Quantitative bias analysis

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Quantitative bias analysis

Objective: To quantify the magnitude and direction of systematic error (bias)

Quantitative bias analysis

Quantify bias from systematic error

- Confounding
- Selection bias
- Misclassification

Quantitative bias analysis

Quantify bias from systematic error

- Confounding
- Selection bias
- Misclassification

Reviewer #2

‘The authors failed to take into account confounding by _____

Quantitative bias analysis

1. Given confounding by an unmeasured variable, what effect estimate would remain if we were able to adjust for this confounder?

Point estimate with bias →
Point estimate taking into account bias

Quantitative bias analysis

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2. How strong would an unknown confounder have to be to fully explain the observed effect?

Quantitative bias analysis

1. Simple bias analysis
2. Probabilistic bias analysis

Quantitative bias analysis

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2. Probabilistic bias analysis

1. Given confounding by an unmeasured variable, what effect estimate would remain if we were able to adjust for this confounder?

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$$\mathrm{ARR} = \mathrm{RR} \times \frac{P_{C1}(\mathrm{RR}_{CD} - 1) + 1}{P_{C0}(\mathrm{RR}_{CD} - 1) + 1}$$

P_{C_1}: Prevalence of confounder among exposed
P_{C_0}: Prevalence of confounder among unexposed
RR_{CD}: Relative risk of confounder associated with outcome

Schneeweiss S. Sensitivity analysis and external adjustment for unmeasured confounders in epidemiologic database studies of therapeutics. *Pharmacoepidemiology & Drug Safety* 2006 May. 15(5):291-303. (.pdf format)

$$RR = \frac{ARR}{\left[\frac{P_{C1}(RR_{CD}-1)+1}{P_{C0}(RR_{CD}-1)+1}\right]}$$

P_{C_1}: Prevalence of confounder among exposed
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RR_{CD}: Relative risk of confounder associated with outcome

$$RR = \frac{ARR}{\left[\frac{P_{C1}(RR_{CD}-1)+1}{P_{C0}(RR_{CD}-1)+1}\right]}$$

P_{C1}
P_{C0}
RR_{CD}

Bias parameters

Example

Does male circumcision protect against HIV infection?

Possible confounder: Being Muslim

RR not adjusted for religion: 0.35 (95% CI 0.28 to 0.44)

Tyndall et al., 1996

$$RR = \frac{ARR}{\left[\frac{P_{C1}(RR_{CD}-1)+1}{P_{C0}(RR_{CD}-1)+1}\right]}$$

P_{C1}
P_{C0}
RR_{CD}

Bias parameters


Somalia
Uganda
Kenya
Nairobi
Rwanda
Burundi
Tanzania

$$RR = \frac{ARR}{\left[\frac{P_{C1}(RR_{CD}-1)+1}{P_{C0}(RR_{CD}-1)+1}\right]}$$

P_{C1} **0.8**

P_{Co} **0.1**

RR_{CD} **0.65**

$$RR = \frac{0.35}{\frac{0.8(0.65-1)+1}{0.1(0.65-1)+1}} = 0.47$$

http://www.drugepi.org/dope-downloads

Sensitivity Analysis

- Sensitivity Analysis of Confounding 2018 (.xls format)
- Schneeweiss S. Sensitivity analysis and external adjustment for unmeasured confounders in epidemiologic database studies of therapeutics. *Pharmacoepidemiology & Drug Safety* 2006 May. 15(5):291-303. (.pdf format)

AutoSave Off | Sensi.Ana_.Confounding.Jun2018.xlsx - Saved

File | Home | SDU | Insert | Page Layout | Formulas | Data | Review | View | Developer | Help | Tell me what you want to do

Templafy | Paste | Cut | Copy | Format Painter | Arial | 10 | Wrap Text | Merge & Center | General | Conditional Formatting | Format as Table | Normal | Bad | Good | Neutral | Check Cell | Explanatory ... | Followed Hyp... | Hyperlink

