Measurement Error

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Plan of Presentation

(1) Introduction to Measurement Error and Concepts

(2) Correcting Prevalences

(3) Mismeasured Exposures:
- Correcting Risk Differences and Ratios
- Categorical Exposures
- Continuous Exposures: Correction & Regression Calibration

(4) Mismeasured Outcomes
- Non-Differential Misclassification: Cts Outcomes, RD's, RR's
- Differential Measurement Error: Binary Outcomes
- Differential Measurement Error: Continuous Outcomes

(5) Mismeasured Confounders

Measurement Error

Can arise from:

(1) Unintentional mis-reporting

(2) Intentional mis-reporting

(3) Technological imprecision

(4) Poor Construct Definition

(5) Transcription error

Measurement Error

Will Vary Depending on Nature of Exposure:

Less likely with: Age, sex, geographic region, marital status

More likely with: self-reported smoking per day, nutrient intake

Will Vary Depending on Outcome:

Less likely with: Death

More likely with: Psychiatric Diagnosis

Measurement Error

Has consequences for analysis:

(1) Estimates are biased

(2) Confidence intervals do not reflect uncertainty from measurement error

(3) Sample size and power calculations are too conservative

(4) Can lead to spurious detection of effect heterogeneity

Some Terminology

Measurement Error: Error in a continuous variable e.g. blood pressure

Misclassification: Error in a binary or categorical variable

Often “measurement error” is also used to describe both e.g. any error in the measurement of something

Measurement error may affect exposures, outcomes, confounders (or effect modifiers, mediators, etc.)

Validation Study: A study intended to obtain a more precise measurement (often a gold standard) of the variable under study

Internal validation study – a validation study with data obtained by sampling from the full study within which the parameter of interest is to be estimated.

External validation study – a validation study with data obtained from a separate population from the main study.

Reliability study: a study with several measurements of the error-prone variable

Some Terminology

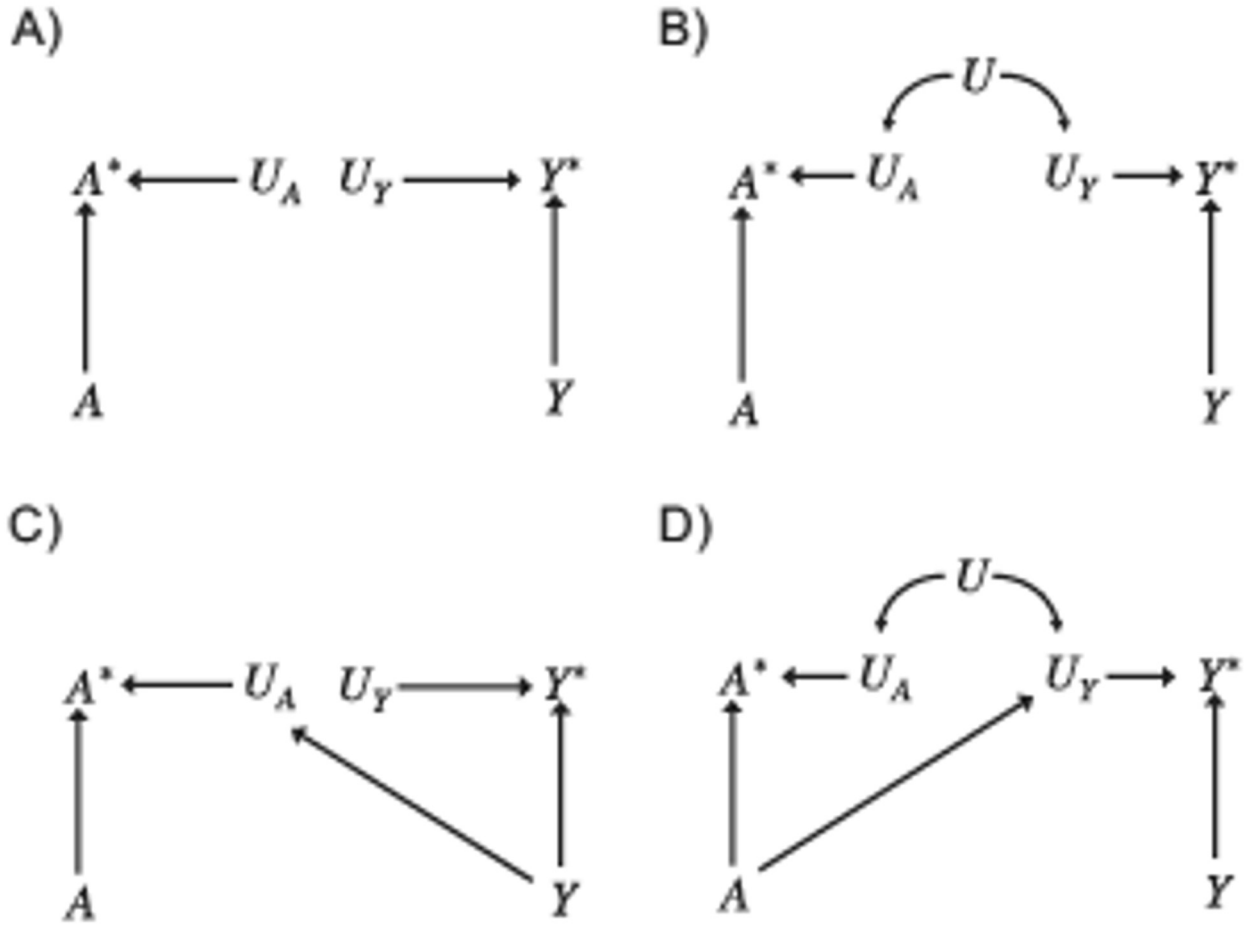
Suppose we have variable X with measurement X*

