How much informative response/non-response bias is too much? A back-of-the-envelope answer

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Abstract

Informative response/non-response bias in survey research may skew effect size estimates, but an upper limit of tolerable bias has not been established. We used simple back-of-the-envelope calculations to estimate how much informative response/non-response bias can be introduced into a survey effort before parameter coverage is lost. Assigning attributes of military combat or sexual trauma exposure and of having/not having disability benefits for posttraumatic stress disorder (“service connection”) to a simulated population of 20,000 “Veterans,” we calculated true associations between combat and service connection and between military sexual trauma and service connection using 2X2 contingency tables and odds ratios. We then simulated response/non-response bias by systematically increasing or decreasing individual cells of the 2X2 contingency tables by a factor of t between 1.01 and 2.00 (equivalent to introducing bias between 1% to 100%) across several sample sizes. We calculated new odds ratios and 95% confidence intervals for each biased contingency table, as well as the maximum possible bias for 13 response/non-response mechanisms. Depending on the cell being manipulated, maximum possible response/nonresponse bias for the association between combat and service connection ranged from 10 to 260 percentage points and for the association between military sexual assault and service connection, 4 to 2,334 percentage points. For larger sample sizes (e.g., 1,000 -3,000), biases as small as 3 to 7 percentage points resulted in 95% confidence intervals that excluded the true odds ratio for some response/non-response mechanisms. Other mechanisms permitted bias of as much as 60 percentage points before parameter coverage was lost. Application of our method to a real-world example showed that realized bias in the real-world sample was not so extreme as to lose parameter coverage. Back-of-the-envelope techniques could help investigators

identify and plan for high-risk response/non-response scenarios. The provided Microsoft Excel worksheets could be adapted to this purpose.

Introduction

Mailed surveys are frequently used to define the scope and magnitude of potential public health problems when alternative methods, such as medical chart or death record review, will not suffice. The risks that informative survey response/non-response bias carry for prevalence estimates are well-recognized, as are the policy implications: under or overestimating any given disease's burden may lead to under or over funding its management. Relatively less attention has been paid to the impacts of informative survey response/non-response bias on measures of association, such as odds ratios, cf [1]. Yet the policy implications of biased odds ratios could be as profound as those associated with under or overestimating disease prevalence: deflated odds ratios could result in important, causal factors being overlooked completely, while inflated odds ratios could misdirect prevention efforts toward one factor at the expense of other, more influential factors. At extreme levels of bias, odds ratios' directions could actually reverse, causing one to treat protective factors as risk factors and vice-versa, thus worsening the problem at hand.

Ample evidence shows that representative survey response—that is, respondents do not differ systematically from non-respondents—will result in unbiased effect size estimates, even if the 95% confidence intervals are very wide [2]. The latter may occur if the response rate is very low (albeit representative) or if the original sample size was small. Non-representative survey response has variable impacts on effect size estimates, which depend critically on both the type of effect size being estimated and on the mechanism of response/non-response. For example, Westreich [3] showed that if survey response status were causally related only to the outcome of interest, risk ratios and risk differences would be biased, but not odds ratios. Conversely, except

under special circumstances, risk ratios, odds ratios, and risk differences would all be biased in expectation were response status causally related to both exposure and outcome.

Even when survey response/nonresponse status is informative—that is, somehow related to either the exposure or outcome of interest, or both—common sense tells us that smaller amounts of bias should impact resulting effect sizes and confidence intervals less than larger amounts of bias. The question, therefore, is how much bias is too much? And does that question’s answer differ according to the response/nonresponse mechanism? For example, would over representation by individuals with both exposure and outcome impact bias more substantially than might similar over representation by individuals without the exposure or outcome? In the present study, we attempt to answer these questions using a simple, back-of-the-envelope approach followed by a real-world example.

Materials and Methods

Population Simulation

The method we propose requires nothing more than an informed guess or estimate of the proportions of individuals in a population with the exposure and outcome of interest, the exposure of interest but not the outcome, and the proportion of unexposed individuals with and without the outcome. In the present analysis, we use a simulated population’s 2X2 contingency table as the basis for the exercise simply because we had one available. While any outcome or exposure could be used for the exercise that follows, we selected two exposures, combat and military sexual trauma, and one outcome, service connection for posttraumatic stress disorder (PTSD). “Service connection” is Department of Veterans Affairs (VA) parlance for receipt of disability benefits for a condition—in this case, PTSD—caused or aggravated by military

service. The exposures were selected such that one, combat, was positively associated with the outcome and the other, military sexual trauma, negatively associated [4].

