias, which after all is the ultimate objective of this assessment.

There are limitations to the strategy that was evaluated here. First, as just mentioned, the analyses will only yield unbiased estimates of efficacy if attrition is *ignorable* based on the self-rated intentions. This approach assumes covariate-dependent attrition and will not reduce bias associated with unmeasured variables or other variables that are not included in the efficacy analyses. Nevertheless, it may reduce at least a portion of the attrition bias [8], as was seen in the bias reduction shown in results from our simulation study. Furthermore, it is unclear how the adjustment would perform under conditions not examined in this simulation study. For instance, we did not consider the ramifications of an *Intent* x *Group* interaction, a random slope,

a complex covariance structure, or allowing for different missing data mechanisms for different observations. The main point of this study is that the nonresponse mechanism could effectively be converted or approximated to an ignorable one through additional data collection.

An alternative to the covariate adjustment used here is inverse probability weighting [e.g., 17,18]. The simulations, of course, assume that an appropriate data analytic model was chosen, in this case mixed-effects linear regression analyses. Also, we acknowledge that the strategy examined here ignores the limitations on generalizability that result from distinctions between those who volunteer and those who refuse an invitation to participate in an RCT. Likewise, the strategy does not mitigate the problem of reduced statistical power with incomplete data.

In conclusion, although RCTs are indispensable for study of efficacy, nonignorable attrition can compromise the validity of RCT results and must be carefully considered. With substantial attrition, the baseline group equivalence in the randomized experiment is compromised, and the trial assumes characteristics of an observational study. Accounting for participants' *Intent to Attend* the next assessment session will reduce attrition bias under the conditions illustrated here. The item adds little burden to the assessment battery and can be used for both data analyses and, more importantly to identify participants at risk of attrition, who might very well benefit from accommodation to their discontent with the RCT experience.

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