Non-Differential vs. Differential Measurement Error: We say that the measurement error of X is non-differential with respect to V if X* is independent of V conditional on X; otherwise it is differential (i.e. X* depends not just on X and random error but also on V)

Suppose we have two variables with measurement error e.g. X and Y with measurements X* and Y*

Independent vs. Dependent Error: We say that the measurement errors of X and Y are independent conditional on V if X* and Y* are independent conditional on (X,Y,V); otherwise they are dependent (i.e. correlation between the measurement errors)

Some Terminology



A) Independent non-differential
B) Dependent non-differential
C) Independent differential
D) Dependent differential

(cf. Hernan and Cole, 2009; VanderWeele and Hernan, 2012)

Major Approaches to Measurement Error

Three Broad Classes of Approaches for Measurement Error:

(1) Conservative Inference: Sometimes measurement error biases results towards the null and investigators appeal to these results arguing for conservative inferences

(2) Sensitivity Analysis: We can use sensitivity analysis to assess how strong measurement error would have to be to alter inferences

(3) Correction: We can use internal or external validation studies to try to assess the extent of measurement error and correct for it

Approaches 1 and 2 are often sufficient for evaluating evidence

Approach 3 is often important when more precise estimates are needed (e.g. assessing cost effectiveness)

Approaches 2 and 3 often use similar results but differ in sources of parameters and in standard errors

Sensitivity and Specificity

Se = Pr(X^* = 1|X = 1)

= sensitivity =probability that someone exposed is classified as exposed

Fn= probability that someone exposed is classified as unexposed

= false-negative probability = Pr(X^* = 0|X = 1) = 1 – Se

Sp= probability that someone unexposed is classified as unexposed

= specificity = Pr(X^* = 0|X = 0)

Fp= probability that someone unexposed is classified as exposed

= false-positive probability = Pr(X^* = 1|X = 0) = 1 – Sp

Positive and Negative Predictive Values

Positive Predictive Value (PPV): $\Pr(X=1|X^*=1)$

Negative Predictive Value (NPV): $\Pr(X=0|X^*=0)$

Let p_X be the prevalence of a X then:

$$\text{PPV} = \Pr(X=1|X^*=1) = \frac{\text{Se } p_X}{\text{Se } p_X + (1 - \text{Sp})(1 - p_X)}$$

$$\text{NPV} = \Pr(X=0|X^*=0) = \frac{\text{Sp } (1 - p_X)}{(1 - \text{Se}) p_X + \text{Sp } (1 - p_X)}$$

Correcting Prevalence

Suppose we have measured the prevalence of X* as p_{X^*}

Then the prevalence p_X of the true exposure X is given by:

$$p_X = (p_{X^*} - 1 + Sp) \,/\, (Se + Sp - 1)$$

$$Var(\hat{p}) \approx \frac{1}{\left(Se + Sp - 1\right)^2} \frac{p_{X^*}(1 - p_{X^*})}{n}$$

