Multiple bias analysis: an application to quantify systematic error in measures of abortion related maternal mortality

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The launch of the UN Millennium Development Goals (MDGs) in 2000 brought heightened global attention to the measurement of maternal mortality as the fifth MDG aims to reduce maternal mortality to three quarters of 1990 levels by 2015[1]. To document such a reduction, however, countries must have the capacity to accurately measure maternal deaths, a task which has proven to be a decades-long challenge.[2-5] Weak infrastructure, lack of functional civil vital registration systems, and misclassification of maternal deaths have posed significant obstacles to the accurate measurement of maternal mortality in much of the developing world.[4, 6-8] In 2010, the World Health Organization(WHO) and the Institute for Health Metrics and Evaluation (IHME) independently attempted to quantify country-specific levels and trends of maternal mortality using distinct modeling approaches to compensate for incomplete and biased data.[9-11] Differences between the estimates published by the two institutions have resulted in confusion about global and national levels of maternal mortality. In addition, wide confidence intervals have resulted in debate as to whether these estimates demonstrate meaningful temporal trends.[10] Given the lack of valid maternal mortality estimates, there is growing consensus that it is critical to strengthen national systems for the collection of all vital statistics, including cause-specific maternal mortality data.[3, 12, 13] Strengthening health systems and improving infrastructure are necessary for the sustainable collection of high quality maternal mortality data; however, such progress is a long-term goal that will require a sustained, multi-year commitment by the international community and national governments alike. In the short-term, it is imperative novel

approaches to measure maternal mortality and to better understand existing maternal mortality data.

Despite the problems with data quality, evidence suggests that abortion related policies may play a key role in maternal mortality reduction globally. Since the MDGs were established, two of the most precipitous national reductions in maternal mortality occurred following a liberalization of abortion laws in both Nepal and Ethiopia.[14, 15] Additionally, eight out of nine countries that are 'on track' to achieve MDG 5 allow abortion on broad grounds until at least ten weeks gestation.[16] It is plausible that in countries where abortion is legally available, not only is unsafe abortion related maternal mortality greatly reduced, but governments are also more effectively able to focus on other causes of maternal mortality, and thereby leading to faster reductions in maternal mortality compared to countries where unsafe abortion is a major cause of maternal death.

Though declines in maternal mortality from Nepal, Ethiopia support the role of abortion policy reform in reducing maternal death, unsafe abortion is likely the least well-measured, and most substantially under-estimated cause of maternal death.[17-21] The literature widely reports that unsafe abortion accounts for 13% of maternal mortality,[17, 21, 22] but the WHO has long cautioned that measures of unsafe abortion uniquely suffer from underreporting and uncertainty.[23] To better understand the role of unsafe abortion in maternal mortality, and to document changes in cause specific maternal deaths as a necessary part of the MDGs, the field of global reproductive health needs a straightforward, quantitative framework through which to assess the expected direction and magnitude of biases that exist in studies of abortion related maternal mortality. In this commentary, we will present a simple framework for identifying bias in studies of abortion related mortality, suggest an epidemiologic approach to the quantification of systematic error (multiple bias analysis), outline the necessary steps for investigators interested in conducting multiple-bias analyses in their own data, and suggest approaches for reporting such analyses in the literature.

Bias in Studies of Abortion and Maternal Mortality

At present, the cause-specific maternal mortality can be assessed with facility-based data (i.e. studies collecting primary data in medical facilities, medical chart records, and autopsy records where available) and verbal autopsy data (data collected with a WHO validated tool designed to gather detailed, quantitative data on the circumstances of death to attribute cause of death in settings that lack comprehensive vital registration systems).[10, 20] In countries where unsafe abortion is common, it is often also illegal (or heavily restricted), and/or highly stigmatized. In these settings, women who experience abortion related complications are less likely than women experiencing other kinds of pregnancy-related complications to seek care in medical facilities for fear of legal, social, or religious repercussions, and both women and their family members are less likely to disclose abortion-related experiences.[20, 21, 24, 25]