We used the R `simStudy` package to simulate a population of 20,000 “Veterans” with characteristics derived from a real-world dataset of Veterans who had applied for PTSD service connection in 2016 [5]. Characteristics assigned to our simulated population included male or female gender, exposure to combat and/or military sexual trauma, and whether the “Veteran” was service connected for posttraumatic stress disorder (PTSD). As Redd et al. [6] have described, in the real world, far fewer women than men apply for PTSD service connection. Here, we assigned female gender to half the population. Mirroring the real-world data, combat exposure was assigned based on sex, such that males had 69% probability of combat exposure and females, 58% probability. Assignment of military sexual trauma exposure depended on both sex and combat exposure such that, of combat positive males and females, 0.6% and 40.4% had military sexual trauma exposure, respectively. Of the combat-negative males and females, 5.1% and 49.3% had military sexual trauma exposure, respectively. Again mirroring the real world population, the probability of the outcome, service connection for PTSD, was assigned as follows: for males without combat or military sexual trauma exposure, 14%; for males without combat exposure but positive military sexual trauma exposure, 1%; for males with combat exposure and no military sexual trauma exposure, 41%; and for males with both combat and military sexual trauma exposure, 0.2%. For females who had neither combat nor military sexual trauma exposure, the probability of service connection was assigned 9%; for those without combat exposure but positive military sexual trauma exposure, 14%; for females with combat but no military sexual trauma exposure, 14%; and for females with both combat and military sexual trauma exposure, 0.9%. The simulated population is available in **Supplementary File S1**.

How much bias is too much? A back-of-the-envelope approach

In the present analysis, we focus solely on odds ratios, though the strategy could easily be applied to relative risks or risk differences. Using a typical 2X2 contingency table to calculate odds ratios between combat and service connection and the odds ratios between military sexual trauma and service connection, we started from the premise that the size of respondent pool N is fixed (see **Supplementary File S2. Appendix**). Over or under representation by any one group fitting into the cell of a 2X2 contingency table (e.g., those who are exposed and have the outcome of interest) must therefore be offset by a similar change in another cell or cells (e.g., those who are unexposed and don't have the outcome of interest). Using the true, known 2X2 contingency tables for our simulated population as our base, we systematically increased each cell by a factor of t while decreasing one other cell by a commensurate amount, where t ranged from 1.01 to 2.0. This corresponded to introducing an informative over response bias in the increased cell of 1% to 100%. The maximum possible over response bias for each of the 12 possible increase/decrease pairs was calculated as $t = \frac{d}{i} + 1$, where d = the original size of the offsetting cell (that is, the cell being decreased) and i = the original size of the cell being increased (see **S2. Appendix**).

There are, of course, numerous ways one cell could be increased by a factor of t and the offset, removed from more than one cell in any manner of different proportions. In the present study, we examined just one example, where we increased the “a” cell (exposed/has outcome; see S2. Appendix) and evenly distributed the offset across the remaining 3 cells. The maximum possible bias for this scenario is $t = 3\frac{d}{i} + 1$, where d = original size of the smallest of the 3 cells being decreased and i = the original size of the cell being increased.

Parameter coverage signifies whether an estimate's confidence intervals (CI) contain the true value [7]. Within the range of t that we studied, we calculated odds ratios for each biased 2X2 table and used Woolf's [8] method to calculate 95% confidence intervals (CI) around each biased odds ratio. This allowed us to estimate at what level t the biased 95% confidence intervals would no longer include the true odds ratio—arguably, the point at which bias is “too much.” Because confidence intervals are sensitive to sample size, we repeated this exercise using a range of sample sizes commonly found in survey research (100, 200, 300, 500, 1000, 2000, and 3000). We used values from the simulated population's 2X2 contingency table to proportionately populate the 2X2 cells for each of the 7 sample sizes. For example, if the population value for cell “a” was 3,505 (17.5% of the simulated population), then the value for cell “a” in the 100-person sample was 17.5% X 100, or 175. To facilitate calculations, we used Microsoft Excel. Because these were back-of-the-envelope calculations, we did not concern ourselves with rounding decimals to whole numbers. In the real world, the 2X2 contingency table would contain only whole numbers. The “Fill Down” function in Excel also automatically calculated negative cell sizes and returned invalid 95% confidence intervals once maximum bias was reached. These invalid results were not interpreted and are highlighted in orange in **Supplementary File S3**.