The variance assumes known Se and Sp

In general, sensitivity and specificity need to be obtained by a validation study in which we can measure the gold standard of the exposure

This could be considerably smaller than the primary sample measuring X^*_{12}

In this case, the variance is more complex

Correcting Risk Differences

Suppose we have mismeasured the exposure A as A* but we have not mismeasured the outcome Y

Our observed data is:

	A^*	1	0	
Y	1	A_1^*	A_0^*	M_1
	0	B_1^*	B_0^*	M_0
		N_1	N_0	

The cells themselves can be corrected using:

$A_1 = (A_1^* - Fp\ M_1) / (Se + Sp - 1)$

$A_0 = (A_0^* - Fn\ M_1) / (Se + Sp - 1)$

$B_1 = (B_1^* - Fp\ M_0) / (Se + Sp - 1)$

$B_0 = (B_0^* - Fn\ M_0) / (Se + Sp - 1)$

Correcting Risk Differences

Suppose we have mismeasured the exposure A as A* but we have not mismeasured the outcome Y

Our observed data is:

	A^*	1	0	
Y	1	A_1^*	A_0^*	M_1
	0	B_1^*	B_0^*	M_0
		N_1	N_0	

The observed risk difference is $A_1^*/N_1 - A_0^*/N_0$

To get a corrected risk difference we use:

$$\frac{(A_1^* - Fp\, M_1)}{(N_1 - Fp\,\{M_1+M_0\})} - \frac{(A_0^* - Fn\, M_1)}{(N_0 - Fn\,\{M_1+M_0\})}$$

Correcting Risk Differences

Consider data on heavy drinking and breast cancer (Willett et al., 1987):

	A^*	1	0	
Y	1	*162*	*439*	*601*
	0	16,817	*72,120*	*88,937*
		16,979	*72,559*	

Observed RD is $A_1^*/N_1 - A_0^*/N_0 = 0.00954 - 0.00605 = 0.00349$

If Se = 68.8% and Sp=92.8% (Willett et al., 1985) the corrected RD is:

$$\frac{(A_1^* - Fp\, M_1)}{(N_1 - Fp\,\{M_1+M_0\})} - \frac{(A_0^* - Fn\, M_1)}{(N_0 - Fn\,\{M_1+M_0\})}$$

$$= 0.0113 - 0.0056 = 0.00564$$

Similar procedures can be used for odds ratios, risk ratios, etc.

Exposure Misclassification

The *p*-value for the test for no exposure-response association preserves type I error (is conservative) when the exposure is binary and misclassification is non-differential

- Bross, I. (1954). Misclassification in 2x2 tables *Biometrics* 1954; 10:478-486

- Lagakos, S. W. (1988). Effects of mismodeling and mismeasuring explanatory variables on tests of their association with a response variable. *Stat Med* **7**, 257-274.

- Tosteson, T and Tsiatis, A. A. (1988). The asymptotic relative efficiency of score tests in a generalized linear model with surrogate covariates. *Biometrika* **75**, 507-514.

Exposure Misclassification

When the exposure is binary, misclassification biases estimates towards the null provided Se+Sp>1 (Lash et al. 2021)

Because of this, often measurement error of a binary exposure is ignored and it is argued that the measurement error is conservative

Note: sometimes bias towards the null is not “conservative” with respect to the conclusion being drawn; and can thus be problematic e.g. assessment of side effects

When the exposure is not binary, non-differential misclassification of the exposure can bias results away from the null (Dosemeci et al., 1990)

Measurement error cannot be ignored in these circumstances

With information on the different misclassification probabilities it is still possible to obtain corrected estimates using a procedure analogous to what was described above

Exposure Misclassification

Even with a non-binary exposure we can sometimes conclude that we have the direction of the effect correct

Weinberg et al. (1994): Under non-differential measurement error of exposure A, if E[Y|A] is increasing in A and E[A*|A] is increasing in A then sign{Cov(Y,A)}=sign{Cov(Y,A*)}

i.e. under these monotonicity assumptions (in expectation) we won't have effect reversal

We can reason about the sign of the effect

This can be generalized to some cases of differential and dependent measurement error (VanderWeele and Hernan, 2011)