Because of social and legal barriers, facility based data are unlikely to accurately capture the magnitude of abortion-related mortality in a facility's catchment area. For example, if women who experience unsafe abortions are systematically less likely to seek medical services when experiencing complications than women who experience complications from other obstetric causes, the proportion of maternal mortality related to unsafe abortion in a facility's catchment area would be underestimated using facility based data.[26] Additionally, studies of cause-specific maternal mortality that are conducted in referral facilities may only capture women with the most severe maternal complications. If women who have unsafe abortions systematically experience more severe complications prior to death than women who experience other maternal causes of death, data from referral facilities would overestimate actual rates of abortion-related mortality.[27]

While verbal autopsy studies may provide some advantages over facility-based estimates in the estimation of community-level distribution of cause-specific maternal mortality, concerns over selection bias persist: fear of social, religious, and legal ramifications may lead family members of women who suffered an abortion-related death to be less likely to participate in studies as compared to family members of women who died from other maternal causes.[28, 29] Additionally, in comparison to other obstetric complications, women are less likely to admit to family members that they are experiencing abortion-related complications which can lead abortion-related deaths to be

systematically misclassified as non-abortion-related maternal deaths, or even as non-maternal deaths.[25]

Some biases are common to both facility-based and verbal autopsy studies. Because women who experience complications from unsafe abortion often experience symptoms like heavy bleeding and infection, the literature suggests that clinicians who assign cause of death in facility-based studies as well as in verbal-autopsy forms can unintentionally misclassify unsafe-abortion related deaths as deaths from other causes (e.g., hemorrhage or sepsis).[2, 30] Abortion-related deaths are more likely than the other maternal causes to be classified as "unknown".[31] If abortion related deaths are more likely to be misclassified as non-abortion related deaths, the misclassification will produce an underestimate of abortion-related deaths as a proportion of all maternal deaths.

To conceptualize the systematic error present in studies of abortion related deaths, we propose a bias framework (Figure 1). We posit that selection bias and misclassification are both are present in both verbal autopsy studies and facility-based studies. If, relative to women who do not experience abortion-related death, women who experience abortion-related deaths are more or less likely to arrive at health facilities and/or are more or less likely to have family members participate in verbal autopsy studies of maternal deaths, bias will arise (i.e., the number of maternal deaths due to abortion measured in a study will differ from the number of maternal deaths due to abortion in the target population). This bias can be described as selection bias.[32] If, relative to women who do not experience abortion-related death, women who experience abortion-related deaths are more (or less) likely to be correctly classified as abortion-related deaths than other types of maternal deaths, bias will arise (i.e., the sensitivity and specificity of abortion related-classification will differ from the sensitivity and specificity for deaths from other maternal causes, and the proportion of maternal deaths due to abortion in the study will differ from the proportion in the study population). This bias can be described as misclassification.[32] The multiple bias analysis framework provides a relatively simple, quantitative strategy for assessing systematic error and resulting bias in any epidemiologic study. While this paper presents a blueprint for multiple bias analysis

of a proportion, the method can be applied to the analysis of multiple biases in more traditional exposure-disease relationships, and regression analyses as well.

Epidemiologic Approaches to Quantify Systematic Error

Studies that measure abortion-related mortality seek to present valid and precise estimates of the underlying 'burden of disease'. To achieve these goals, attention must be given to the potential for both systematic error (the validity of estimates), sources of which are discussed above in the bias analysis framework, and random error (the precision of estimates). A clear consensus has been reached across scientific fields regarding the quantitative reporting of random error: the ubiquitous 95% confidence interval.[33] Techniques for the quantitative assessment of systematic error have existed for decades,[34] and range from simple sensitivity analyses[35] to complex Bayesian uncertainty analysis approaches.[36] Yet, it is only recently that calls have emerged in the epidemiologic literature to evaluate and report levels of systematic error.[36-39] One such technique is multiple bias analysis, a probabilistic extension of basic sensitivity analyses that allows investigators to address multiple non-independent threats to a study's validity in one analysis (e.g, selection and misclassification bias, simultaneously).[36] Multiple bias analysis requires three main components: first, researchers determine which biases (for example information bias and/or selection bias) are likely to exist in their studies. Second, using expert knowledge and data from validation studies (where these studies exist), researchers construct parameters (or distributions) of the probable magnitude of those biases. Third after applying the distributions ("bias parameters") to the data, researchers randomly sample from those parameters over thousands of iterations to generate hypothetical distributions of point estimates had the postulated biases not existed in the study.