We then explored how these techniques might apply in a real-world example, drawing from a previously published survey [5]. As reported elsewhere, 480 male and 480 female ($N = 960$) Veterans who served during Operations Enduring Freedom, Iraqi Freedom, and New Dawn were randomly selected from a sampling frame of 14,630 men and 2,945 women with pending disability claims for PTSD [5]. We used the known values of the 960, originally sampled Veterans to populate a 2X2 contingency table for the association between military sexual trauma exposure and PTSD service connection. Using the population's known values, we created

spreadsheets based on an expected response rate of 50% ($N = 480$) and on the actual response rate of 42.7% ($N = 410$). As above, we then systematically increased one cell in the 2×2 contingency table by a factor of t while decreasing another cell(s) by a commensurate amount. We also created an Excel spreadsheet based on the observed values of the actual survey respondents ($N = 410$) and systematically increased each cell in that 2×2 contingency table by a factor of t while decreasing another cell(s) by a commensurate amount. Finally, using the respondent's observed values, we created an Excel spreadsheet that worked "backwards" to estimate the true, population values of the 2×2 contingency table given a specified level of t and one of the 13 response/non-response mechanisms assessed (see **S2. Appendix**, Equation 6). **Supplementary file 4** provides the Excel spreadsheets for the real-world example.

Results

Attributes of the simulated population

Table 1 shows the simulated population's attributes (though, again, one does not need a simulated population for this exercise). As can be seen, attributes mapped closely to our intentions, though we had slightly more women (50.4%) than men. **Table 2** shows the simulated population's 2×2 contingency tables for the associations between service connection and combat and between service connection and military sexual trauma. The true, population odds ratio between combat and PTSD service connection was 2.66, and between military sexual trauma and service connection, 0.35.

[Table 1 goes here]

[Table 2 goes here]

Back-of-the-envelope results: simulated population

Supplementary File S3 provides the Microsoft Excel spreadsheet for all the back-of-the-envelope calculations of the simulated population. Although not a defined objective, **Supplementary File S3** nicely demonstrate the risks for data sparsity at smaller samples. At sample size 100, for instance, there were only 2.5 “Veterans” with military sexual trauma and service connection in expectation.

Table 3 shows the maximum bias that could be introduced into one cell of the 2X2 contingency table before the offsetting cell reached zero. For the odds ratio between combat and PTSD service connection, the maximum possible bias in cell “b” (exposed, not service connected) was just 10 percentage points before the offsetting cell “c” (unexposed, service connected) reached zero. Conversely, cell “c” could be increased by almost 11-fold before the offset in “b” reached zero. Less common in the simulated population than combat, the range of maximum bias was wider for the association between military sexual trauma and service connection. Cell “d” (unexposed, not service connected) could be increased by no more than 4 percentage points before cell “a” (exposed, service connected) reached zero. Cell “a” could be increased almost 24-fold before cell “d” reached zero.

[Table 3 goes here]

Table 4 shows the approximate point where bias in one cell of the 2X2 contingency table, offset by another cell or cells, resulted in 95% confidence intervals that excluded the true value for the association between combat and PTSD service connection. **Table 5** shows the same for the association between military sexual assault and PTSD service connection. Compared to other combinations, less bias was needed to generate 95% confidence intervals that excluded the true odds ratio when the increased cell was offset by the originally smallest cell (cells “a,” “b,” or “d”

offset by “c” in Table 4 or cells “b,” “c,” or “d” offset by “a” in Table 5). At sample size 500 for combat, for example, when using “c” (unexposed, service connected) as the offset, increasing “b” (exposed, not service connected) just 5 percentage points or “d” (unexposed, not service connected) just 6 percentage points resulted in 95% confidence intervals that excluded the true odds ratio, whereas cell “a” (exposed, service connected) could be doubled if “d” were the offsetting cell and still generate 95% confidence intervals that included the true value.

[Table 4 goes here]

[Table 5 goes here]

Because confidence intervals widen with smaller sample sizes, both tables unsurprisingly show that more bias could be introduced into the cell of a 2X2 contingency table at smaller sample sizes than at larger sizes and still have 95% confidence intervals that included the true odds ratio. This tolerance of bias comes at the expense of accuracy and precision. For example, as listed in the sample size 100 sheet in the **Supplementary File S3**, when cell “b” (exposed to combat, not service connected) was increased 80 percentage points and offset by “c” (unexposed, service connected), the resulting odds ratio between combat and PTSD service connection was 127.82 with 95% confidence intervals 0.17 to 97,648.74. **Table 6** shows the biased odds ratios for sample size 3,000 when one cell was increased by 1 percentage point or by 100 percentage points and offset by another cell or cells. Because odds ratio estimates for any given level of bias did not, essentially, differ across sample sizes (see **Supplementary File S3**), only results for sample size 3,000 are shown in the Table. At 1% bias, the odds ratio estimates were unsurprisingly close to the true value, regardless of the response/non-response mechanism. At 100% bias, odds ratio estimates for the association between combat and PTSD service connection ranged from 0.01 to 136.31 and for the association between military sexual trauma

and PTSD service connection, 0.04 to 3.75. Thus, depending on the response/non-response bias mechanism, odds ratios sometimes completely reversed direction at higher levels of bias.