Continuous Exposures

Suppose continuous exposure A is measured with non-differential error:

$$A^* = A + \varepsilon$$

And we fit either a linear or logistic regression model with the mis-measured exposure A*:

$$E[Y|A^*=a,C=c] = \theta_0 + \theta_1 a^* + \theta_2' c$$
$$\text{logit}[Y=1|A^*=a,C=c] = \theta_0 + \theta_1 a^* + \theta_2' c$$

We need one parameter to carry out the correction

$$\lambda = \text{Var}(A|C) / \text{Var}(A^*|C) = \text{Cor}(A,A^*)^2$$

i.e. the proportion of variance in A* that is explained by the true exposure A versus by error

This could be obtained in a validation study or by sensitivity analysis

Continuous Exposures

If we specify the parameter $\lambda = Var(A|C) / Var(A^*|C)$
then the relation between the regression coefficients with the true exposure

$$E[Y|A=a,C=c] = \beta_0 + \beta_1 a + \beta_2' c$$
$$\text{logit}[Y=1|A=a,C=c] = \beta_0 + \beta_1 a + \beta_2' c$$

And the misclassified exposure

$$E[Y|A^*=a,C=c] = \theta_0 + \theta_1 a^* + \theta_2' c$$
$$\text{logit}[Y=1|A^*=a,C=c] = \theta_0 + \theta_1 a^* + \theta_2' c$$

is given by: $\beta_1 = \theta_1 / \lambda$

Once again, bias is towards the null
If λ is known or specified in a sensitivity analysis we can apply this to the estimate and confidence interval; otherwise correction of the confidence interval is more complicated (e.g. Carroll et al., 2006)

See Additional Slides on correcting differential exposure measurement error

Regression Calibration

If we have a validation study with data on A and A* we can estimate the parameter $\lambda = Var(A|C) / Var(A^*|C)$ and divide the estimate by our estimate of λ (sometimes called “regression calibration”, Rosner et al., 1992)

We can also carry out correction more directly using another procedure also called “regression calibration” (Carroll et el., 2006):

1. Regress A on A* and C in the validation study
2. Estimate fitted values for A from this regression model based on data on A* and C in the main study
3. Regress Y on the fitted values, adjusting for C, to obtain a corrected estimate
4. Standard errors must be obtained through bootstrapping or other corrections

A similar procedure can be employed in logistic models or if data is available from a replication study (multiple measures of exposure subject to error)

Over-Correction

If we use data from a validation study to estimate $\lambda = Cor(A,A^*)^2$
or if we use regression calibration, this assumes that we have access to the actual measurement of A in the validation study i.e. a gold standard

If our actual measurement of A is not in fact the true exposure value A but just a more precise version, then regression calibration will "over-correct" the measurement error and inflate the estimate above the truth

Rather than using a "gold-standard" we would effectively be using an "alloyed gold standard" (Wacholder et al., 1993)

It is good to pose the question of how perfect the supposed "true" measurement is whenever validation studies are used for corrected estimate

DeVellis (2017) in the context of scale construction and reliability suggests not correcting based on reliability

[Note: if we use $\lambda = Var(A|C) / Var(A^*|C)$ with an "alloy" we will underestimate effects; with an "alloyed gold standard" we do not have $Var(A|C) / Var(A^*|C) = Cor(A,A^*)^2$]

Outcome Measurement Error

Mismeasured and Misclassified Outcomes

- Non-Differential Misclassification: Cts Outcomes, RD's, RR's
- Differential Measurement Error: Binary Outcomes
- Differential Measurement Error: Continuous Outcomes

Continuous Outcome Measurement Error

Suppose now that a continuous outcome Y is measured with non-differential measurement error such that $Y^* = Y + \varepsilon$

If we fit the regression model

$$E[Y^*|A=a,C=c] = \beta_0 + \beta_1 a + \beta_2' c$$

Our estimate of β_1 remains unbiased

We can ignore the measurement error in this case (it is essentially just incorporated into the error term of the regression model)

Outcome Misclassification: Risk Differences

Suppose now that the outcome is binary and non-differentially misclassified
Suppose sensitivity is Se and Specificity is Sp

Recall that if an outcome Y is misclassified we can obtain corrected prevalence by $p_y = (p_{y^*} - 1 + Sp) / (Se + Sp - 1)$