Multiple bias analysis techniques are a helpful tool through which researchers can attempt to quantify bias in their data, but indeed, bias analysis techniques are not without critics. Some argue that the results of such analyses are themselves biased by the values chosen by the author for each bias parameter.[40] There is no disputing that the parameters chosen, by their nature, dictate the results of bias analyses. However, by virtue of making *a priori* statements of the presumed biases and their supposed magnitude in a

study, an author establishes a clear, transparent process by which systematic error was assessed.[38] That process can be followed by readers, who can make their own assessments about the correctness or incorrectness of the authors' bias parameters, and about how results would change if the parameters had been different. Other, less complex techniques exist for the quantification of bias in studies, such as simple bias analysis (commonly known as sensitivity analysis)[36, 41] in which authors adjust for a single hypothesized value of bias, or multidimensional bias analysis, an elaboration of sensitivity analysis that allows for the simultaneous examination of multiple hypothesized values of bias.[36, 42]

A Multiple Bias Analysis Plan

The analysis plan described in detail below is intended as guide for the implementation of multiple bias analysis in eight simple steps:

Step 1. Specify the shape and width of probability distributions for the selection probabilities of abortion related deaths and non-abortion related deaths (i.e. the probability that abortion related deaths that should be captured by a study are, in fact, enumerated by that study). Under ideal circumstances, selection probabilities would be determined via internal validation studies, however, given that few internal validation studies exist in the literature, selection probabilities should be approximated using 1) data from validation studies of maternal mortality conducted in similar regions/populations, 2) adjustment factors commonly used in the demographic literature to adjust for underestimation of maternal death in studies of maternal mortality and abortion related mortality. While these sources of probability distributions are imperfect proxies for the real selection probabilities in each of the studies of interest, the assumption is made that selection bias performs similarly in studies in the same region of the world, and therefore, by constructing probability distributions of a range of possible values of selection bias, we can explicitly state the range of selection bias that one assumes, and model what the data would have looked like given a random sampling of those possible values. Trapezoidal distributions are the most commonly employed shape for probability distributions in the multiple-bias analysis literature30,57 as they allow for the specification of the range of most likely values (between mode 1 and mode 2) and the range of all possible values (between minimum and maximum specified values).

Step 2. Specify shape and width of probability distributions for the sensitivity and specificity of classifying abortion related deaths for each study. Specify probability distributions for the sensitivity and specificity of classifying abortion related deaths for each study. As in Step 1, two sources of information should be used to specify these probability distributions: 1) Data from validation studies of verbal autopsy algorithms conducted in the same country or in similar populations, 2) Data from validation studies conducted in the same country (or in similar populations) of cause of death classification from clinical case notes against autopsy diagnoses. While these two sources of data are again imperfect, there is a substantial validation literature testing the sensitivity and specificity of cause of death classification in different parts of the world that was used to inform our choices of bounds for the range of possible values of sensitivity and specificity.

Step 3. Using crude data from each of the studies, calculate the proportion of abortion related deaths in each study with the following formula:

1. $\mathbf{Y_0} = \frac{X_{0ARD}}{Total_{MD}}$,

where $\mathbf{Y_0}$ is the proportion of observed abortion related deaths (ARD), X_{0ARD} is the number of abortion related deaths identified by the study and $Total_{MD}$ is the total number of maternal deaths identified by *Study A.*

Step 4. Construct a probability distribution and a 95% confidence interval of the proportion calculated in *Step 3* using the following formulae:

1. $SE=sqrt(Y_0*(1-Y_0)/(Total_{MD}))$, where SE is the standard error of Y_0, and Y_0 is the proportion observed abortion related deaths in the study.
2. $95\%\ CI = Y_0 \pm SE$

Step 5. Adjust for selection bias in the study using the following formulae:

1. $\mathbf{X_{1ARD}} = \left(\frac{X_{0ARD}}{W_1}\right)$ where X_{1ARD} is the number of abortion related deaths adjusted for selection bias, X_{0ARD} is the number of abortion related deaths identified by the study, and where W_1 is the a priori specified trapezoidal distribution of all possible values for the selection probability for abortion related deaths.