[Table 6 goes here]

Real world example

In our real-world example, **Supplementary Table 1** shows that, whether using the expected sample size of 480 or the realized sample size of 410, parameter coverage for the association between military sexual trauma and service connection was not lost for most response/non-response mechanisms until bias reached 20 percentage points or more. For the response/non-response mechanisms of “c” (unexposed/service connected) offset by “a” (exposed, service connected) and “d” (unexposed/not service connected) offset by “b” (exposed, not service connected), bias in the increased cell of 9 to 10 percentage points was enough to lose parameter coverage. Results were essentially the same when using respondents’ observed values.

The real-world data showed that, relative to the true population values, “c” respondents (unexposed/service connected) were over-represented by 9 percentage points, and most of the offset occurred in cell “d” (unexposed, not service connected). **Supplementary Table 1** indicates that parameter coverage would not be lost under this mechanism until the bias in “c” increased by 30 percentage points. **Supplementary Table 2** shows how well our back-of-the-envelope approach fit the actual data. The first row shows the 2X2 contingency table for the association between military sexual trauma exposure and PTSD service connection based on the known population values. Row 2 shows estimated values for the 2X2 contingency table if cell “c” (unexposed/service connected) were increased by 9 percentage points and offset by cell “d” (unexposed, not service connected). Row 3 shows the observed respondent results. As can be seen, respondent’s observed values map closely to the second row. Results do not map perfectly

to row 2, however, because there was also an observed, slight, over response in cell “a” and slight offset in cell “b.” The final row shows that using Equation 6 from the Appendix allows one to closely approximate the original population values for cell “c” and cell “d” based on respondents’ observed values. Because the observed bias in cell “c” was less than 30 percentage points, the estimated odds ratios for rows 2 - 4 all lie within the true value’s 95% confidence intervals.

Discussion

Back-of-the-envelope calculations showed that there was an upper limit to how much over response bias could be introduced into a single cell before an offsetting cell reached zero. In scenarios where over response was offset by under response in the smallest cell, the maximum bias was sometimes just a few percentage points. For other scenarios, such as when the offset was evenly distributed across the remaining 3 cells, over response could be as much as 2,334 percentage points before an offsetting cell reached 0. Back-of-the-envelope calculations also confirmed that the specific mechanism of informative response/non-response bias strongly influenced how much bias could be introduced into a sample before 95% confidence intervals excluded the true value. For certain response/nonresponse mechanisms, it took very little bias—often less than 10 percentage points in the over responding cell—before the 95% confidence intervals excluded the true value. Other response/non-response scenarios were more forgiving, allowing even a doubling of respondents in one cell without losing parameter coverage. Because confidence intervals are sensitive to sample size, however, the true odds ratio was more often excluded at larger sample sizes than at smaller samples given the same amount of bias.

Simulating plausible alternative realizations, as we did here, allows one to concretely see various potential counterfactual situations and their resulting impact on inferences [7]. Such

practices are common in many disciplines, including engineering product design, operation research, and strategic decision making, e.g., [9, 10]. In this age of inexpensive computation, simulated models using computer algorithms may be used to create highly sophisticated counterfactual situations. Conversely, back-of-the-envelope techniques are intended to arrive at approximated answers quickly, usually using very simple maths. This makes the approach highly accessible, regardless of one's statistical sophistication or programming prowess.

By systematically altering cell counts and using simple algebra, we were able to identify, very concretely, the impact of different response/non-response mechanisms on informative bias using several different sample sizes. Similarly, other investigators could input plausible cell sizes into 2X2 contingency tables prior to launching survey efforts to help identify response/non-response scenarios at high-risk of generating unacceptable bias. Dynamic monitoring of partial R-indicators [11] coupled with adaptive recruitment methods could then help investigators avoid over or under recruiting individuals with specific exposure/outcome combinations, e.g., [12]. For completed projects, research consumers could use the approach to identify the impact and degree of likely response/non-response mechanisms on effect size estimates. If readers suspected that a survey effort over selected participants with the exposure and the outcome of interest, for example, they could input study results into a 2X2 contingency table and then quickly estimate how much bias would be needed in that cell to generate a statistically different effect size. The Excel spreadsheets that accompany this manuscript could be adapted for such calculations, or readers could create their own. Our approach also produces the biased odds ratio in expectation, thus allowing investigators and readers to examine different response/nonresponse mechanisms' impacts on both the effect size estimate and the confidence intervals. Our real-world example

showed that, while our respondents differed systematically from the underlying population, the bias was not so severe as to lose parameter coverage.