For a the risk difference of RD* with the observed data it is straightforward to obtain a corrected RD by the formula:

$RD = RD^* / (Se + Sp - 1)$

Sometimes this formula is written as: $RD = RD^* / (1 - Fn - Fp)$

The denominator will always be <= 1 so the division will increase the observed risk difference in magnitude
If Fn+Fp > 1 (severe error) we will get the direction of the effect wrong! But…
Provided Fn + Fp < 1, the observed risk difference is biased towards the null

Outcome Misclassification: Risk Ratios

Consider risk ratios now for a misclassified binary outcome
Recall $p_y = (p_{y^*} - 1 + Sp) / (Se + Sp - 1)$

Suppose the sensitivity and specificity are the same for the exposed and the unexposed (i.e. non-differential misclassification)

Let p_1 and p_0 denote the probability of the outcome with and w/o exposure
Then the corrected risk ratio is just:

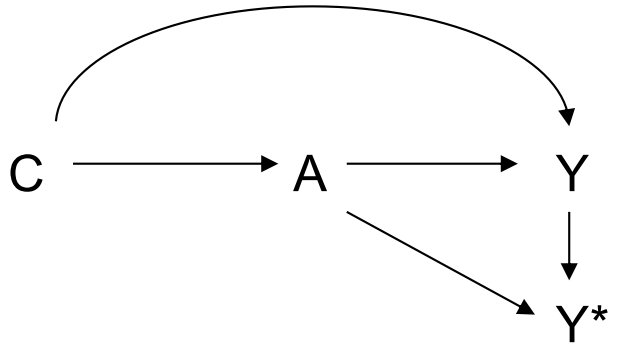
$$p_1/p_0 = (p_{1^*} - 1 + Sp) / (p_{0^*} - 1 + Sp)$$

The correction does not depend on sensitivity
If specificity is perfect Sp=1 (i.e. no detecting of disease when absent) then the risk ratio will always be unbiased even if sensitivity is imperfect
If specificity is imperfect we still get bias towards the null

Even under differential misclassification we can just apply the formula $p_y = (p_{y^*} - 1 + Sp) / (Se + Sp - 1)$ twice with different Se and Sp

Differential Measurement Error in a Binary Outcome

Consider differential misclassification of a binary outcome such that the measurement of the outcome depends on the exposure



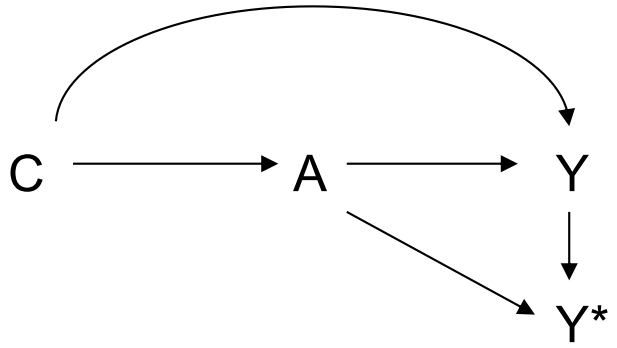
Let s_a=P(Y*=1|Y=1,A=a,C=c) be the sensitivity for Y when A=a
Let f_a=P(Y*=1|Y=0,A=a,C=c) be the false positive prob. when A=a (i.e.1-Sp)

Result (VanderWeele and Li, 2019 AJE): If $p_1/p_0 \geq 1$ then $p_1/p_0 \geq (p_1^*/p_0^*) / \max(s_1/s_0 , f_1/f_0)$; and if $p_1/p_0 \leq 1$ then $p_1/p_0 \leq (p_1^*/p_0^*) / \min(s_1/s_0 , f_1/f_0)$.