2. $\mathbf{X_{1NARD}} = \left(\frac{X_{0NARD}}{W_2}\right)$ where X_{1NARD} is the number of non-abortion related maternal deaths adjusted for selection bias, X_{0NARD} is the number of non abortion related maternal deaths identified by the study, and where W_2 is the selection probability for non-abortion related maternal deaths.

3. $\mathbf{Y_1} = \frac{\left(\frac{X_{0ARD}}{W_1}\right)}{\left(\frac{X_{0ARD}}{W_1} + \frac{X_{0NARD}}{W_2}\right)}$ where $\mathbf{Y_1}$ is the proportion of abortion related deaths observed in the study adjusted for selection bias, and other notation is as above.

Note, the proportion of abortion related deaths should be adjusted in the order in which the biases occurred.[53] Given that subjects must, by necessity, be selected into any study before misclassification can occur, adjustment for selection bias comes first, then misclassification bias.

Step 6. Adjust for misclassification in the study. Given that misclassification can only occur among subjects selected into any study, Y_1 (the proportion of abortion related deaths observed in the study adjusted for selection bias) should be utilized as the baseline for misclassification adjustment via the following formulae:

1. $\mathbf{X_{2ARD}} = \left[\left(X_{1ARD} * W_3\right) + \left(X_{1NARD} - X_{1NARD} * W_4\right)\right]$ where X_{2ARD} is the number of abortion related deaths adjusted for selection bias and misclassification, X_{1ARD} is the number of abortion related deaths adjusted for selection bias and X_{1NARD} is the number of non abortion related maternal deaths adjusted for selection bias, and where $\mathbf{W_3}$ is the sensitivity of classification of abortion-related death and W_4 is the specificity of classification of abortion related death.

2. $\mathbf{X_{2NARD}} = [\left(X_{1NARD} * W_3\right) + (X_{1ARD} - \left(X_{1ARD} * W_4\right)]$ where X_{2ARD} is the number of non-abortion related deaths adjusted for selection bias and misclassification, X_{1ARD} is the number of abortion related deaths adjusted for selection bias and X_{1NARD} is the number of non abortion related maternal deaths adjusted for

selection bias, where $\mathbf{W_3}$ is the sensitivity of classification of abortion related death and W_4 is the specificity of classification of abortion related death.

3. $\mathbf{Y_2} = \frac{X_{2ARD}}{X_{2ARD} + X_{2NARD}}$ where Y_2 is the proportion of abortion related deaths adjusted for selection bias and misclassification, and where X_{2ARD} is the number of abortion related deaths adjusted for selection bias and misclassification and X_{2NARD} is the number of non abortion related maternal deaths adjusted for selection bias and misclassification.

Step 7. After adjusting for both sources of bias (selection bias and misclassification) incorporate random error into the new estimate. Using the same formulae that were employed in Step 1, construct a probability distribution and a range of possible values for the proportion:

1. $SE=sqrt(Y_2*(1-Y_2)/(Total_{MD}))$, where SE is the standard error of Y_2, and Y_2 is the proportion of observed abortion related deaths in the study adjusted for selection bias and misclassification.
2. $95\%\ CI = Y_2 \pm SE$.

Step 8. Model 50,000 Monte Carlo simulation trials for each simulation experiment under different probability distribution scenarios; twenty-one scenarios in total.

A Working Example of Multiple Bias Analysis

The following is a working example of a multiple bias-analysis to evaluate the influence of selection bias and misclassification in a hypothetical study (*Study A*) of maternal deaths from the maternity ward at the main referral hospital in a major urban center in East Africa over a seven year period. Data were collected from case notes from the maternity ward of the hospital, and extraction of data files from the study period was reported as 80% of the all maternal deaths identified in case notes. Maternal death was defined by the ICD-10 definition. The study identified 253 maternal deaths, of which 52 were abortion related.