Limitations

Defining bias as “too much” when the true effect size is no longer included within the 95% confidence intervals is defensible, but only as a starting point to the conversation. A proper definition of “too much” bias should also account for distortion in the effect size itself. Most would agree that an odds ratio 48 times larger than the true value (i.e., sample size 100, cell “b” increased 80 percentage points and offset by “c”), represents unacceptable bias even if the 95% confidence intervals contained the true value. Woolf’s confidence interval is also uninformative when any cell count in a 2X2 contingency table is 0. If desired, smoothed logit intervals could be used under those circumstances [13]. We considered only univariate odds ratios, though the idea should extend easily to risk ratios and risk differences. Although calculations would be more complex, the technique should also be able to accommodate more complex associations, such as stratified analyses or contingency tables with more than 4 cells. As our real-world example showed, it is also too simplistic to assume that over response will occur in only one exposure/outcome category or be offset by under response in only one other exposure/outcome category. It is easy enough to explore these other possibilities, however, by increasing the number of response/nonresponse mechanisms considered in the spreadsheet. Investigators do not need to know the true distribution of exposures and outcomes in the population to populate the starting 2X2 contingency table, but they do need some reasonable estimate. For situations where there is no prior information, this approach will not be helpful.

Conclusions

Biased effect estimates may confuse the epidemiology of important public health problems. Unfortunately, even relatively small amounts of bias may distort odds ratios by a statistically significant amount, depending on the response/non-response mechanism. Our back-of-the-envelope approach could help investigators plan for and possibly avoid these issues.

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Supporting Information Captions

S1. Excel File of Simulated Population of 20,000 “Veterans”

S2. Appendix (attached)

S3. Microsoft Excel Worksheets of Biased Odds Ratios and Confidence Intervals Across Sample Sizes.

S4. Microsoft Excel Worksheets of Real-World Example

S4. Supplementary Tables 1-2 (attached)

Table 1.

Attributes of the Simulated Population

Attributes	Total Population		“Men”		“Women”	
	N = 20,000		n = 9,916		n = 10,084	
	n	%	n	%	n	%
Combat Exposure	12,630	63.2	6,833	68.9	5,797	57.5
Military Sexual Trauma Exposure	4654	23.3	231	2.3	4,423	43.9
Service Connected for PTSD	4,434	22.2	3,241	32.7	1,193	11.8

Table 2.

Simulated Population's True 2X2 Contingency Tables for the Association between Combat and Posttraumatic Stress Disorder Service Connection and between Military Sexual Trauma and Posttraumatic Stress Disorder Service Connection

		PTSD Service Connection				PTSD Service Connection			
		+	-			+	-		
Combat Exposure	+	3,505	9,125	12,630	Military Sexual Trauma	+	505	4,149	4,654
	-	929	6,441	7,370		-	3,929	11,417	15,346
		4,434	15,566	20,000			4,434	15,566	20,000
OR _{combat/SC} = 2.66					OR _{military sexual trauma/SC} = 0.35				

Bold face numbers indicate the marginal totals. OR = odds ratio. SC = service connection.

Table 3.

Maximum Possible Bias in the Associations between Combat and Posttraumatic Stress Disorder Service Connection and between Military Sexual Trauma and Posttraumatic Stress Disorder Service Connection When One Cell in a 2X2 Contingency Table is Increased

Cell in the 2X2 Contingency Table that was Increased		Cell(s) in the 2X2 Contingency Table that was Decreased by a Commensurate Amount		Maximum Possible Bias in the “Increased” Cell Relative to the “Decreased” Cell(s) in Percentage Points	
Letter Code	Exposure/ Outcome Status	Letter Code	Exposure/ Outcome Status	For the Odds Ratio between Combat and PTSD Service Connection	For the Odds Ratio between Military Sexual Trauma and PTSD Service Connection
a	+/+	b	+/-	260	822
a	+/+	c	-/+	27	778
a	+/+	d	-/-	184	2,261
b	+/-	a	+/+	38	12
b	+/-	c	-/+	10	95
b	+/-	d	-/-	71	275
c	-/+	a	+/+	377	13
c	-/+	b	+/-	982	106
c	-/+	d	-/-	693	291
d	-/-	a	+/+	54	4
d	-/-	b	+/-	142	36
d	-/-	c	-/+	14	34
a	+/+	b,c,d	All others ¹	80	2,334

Based on a simulated population. Maximum possible bias represents the point where the “decreased” cell will equal zero based on sample size 20,000. Letter codes correspond to the 2X2 contingency table presented for OR₁ (Equation 1, Appendix). ¹Cells b, c, and d were each reduced by 1/3 of the increase in cell a. PTSD = posttraumatic stress disorder. “+/+” = has the exposure and outcome. “+/-” = has the exposure but not the outcome. “-/+” = does not have the exposure but has the outcome. “-/-” = has neither exposure nor outcome.

Table 4.