The term $\max(s_1/s_0 , f_1/f_0)$ is the maximum effect of A on Y* not through Y
To explain away a risk ratio of magnitude RR we need this to be at least as large as RR; this is an “E-value” for differential measurement error

Differential Measurement Error in a Continuous Outcome

Consider differential misclassification of a continuous outcome such that the measurement of the outcome depends on the exposure



We want: $E[Y|A=a,C=c] = \beta_0 + \beta_1 a + \beta_2' c$

We can estimate: $E[Y^*|A=a,C=c] = \theta_0 + \theta_1 a + \theta_2' c$

If we specify: $E[Y^*|A=a,Y=y,C=c] = \gamma_0 + \gamma_1 a + \gamma_2 y + \gamma_3' c$

Then: $\beta_1 = (\theta_1 - \gamma_1) / \gamma_2$

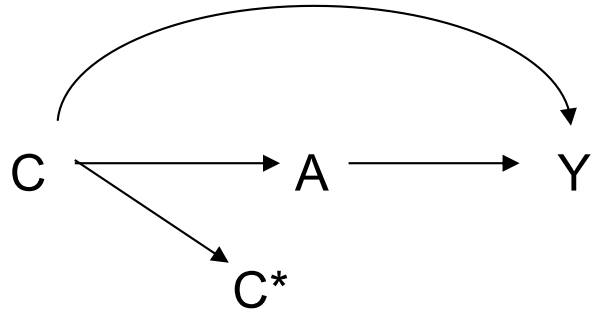
If $\gamma_2=1$ this is just $\beta_1 = (\theta_1 - \gamma_1)$ i.e. we subtract off the effect of A on Y* (conditional on Y i.e. not through Y) from our estimate

This can be done for continuous or binary exposures

Confounder Measurement Error

Our confounding variables may be measured with error

Similar issues arise if some variable C* is serving as a proxy for the true confounder C



We may be think that the variable C is a confounder but only have some error-prone measurement of it, C*

Should we control for such a variable?

Intuition suggests yes. Under what circumstances is this reasonable?

Confounder Measurement Error

Suppose we have one binary confounder subject to non-differential misclassification i.e. $P(C^*=c^*|C=c,A=a,Y=y) = P(C^*=c^*|C=c)$

Define the true effect on the risk difference scale as:

$RD_T = \sum_c \{E[Y|A=1,c] - E[Y|A=0,c]\}P(c) = E[Y_{a=1}] - E[Y_{a=0}]$

Define the observed adjusted effect as :

$RD_{obs} = \sum_c \{E[Y|A=1,c^*] - E[Y|A=0,c^*]\}P(c^*)$

Define the crude effect as: $RD_{cr} = E[Y|A=1] - E[Y|A=0]$

When will adjustment for a confounder subject to non-differential misclassification (the "observed adjusted" effect) be between the true effect and the crude?

In other words, will controlling for the mismeasured confounder or "proxy" confounder partially control for confounding bias?

Confounder Measurement Error

Results are available under additional monotonicity assumptions (Ogburn and VanderWeele, 2011)

Monotonicity: We say that the effect of C on Y is monotonic if E[Y|A=a,C=c] is either non-decreasing or non-increasing in c for both levels of a; we say that the effect of C on A is monotonic if E[A|C=c] is non-decreasing or non-increasing in c

Result 1 – Binary Confounder: If the effect of C on Y is monotonic then the partial control result holds if C is binary and subject to non-differential misclassification

Result 2 – Polytomous Confounder: If the effect of C on Y is monotonic and the effect of C on A is monotonic then the partial control result holds if C is polytomous and subject to non-differential misclassification; the result also holds if C is coarsened

Confounder Measurement Error

The issue arises when the effect of the true confounder C is in different directions for treated and control subjects

Example: If

- The exposure A is type 2 diabetes
- The outcome Y is hypertension
- The confounder C is the drug thiazide
- Thiazide will generally decrease hypertension, but it can exacerbate hypertension amongst those with type 2 diabetes

If the confounder C were obtained by self-report and thus subject to measurement error, control for the error-prone variable is not guaranteed to reduce bias

Confounder Measurement Error

Implications

Think carefully about whether the confounder may operate in different direction for the treated and control subjects

If so, controlling for a mis-measured confounder is not guaranteed to reduce bias

However, violations of the monotonicty conditions are necessary but not sufficient to violate the partial control result

Not all monotonicity violations will result in increased bias when controlling for a mismeasured variable

It may still be better to condition in practice even if monotonicity is violated but conclusions are less definitive

Measurement error of confounders will only partially adjust for confounding; we can also treat this as unmeasured confounding (previous lecture); see also additional slides for continuous mismeasured confounders