Step 1: A literature review was conducted of studies in the same geographic region as *Study A* found the lowest reported selection probability to be 0.02 (i.e. only 2% of

potential abortion-related deaths were missed by the study) and the highest reported selection probability to be 0.5. The two modal values were the most commonly reported selection probabilities or adjustment factors, for *Study A*, the most commonly reported selection factors were 0.2 (i.e. 20% of abortion-related deaths were missed) and 0.25 (i.e. 25% of abortion-related deaths were missed). Three iterations of trapezoidal modes were modeled for each selection probability, with varying widths between the modal values (narrow, medium, and wide), to examine/assess the implications of modal value selection on the final results (Table 1)

Step 2: Trapezoidal distributions were also employed to model the range of possible values for sensitivity and specificity of cause of death classification. From the literature review in *Step 1*, the lowest and highest reported sensitivities and specificities for abortion related mortality were selected as the upper and lower bounds of the probability distributions. The two modal values were chosen as representative of the most commonly reported selection probabilities or adjustment factors. As in *Step 1*, three iterations of trapezoidal modes were modeled for each parameter (sensitivity and specificity), with varying widths between the modal values (narrow, medium, wide) to test the implications of modal value selection on the final results. In all, twenty-one possible combinations of varying widths of selection probabilities and classification distributions were tested for each study (Table 1)

Step 3: The proportion of abortion related deaths was calculated: $\mathbf{Y_0=0.206}$

Step 4: A 95% confidence interval of the proportion of abortion related deaths was calculated: **0.196, 0.316**

Step 5: Adjustment was made for selection bias using a priori specified trapezoidal distributions of all possible values for the selection probability for abortion related deaths (Table 1).

Step 6: Adjustment was made for misclassification in Study A using a priori specified trapezoidal distributions of all possible values for the sensitivity of classification of abortion-related deaths and the specificity of classification of abortion related deaths.

Step 7: A probability distribution and a range of possible values for the bias adjusted proportions was constructed (Table 1)

Step 8. 50,000 Monte Carlo simulation trials were modeled for each of the twenty-one

different simulation experiments (Table 1)

Summary of Bias Analysis Results

Table 2 presents the multiple bias analysis results for hypothetical *Study A*. *Study A* reported a median of 0.206 (20.6% of maternal deaths were abortion related). After adjustment for selection bias under three distribution scenarios, the median increased, on average, to 0.370. After additional adjustment for misclassification, the median proportion of abortion related deaths had increased, on average, to 0.306. After including random error into the multiple bias analysis, the median was, on average, 0.308; approximately 20% greater than the reported proportion of abortion related deaths. Had the authors of *Study A* reported a 95% confidence interval around their reported median, the range would have been: 0.196-0.316. After adjustment for selection bias under three scenarios, the potential range widened to: 0.242-0.550. After adjustment for selection bias and misclassification under 9 scenarios, the potential range was: 0.203-0.458. After including random error in the multiple bias analysis of selection bias and misclassification, the potential range widened further to: 0.169-0.485.

In this example, we applied a multiple bias analysis framework to estimates of abortion related mortality and performed multiple bias analyses (adjusting for selection bias and misclassification, and integrating random error) on estimates of the proportion of abortion related mortality reported by a hypothetical study, *Study A*. We hypothesized that both selection bias and misclassification were present in *Study A*, however, because no internal validation studies was conducted, we generated the prior probability distributions for selection bias and misclassification from existing external validation studies, and commonly employed demographic adjustment factors. Despite our best efforts to accurately represent the range of potential selection bias and misclassification, we could not be certain about the extent of systematic error, nor the magnitude or direction of the resulting bias. Consequently, we developed and tested 21 different scenarios for *Study A*, exploring all possible combinations of prior probability distributions in order to identify trends in the generated bias-adjusted estimates for abortion related mortality.

Our finding that, under all twenty-one scenarios of multiple bias analysis, the median proportion of abortion related deaths increased provides quantitative evidence that systematic error, specifically selection bias and misclassification, may indeed result in estimates of the proportion of abortion related maternal deaths that underestimate the true proportion of abortion related maternal deaths. For *Study A*, which initially found less than 20% of maternal deaths to be abortion-related, the proportion of abortion-related mortality was underestimated by an average of twenty percent.