The Association between Combat and Posttraumatic Stress Disorder Service Connection: Amount of Bias in One Cell of a 2X2 Contingency Table That Could Occur Before the 95% Confidence Intervals No Longer Contains the True Odds Ratio

Box that was Increased		Box(es) Commensurately Decreased		Amount of Change in the “Increased” Box (in Percentage Points) that Resulted in 95% Confidence Intervals that Excluded the True Odds Ratio							
Letter Code	Exposure/ Outcome Status	Letter Code	Exposure/ Outcome Status			Sample size					
				20K	3K	2K	1K	500	300	200	100
a	+/+	b	+/-	6	20	20	30	40	50	70	90
a	+/+	c	-/+	2	4	5	7	10	20	20	Max
a	+/+	d	-/-	30	>100	>100	>100	>100	>100	>100	>100
b	+/-	a	+/+	2	6	7	10	20	20	20	30
b	+/-	c	-/+	1	3	3	4	5	7	8	Max
b	+/-	d	-/-	4	9	10	20	20	30	30	50
c	-/+	a	+/+	6	20	30	30	50	60	70	100
c	-/+	b	+/-	10	30	40	50	70	90	>100	>100
c	-/+	d	-/-	8	20	30	40	50	70	80	>100
d	-/-	a	+/+	8	20	20	30	40	40	40	50
d	-/-	b	+/-	5	20	20	20	30	40	50	70
d	-/-	c	-/+	1	3	3	5	6	8	10	Max
a	+/+	b,c,d	All others ¹	4	9	20	20	30	40	40	Max

Back-of-the-envelope calculations based on a simulated population. Letter codes correspond to the 2X2 contingency table presented for OR₁ (Equation 1, Appendix). ¹Cells b, c, and d were each reduced by 1/3 of the increase in cell a. Max = 95% confidence intervals included the true odds ratio up to the point when maximum bias was reached (see Table 3).

“+/+” = has the exposure and outcome. “+/-” = has the exposure but not the outcome. “-/+” = does not have the exposure but has the outcome. “-/-” = has neither exposure nor outcome.

Table 5.

The Association between Military Sexual Trauma and Posttraumatic Stress Disorder Service Connection: Amount of Bias in One Cell of a 2X2 Contingency Table That Could Occur Before the 95% Confidence Intervals No Longer Contains the True Odds Ratio

Box that was Increased		Box(es) Commensurately Decreased		Amount of Change in the “Increased” Box (in Percentage Points) for Each Sample Size that Resulted in 95% Confidence Intervals that Excluded the True Odds Ratio							
Letter Code	Exposure/ Outcome Status	Letter Code	Exposure/ Outcome Status	Sample size							
				20K	3K	2K	1K	500	300	200	100
a	+/+	b	+/-	5	20	20	30	40	50	60	90
a	+/+	c	-/+	5	20	20	30	40	50	60	90
a	+/+	d	-/-	6	20	20	30	40	60	70	>100
b	+/-	a	+/+	2	3	4	5	7	10	Max	Max
b	+/-	c	-/+	20	40	40	50	60	60	70	80
b	+/-	d	-/-	9	30	30	40	60	70	90	>100
c	-/+	a	+/+	2	4	4	6	8	10	Max	Max
c	-/+	b	+/-	20	40	50	60	60	70	80	90
c	-/+	d	-/-	10	30	30	40	60	70	90	>100
d	-/-	a	+/+	1	2	2	3	3	Max	Max	Max
d	-/-	b	+/-	2	4	5	6	9	20	20	20
d	-/-	c	-/+	2	4	5	6	8	20	20	20
a	+/+	b,c,d others ¹	All	6	20	20	30	40	50	60	100

Back-of-the-envelope calculations based on a simulated population. Letter codes correspond to the 2X2 contingency table presented for OR₁ equation (Equation 1, Appendix). ¹Boxes b, c, and d were each reduced by 1/3 of the increase in Box a. Max = 95% confidence intervals included the true odds ratio up to the point when maximum bias was reached (see Table 3). “+/+” = has the exposure and outcome. “+/-” = has the exposure but not the outcome. “-/+” = does not have the exposure but has the outcome. “-/-” = has neither exposure nor outcome.

Table 6.

Biased Odds Ratios between Combat Exposure and Posttraumatic Stress Disorder Service Connection and between Military Sexual Trauma and Posttraumatic Stress Disorder Service Connection When One Cell in a 2X2 Contingency Table is Increased by 1 or 100 Percentage Points.