Confounder Measurement Error

This issue has a long history in the epidemiologic literature

Greenland (1980) argued that for a binary confounder subject to non-differential misclassification the "observed adjusted" effect would always lie in between the true effect and the crude

Fung and Howe (1984) presented evidence from simulations arguing that the partial control result holds for non-differentially mismeasured polytomous confounders

However, Brenner (1992) set the record straight by showing by counterexample that it need not hold with polytomous confounders, and contrasting this failure with the binary case

Subsequently, a number of methodological and applied papers reference the partial control result

It is included in most textbooks on epidemiologic methods

However, counter-examples can even arise with a binary confounder (Ogburn and VanderWeele, 2011; cf Appendix Slides)

Conclusions

(1) Measurement error and misclassification is common; if it is almost everywhere, can conclusions be drawn?

(2) Often non-differential measurement error of the outcome will be unbiased or biased towards the null

(3) Often non-differential measurement error of the exposure will be biased towards the null, but care is needed for categorical exposures

(4) It is often preferable to include misclassified confounders to nothing

(5) With differential misclassification we really need sensitivity analysis

(6) When biases towards the null are problematic (e.g. side effects) we need sensitivity analysis or validation studies

(7) When precise estimates are needed (e.g. cost effectiveness) we need validation studies

Additional Slides

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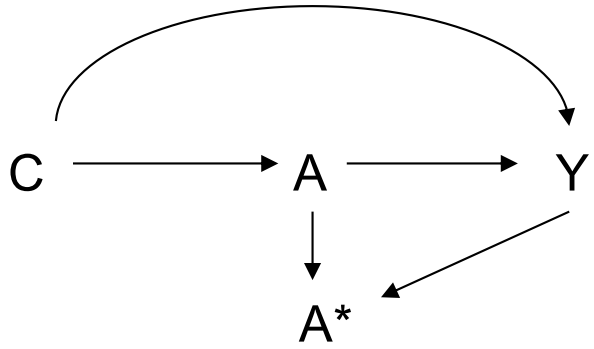
Differential Measurement Error of a Continuous Exposure

Consider differential measurement error of a continuous exposure when the outcome affects the exposure measurement (VanderWeele and Li, 2019)



Consider a linear regression model or logistic with a rare outcome

$$E[Y|A=a,C=c] = \beta_0 + \beta_1 a + \beta_2' c$$
$$\text{logit}[Y=1|A=a,C=c] = \beta_0 + \beta_1 a + \beta_2' c$$

Suppose further that: $E[A^*|A,Y,C] = \gamma_0 + a + \gamma_1 y + \gamma_2' c$

and let $\lambda = Var(A|C) / Var(A^*|C,Y)$

[If σ_u^2 is the error variance in this regression and σ_a^2 is the variance for A conditional on C then let $\lambda = \sigma_a^2 / (\sigma_a^2 + \sigma_u^2)$

Differential Measurement Error of a Continuous Exposure

Suppose further that: $E[A^*|A,Y,C] = \gamma_0 + a + \gamma_1 y + \gamma_2' c$

and let $\lambda = Var(A|C) / Var(A^*|C,Y)$

[If σ_u^2 is the error variance in this regression and σ_a^2 is the variance for A conditional on C then let $\lambda = \sigma_a^2 / (\sigma_a^2 + \sigma_u^2)$

The relations between:

$$E[Y|A=a,C=c] = \beta_0 + \beta_1 a + \beta_2' c$$

$$\text{logit}[Y=1|A=a,C=c] = \beta_0 + \beta_1 a + \beta_2' c$$

And:

$$E[Y|A^*=a,C=c] = \theta_0 + \theta_1 a^* + \theta_2' c$$

$$\text{logit}[Y=1|A^*=a,C=c] = \theta_0 + \theta_1 a^* + \theta_2' c$$

are given by: $\beta_1 = [\theta_1 - \gamma_1/(\sigma_a^2 + \sigma_u^2)] / \lambda$

Before scaling by $1/\lambda$ we essentially subtract off the effect of Y on A*

The effect we subtract off $\gamma_1/(\sigma_a^2 + \sigma_u^2)$ is standard deviations of A* (conditional on Y,C)

Cf. VanderWeele and Li (2019) for a binary exposure with differential misclassification