Discussion

Findings from multiple bias analyses of abortion related mortality have broad reaching implications for the way we understand the distribution of cause of maternal death in a range of scenarios. If, as our data suggest, abortion related deaths account for a larger proportion of maternal deaths than previously thought, these methods can be used to more accurately determine a potential range of abortion related mortality in local and country specific contexts. These data might also be used to help policy makers and program planners target funds towards increasing access to family planning and safe abortion services at the community level, and, where abortion remains illegal, focusing on providing widespread access to contraception and comprehensive post abortion care. Such policies and programs will be fundamental to addressing the issue of mortality resulting from unsafe abortion. Our finding that the range of possible values of the proportion of abortion related deaths increased with multiple bias analysis is further evidence that the current estimates of abortion related mortality are not precise, and that those ranges vary widely by study site. This finding serves as a reminder to all investigators interested in quantifying the proportion of abortion related deaths in any setting, that, given the limitations of our data, we should report the observed proportion of abortion related deaths along with their appropriate confidence intervals in order to ensure readers are aware of the imprecision and potentially biased nature of our estimates.

Multiple bias analysis provides authors with a set of mathematical and statistical tools to estimate the effect of biases across a range of plausible magnitudes on the parameters estimated from the study data. In circumstances where systematic error is

known to be present, some form of bias analysis should not only be considered a necessary analytic step, it can also serve as a useful framework to help consumers of the literature interpret results vis-á-vis the magnitude and likelihood of potential biases. When authors report the results of traditional epidemiologic analyses, they traditionally do not quantify the role of bias in those results, implicitly making the assumption that biases do not exist or are unlikely to change their results. Multiple bias analysis allows investigators to exchange those implicit assumptions for explicit assumptions through the quantification of selection bias and sensitivity/specificity.

Multiple bias analysis is particularly applicable to the field of global reproductive health where issues of selection factors, willingness to participate in studies, misreporting, and underreporting of sensitive behaviors have long been acknowledged as obstacles to the collection of high quality data. With some fairly simple steps, reporting results of multiple bias analyses in estimates of abortion related mortality, predictors of unsafe abortion, and other abortion related reproductive health questions that suffer from similar biases, would not only improve reporting practices in the field, but would provide a guide for readers to understand the biases that exist in the data and how those biases might impact the observed data. It would also provide policymakers with a more accurate understanding of the potential impact of policies that target the underlying causes of unsafe abortion and abortion related mortality.