Cell in the 2X2 Contingency Table that was Increased		Cell(s) in the 2X2 Contingency Table that was Decreased by a Commensurate Amount		Biased Odds Ratio			
Letter Code	Exposure/ Outcome Status	Letter Code	Exposure/ Outcome Status	Between Combat and PTSD Service Connection		Between Military Sexual Trauma and PTSD Service Connection	
				When 1% Bias is Introduced	When 100% Bias is Introduced	When 1% Bias is Introduced	When 100% Bias is Introduced
a	+/+	b	+/-	2.70	8.65	0.35	0.81
a	+/+	c	-/+	2.80	13.02	0.36	0.81
a	+/+	d	-/-	2.68	2.43	0.35	0.68
b	+/-	a	+/+	2.57	0.45	0.32	0.06
b	+/-	c	-/+	2.92	136.31	0.35	3.75
b	+/-	d	-/-	2.60	0.01	0.35	0.11
c	-/+	a	+/+	2.63	0.98	0.32	0.07
c	-/+	b	+/-	2.64	1.48	0.35	3.34
c	-/+	d	-/-	2.63	1.14	0.35	0.12
d	-/-	a	+/+	2.64	0.32	0.28	0.04
d	-/-	b	+/-	2.71	18.11	0.37	2.64
d	-/-	c	-/+	2.89	9.55	0.37	3.59
a	+/+	b,c,d	All others ¹	2.72	36.28	0.36	0.76

Results based on sample size 3,000 of a simulated population. The true odds ratio between combat and PTSD service connection is 2.66. The true odds ratio between military sexual trauma and PTSD service connection is 0.35. Letter codes correspond to the 2X2 contingency table presented for OR₁ equation (Equation 1, Appendix). ¹Cells b, c, and d were each reduced by 1/3 of the increase in cell a. PTSD = posttraumatic stress disorder. “+/+” = has the exposure and outcome. “+/-” = has the exposure but not the outcome. “-/+” = does not have the exposure but has the outcome. “-/-” = has neither exposure nor outcome.

S2. Appendix

The following shows the usual 2X2 contingency table for calculating an odds ratio, and the odds ratio (OR_1) formula:

		Outcome		
		+	-	
Exposure	+	a	b	a+b
	-	c	d	c+d
		a+c	b+d	a+b+c+d = N

$$OR_1 = \frac{ad}{bc} \quad (1)$$

We started from the premise that the size of respondent pool N is fixed; therefore, over or under representation by any one group fitting into the cell of a 2X2 contingency table must be offset by a similar change in another cell or cells. If “a” is the number of people responding to a survey with both the outcome of interest and the exposure, changing the size of “a” by factor t and offsetting “a’s” increase by reducing “c,” say, is equivalent to creating a situation of informative, non-random, response/non-response bias. There is over response in cell “a” and under response (non-response) in cell “c.” A biased 2X2 contingency table and odds ratio formula (OR_2) follows:

		Outcome		
		+	-	
Exposure	+	ta	b	$ta+b$
	-	$c-(ta-a)$	d	$c-(ta-a)+d$
		a+c	b+d	$ta+b+c-(ta-a)+d =$ $a+b+c+d = N$

$$OR_2 = \frac{ta*d}{b*(c-(ta-a))} \quad (2)$$

If we change the size of “b” relative to “d,” keeping everything else the same, we get the following:

		Outcome		
		+	-	
Exposure	+	a	<i>tb</i>	$a+tb$
	-	c	$d-(tb-b)$	$c+d-(tb-b)$
		a+c	b+d	$a+tb+c+d-(tb-b) =$
				$a+b+c+d = N$

$$OR_3 = \frac{a*[d-(tb-b)]}{tb*c} \quad (3)$$

There are, of course, numerous ways one cell could be increased by factor *t* and the offset, removed from multiple cells in any manner of different proportions. Below we increase cell “a” and evenly distributed the offset across the remaining 3 cells:

		Outcome		
		+	-	
Exposure	+	<i>ta</i>	$b-1/3(ta-a)$	$ta+b-[1/3(ta-a)]$
	-	$c-1/3(ta-a)$	$d-1/3(ta-a)$	$c-[1/3(ta-a)]+d-[1/3(ta-a)]$
		$ta+c-1/3[(ta-a)]$	$b-[1/3(ta-a)]+d-[1/3(ta-a)]$	$ta+b+c+d-(ta-a) =$
				$a+b+c+d = N$

$$OR_4 = \frac{ta*[d-1/3(ta-a)]}{[b-1/3(ta-a)]*[c-1/3(ta-a)]} \quad (4)$$

Note that there is an upper limit to the amount of bias that can be introduced into one cell relative to another. In equation (2), for example, $ta - a$ cannot exceed c , else c will become negative. Solving for t , the formula for maximum bias in this instance is $t = \frac{c}{a} + 1$. The generalized formula for maximum bias is $t = \frac{d}{i} + 1$, where d = the original size of the “decreased” cell and i = the original size of the “increased” cell.