Outcome Misclassification: Logistic Regression

Consider non-differential misclassification for a binary outcome in a logistic regression model

$$\text{logit}[Y^*=1|A=a,C=c] = \theta_0 + \theta_1 a + \theta_2' c$$

The coefficient θ_1 will not be unbiased as with linear regression

One can instead weight the logistic regression using the positive and negative predictive values calculated from the sensitivity and specifity which can be taken as sensitivity analysis parameters (Lin and Lyles, 2010)

$$PPV = Pr(Y=1|Y^*=1) = \frac{Se\ p_y}{Se\ p_y + (1 - Sp)(1 - p_y)}$$

$$NPV = Pr(Y=0|Y^*=0) = \frac{Sp\ (1- p_y)}{(1 - Se)\ p_y + Sp\ (1 - p_y)}$$

Outcome Misclassification: Logistic Regression

Those who have Y*=1 get PPV copies of Y=1 and (1-PPV) copies of Y=0
Those who have Y*=0 get (1-NPV) copies of Y=1 and NPV copies of Y=0

With covariates this becomes somewhat more complex if what is specified is sensitivity or specificity, as then PPV and NPV have to be estimated based on the covariates (even if sensitivity and specificity are independent of the covariates):

$$PPV = Pr(Y=1|Y^*=1,C) = \frac{Se\ p_{y|c}}{Se\ p_{y|c} + (1 - Sp)\ (1 - p_{y|c})}$$

This can be done but is computationally more involved

The approach can also accommodate differential misclassification as different sensitivity and specificity can be given for exposed and unexposed

An alternative approach involves an approximation and iteratively re-weighted least squares (Neuhaus, 1999)

Confounder Measurement Error

Stated in its unqualified form, the partial control result, even for binary confounders, does not always hold

Counterexamples are possible (Ogburn and VanderWeele, 2011)

Crude

	$A=1$	$A=0$
$Y=1$	530	200
$Y=0$	100	170

RD_{crude}	0.301
RR_{crude}	1.556
OR_{crude}	4.505

True

$C=1$	$A=1$	$A=0$
$Y=1$	390	10
$Y=0$	10	20

$C=0$	$A=1$	$A=0$
$Y=1$	140	190
$Y=0$	90	150

RD_{true}	0.304
RR_{true}	1.659
OR_{true}	3.819

Sensitivity $=1$, Specificity $=.9$

Observed

$C'=1$	$A=1$	$A=0$
$Y=1$	404	29
$Y=0$	19	35

$C'=0$	$A=1$	$A=0$
$Y=1$	126	171
$Y=0$	81	135

RD_{obs}	0.270
RR_{obs}	1.532
OR_{obs}	3.391

Confounder Measurement Error

Suppose one continuous confounder X is measured with non-differential error:

$$X^* = X + \varepsilon$$

And we fit either a linear regression model with the mis-measured covariate X* and also regress X* on A and C

$$E[Y|A=a,X^*=x^*,C=c] = \theta_0 + \theta_1 a + \theta_2 x^* + \theta_3' c$$
$$E[X^*|A=a,C=c] = \beta_0 + \beta_1 a + \beta_2' c$$

We only need one parameter to carry out the correction

$$\lambda = Var(X|A,C) / Var(X^*|A,C)$$

i.e. the proportion of variance in X* that is explained by the true covariate X versus by error

This could be obtained in a validation study or by sensitivity analysis

Confounder Measurement Error

If we specify the parameter $\lambda = Var(X|A,C) / Var(X^*|A,C)$ and fit models:

$E[Y|A=a,X^*=x^*,C=c] = \theta_0 + \theta_1 a + \theta_2 x^* + \theta_3' c$

$E[X^*|A=a,C=c] = \beta_0 + \beta_1 a + \beta_2' c$

we have that the true coefficients expressed in terms of the mismeasured (denote with the tilda "~") are given by (Carroll et al., 2006):

$$\theta_1 = \tilde{\theta}_1 - \tilde{\theta}_2\left(\frac{1}{\lambda} - 1\right)\beta_1$$

$$\theta_2 = \frac{\tilde{\theta}_2}{\lambda}.$$

The corrected exposure coefficient depends both on the error in measurement X* and on the association between X* and A

The same results hold for logistic regression (rather than linear) for rare Y

Corrected standard errors can be obtained by bootstrapping or the multivariate delta method (Carroll et al., 2006)