Figure 1: Bias Framework

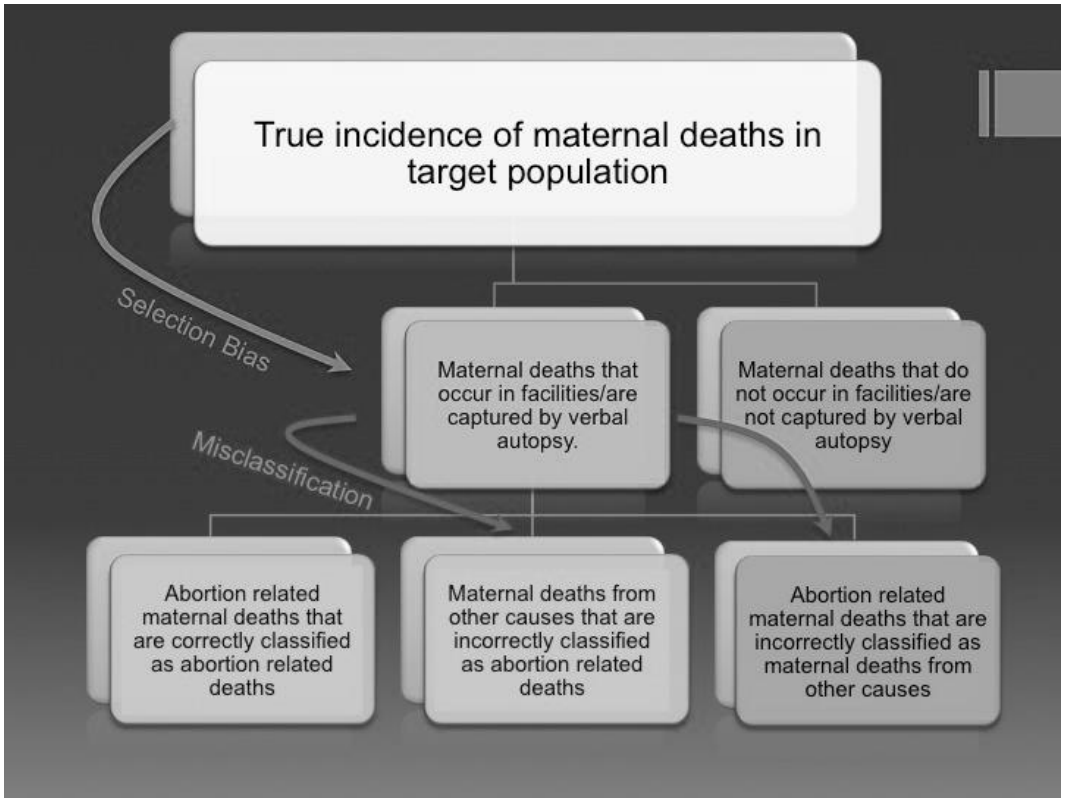

Table 1 Descriptions of trapezoidal probability distributions used for multiple-bias analysis of *Study A*

Study A	Scenario	W_1*	W_2*	W_3*	W_4*	RE
	1	0.2, 0.34, 0.43, 0.78	0.5, 0.7, 0.8, 1.0			None
	2	0.2, 0.30, 0.50, 0.78	0.5, 0.65, 0.85, 1.0			None
	3	0.2, 0.24, 0.53, 0.78	0.5, 0.6, 0.9, 1.0			None
	4	0.2, 0.34, 0.43, 0.78	0.5, 0.7, 0.8, 1.0	0.6, 0.7, 0.8, 0.9	0.91, 0.95, 0.97, 0.99	None
	5	0.2, 0.34, 0.43, 0.78	0.5, 0.7, 0.8, 1.0	0.6, 0.65, 0.85, 0.9	0.91, 0.94, 0.98, 0.99	None
	6	0.2, 0.34, 0.43, 0.78	0.5, 0.7, 0.8, 1.0	0.6, 0.62, 0.82, 0.9	0.91, 0.92, 0.98, 0.99	None
	7	0.2, 0.30, 0.50, 0.78	0.5, 0.65, 0.85, 1.0	0.6, 0.7, 0.8, 0.9	0.91, 0.95, 0.97, 0.99	None
	8	0.2, 0.30, 0.50, 0.78	0.5, 0.65, 0.85, 1.0	0.6, 0.65, 0.85, 0.9	0.91, 0.94, 0.98, 0.99	None
	9	0.2, 0.30, 0.50, 0.78	0.5, 0.65, 0.85, 1.0	0.6, 0.62, 0.82, 0.9	0.91, 0.92, 0.98, 0.99	None
	10	0.2, 0.24, 0.53, 0.78	0.5, 0.6, 0.9, 1.0	0.6, 0.7, 0.8, 0.9	0.91, 0.95, 0.97, 0.99	None
	11	0.2, 0.24, 0.53, 0.78	0.5, 0.6, 0.9, 1.0	0.6, 0.65, 0.85, 0.9	0.91, 0.94, 0.98, 0.99	None
	12	0.2, 0.24, 0.53, 0.78	0.5, 0.6, 0.9, 1.0	0.6, 0.62, 0.82, 0.9	0.91, 0.92, 0.98, 0.99	None
	13	0.2, 0.34, 0.43, 0.78	0.5, 0.7, 0.8, 1.0	0.6, 0.7, 0.8, 0.9	0.91, 0.95, 0.97, 0.99	Standard
	14	0.2, 0.34, 0.43, 0.78	0.5, 0.7, 0.8, 1.0	0.6, 0.65, 0.85, 0.9	0.91, 0.94, 0.98, 0.99	Standard
	15	0.2, 0.34, 0.43, 0.78	0.5, 0.7, 0.8, 1.0	0.6, 0.62, 0.82, 0.9	0.91, 0.92, 0.98, 0.99	Standard
	7	0.2, 0.30, 0.50, 0.78	0.5, 0.65, 0.85, 1.0	0.6, 0.7, 0.8, 0.9	0.91, 0.95, 0.97, 0.99	Standard
	8	0.2, 0.30, 0.50, 0.78	0.5, 0.65, 0.85, 1.0	0.6, 0.65, 0.85, 0.9	0.91, 0.94, 0.98, 0.99	Standard
	9	0.2, 0.30, 0.50, 0.78	0.5, 0.65, 0.85, 1.0	0.6, 0.62, 0.82, 0.9	0.91, 0.92, 0.98, 0.99	Standard
	10	0.2, 0.24, 0.53, 0.78	0.5, 0.6, 0.9, 1.0	0.6, 0.7, 0.8, 0.9	0.91, 0.95, 0.97, 0.99	Standard
	11	0.2, 0.24, 0.53, 0.78	0.5, 0.6, 0.9, 1.0	0.6, 0.65, 0.85, 0.9	0.91, 0.94, 0.98, 0.99	Standard
	12	0.2, 0.24, 0.53, 0.78	0.5, 0.6, 0.9, 1.0	0.6, 0.62, 0.82, 0.9	0.91, 0.92, 0.98, 0.99	Standard