Under specific circumstances, an increase in one cell that is offset by another cell or cells will not bias the odds ratio. For example, when cell “a” is increased by factor t and offset by “d,” the odds ratio will not be biased if the decrease in “d” is equal to $\frac{d}{t}$. Likewise, when “d” is increased by factor t and offset by “a,” the odds ratio will not be biased if “a’s” decrease is equal to $\frac{a}{t}$. Similar logic applies to increases or decreases in cell “b” that are offset by “c,” in increases or decreases in cell “a” that are offset by cell “b,” and so on.

When presented with a biased odds ratio, one may take advantage of these relationships to estimate the true odds ratio OR_I when t is known. If, as in Equation 2, $A = ta$ and $C = c - (ta - a)$, then

		Outcome		
		+	-	
Exposure	+	A	b	A+b
	-	C	d	C+d
		A+C	b+d	A+b+C+d= N

$OR_2 = \frac{A*d}{b*C} \quad (5)$

The correct odds ratio OR_I may be estimated by replacing A with A/t and by replacing C with $C + (A - \frac{A}{t})$:

		Outcome		
		+	-	
Exposure	+	A/t	b	$A/t+b$
	-	$C + (A - \frac{A}{t})$	d	$C + (A - \frac{A}{t})+d$
		$A/t + C + (A - \frac{A}{t})$	b+d	$A/t+b+C + (A - \frac{A}{t})+d=$
		$a+b+c+d= N$		

$$OR_1 = \frac{A/t*d}{b*C+(A-\frac{A}{t})} \quad (6)$$

S4. Supplementary Tables

Supplementary Table 1.

Real World Example: Amount of Bias in One Cell of a 2X2 Contingency Table That Could Occur Before the 95% Confidence Intervals No Longer Contained the True Odds Ratio

Box that was Increased		Box(es) Commensurately Decreased		Amount of Change in the “Increased” Box (in Percentage Points) that Resulted in 95% Confidence Intervals that Excluded the True Odds Ratio between Military Sexual Trauma Exposure and Service Connection		
Letter Code	Exposure/ Outcome Status	Letter Code	Exposure/ Outcome Status	Based on Expected Sample Size N = 480	Based on Realized Sample Size N = 410	Based on Observed Respondents N = 410
a	+/+	b	+/-	20	20	20
a	+/+	c	-/+	30	40	40
a	+/+	d	-/-	>100	>100	>100
b	+/-	a	+/+	30	30	30
b	+/-	c	-/+	>100	>100	>100
b	+/-	d	-/-	40	40	40
c	-/+	a	+/+	10	10	10
c	-/+	b	+/-	20	20	20
c	-/+	d	-/-	30	30	30
d	-/-	a	+/+	20	20	20
d	-/-	b	+/-	9	9	10
d	-/-	c	-/+	20	20	30
a	+/+	b,c,d	All others ¹	40	40	40

“Expected” and “Realized” samples reflect the population’s true values. “Respondent” sample is based on the observed values of respondents, which may be biased. Letter codes correspond to the 2X2 contingency table presented for OR₁ equation (Equation 1, Appendix). ¹Cells b, c, and d were each reduced by 1/3 of the increase in cell a. “+/+” = has the exposure and outcome. “+/-” = has the exposure but not the outcome. “-/+” = does not have the exposure but has the outcome. “-/-” = has neither exposure nor outcome.

Supplementary Table 2.

Real World Example: Fit between Population Values, Observed Values, and Back-of-the-Envelope Estimations for the Association between Military Sexual Trauma Exposure and Service Connection

Source	N	2X2 Contingency Table Values				Odds Ratio	95% CI
		a +/+	b +/-	c -/+	d -/-		
Population's values	410	48.7	49.1	159.3	152.9	0.95	(0.66, 1.50)
BOE expected values ¹	410	48.7	49.1	173.3	138.9	0.79	(0.55, 1.25)
Respondents' observed values	410	51	47	173	139	0.87	(0.60, 1.37)
BOE expected values if working "backward" ²	410	51	47	158.7	153.8	1.05	(0.72, 1.65)

Letter codes correspond to the 2X2 contingency table presented for OR₁ equation (Equation 1, Appendix). "+/+" = has the exposure and outcome. "+/-" = has the exposure but not the outcome. "-/+" = does not have the exposure but has the outcome. "-/-" = has neither exposure nor outcome. BOE=Back-of-the-envelope. ¹Expected value if the *population* value for cell "c" is increased by 9 percentage points and offset by cell "d." Results should approximate the respondents' observed values.

²Expected value if the *respondents'* value for cell "c" is decreased by 9 percentage points and cell "d" is increased a commensurate amount. Results should approximate the population's values.