* Trapezoidal distribution (minimum value, mode 1 value, mode 2 value, maximum value).
W_1: Selection probability for abortion related deaths
W_2: Selection probability for non-abortion related deaths
W_3: Sensitivity of cause of death classification
W_4: Specificity of cause of death classification
RE: Random Error

Table 2 Multiple bias analysis results for Study A: proportion of maternal deaths due to unsafe abortion adjusted for selection bias, misclassification, and random error, after 50,000 simulation trials per scenario.

Bias Model	Scenario (probability distribution/s)	Median	2.5, 97.5 percentiles	Ratio of limits
None (reported)	NA	0.206	0.206, 0.206	1.00
None (conventional, with estimate of precision)	NA	0.206	0.196, 0.316	1.61
Adjusted for misclassification only, no random error	1 (W_1&W_2 narrow)	0.369	0.248, 0.523	2.11
	2 (W_1&W_2 medium)	0.368	0.245, 0.530	2.16
	3 (W_1&W_2 wide)	0.372	0.242, 0.550	2.27
Adjusted for misclassification and selection bias, no random error	4 (W_1&W_2 narrow, W_3&W_4 narrow)	0.305	0.209, 0.431	2.06
	5 (W_1&W_2 narrow, W_3&W_4 medium)	0.308	0.210, 0.438	2.08
	6 (W_1&W_2 narrow, W_3&W_4 wide)	0.302	0.206, 0.432	2.10
	7 (W_1&W_2 medium, W_3&W_4 narrow)	0.305	0.207, 0.437	2.11
	8 (W_1&W_2 medium, W_3&W_4 medium)	0.306	0.207, 0.443	2.14
	9 (W_1&W_2 medium, W_3&W_4 wide)	0.302	0.204, 0.437	2.11
	10 (W_1&W_2 wide, W_3&W_4 narrow)	0.308	0.206, 0.452	2.19
	11 (W_1&W_2 wide, W_3&W_4 medium)	0.310	0.206, 0.458	2.22
	12 (W_1&W_2 wide, W_3&W_4 wide)	0.305	0.203, 0.452	1.96
Adjusted for misclassification and selection bias, random error included	13 (W_1&W_2 narrow, W_3&W_4 narrow)	0.307	0.175, 0.462	2.64
	14 (W_1&W_2 narrow, W_3&W_4 medium)	0.310	0.176, 0.469	2.66
	15 (W_1&W_2 narrow, W_3&W_4 wide)	0.304	0.173, 0.461	2.66
	16 (W_1&W_2 medium, W_3&W_4 narrow)	0.307	0.174, 0.467	2.68
	17 (W_1&W_2 medium, W_3&W_4 medium)	0.309	0.173, 0.473	2.78
	18 (W_1&W_2 medium, W_3&W_4 wide)	0.304	0.170, 0.466	2.74
	19 (W_1&W_2 wide, W_3&W_4 narrow)	0.311	0.173, 0.480	2.77
	20 (W_1&W_2 wide, W_3&W_4 medium)	0.313	0.172, 0.485	2.81
	21 (W_1&W_2 wide, W_3&W_4 wide)	0.308	0.169, 0.480	2.84

W_1: Selection probability for abortion related deaths
W_2: Selection probability for non-abortion related deaths
W_3: Sensitivity of cause of death classification
W_4: Specificity of cause of death classification

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