Templafy | Clipboard | Font | Alignment | Number | Styles

V30

2. Array approach

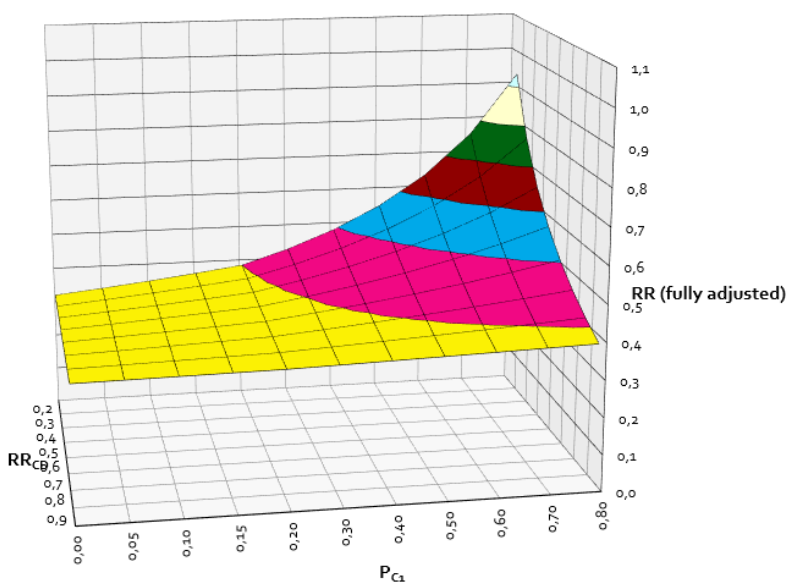
Example: HIV infection and religion

$$RR_{adj} = \frac{ARR}{\frac{P_{C1}(RR_{CD}-1)+1}{P_{C0}(RR_{CD}-1)+1}}$$

% Bias = [(ARR-RRadj.)/RRadj.]*100

	A	B	C	D	E	F
4	fix	X	Y	fix	Z2	Z1
5	ARR	RR_{CD}	P_{C1}	P_{C0}	$RR_{adjusted}$	% Bias
6	0,35	0,2	0,00	0,050	0,34	4,17
7	0,35	0,3	0,00	0,050	0,34	3,63
8	0,35	0,4	0,00	0,050	0,34	3,09
9	0,35	0,5	0,00	0,050	0,34	2,56
10	0,35	0,6	0,00	0,050	0,34	2,04
11	0,35	0,7	0,00	0,050	0,34	1,52
12	0,35	0,8	0,00	0,050	0,35	1,01
13	0,35	0,9	0,00	0,050	0,35	0,50
14	0,35	1,0	0,00	0,050	0,35	0,00
15	0,35	1,1	0,00	0,050	0,35	-0,50
16	0,35	0,2	0,05	0,050	0,35	0,00
17	0,35	0,3	0,05	0,050	0,35	0,00
18	0,35	0,4	0,05	0,050	0,35	0,00
19	0,35	0,5	0,05	0,050	0,35	0,00
20	0,35	0,6	0,05	0,050	0,35	0,00
21	0,35	0,7	0,05	0,050	0,35	0,00
22	0,35	0,8	0,05	0,050	0,35	0,00
23	0,35	0,9	0,05	0,050	0,35	0,00
24	0,35	1,0	0,05	0,050	0,35	0,00
25	0,35	1,1	0,05	0,050	0,35	0,00
26	0,35	0,2	0,10	0,050	0,37	-4,17
27	0,35	0,3	0,10	0,050	0,36	-3,63
28	0,35	0,4	0,10	0,050	0,36	-3,09
29	0,35	0,5	0,10	0,050	0,36	-2,56
30	0,35	0,6	0,10	0,050	0,36	-2,04
31	0,35	0,7	0,10	0,050	0,36	-1,52
32	0,35	0,8	0,10	0,050	0,35	-1,01
33	0,35	0,9	0,10	0,050	0,35	-0,50
34	0,35	1,0	0,10	0,050	0,35	0,00
35	0,35	1,1	0,10	0,050	0,35	0,50
36	0,35	0,2	0,15	0,050	0,38	-8,33
37	0,35	0,3	0,15	0,050	0,38	-7,25
38	0,35	0,4	0,15	0,050	0,37	-6,19
39	0,35	0,5	0,15	0,050	0,37	-5,13
40	0,35	0,6	0,15	0,050	0,36	-4,08
41	0,35	0,7	0,15	0,050	0,36	-3,05
42	0,35	0,8	0,15	0,050	0,36	-2,02
43	0,35	0,9	0,15	0,050	0,35	-1,01
44	0,35	1,0	0,15	0,050	0,35	0,00
45	0,35	1,1	0,15	0,050	0,35	1,00

ARR = 0.35
P_{C0} = 0.05



ARR = 0.35

Start | Notation | Array; TNFa | Array; COX2 | Rule Out; CCB | Rule Out; Zolpidem | External adjust; COX-2 | Internal Adjust Linagliptin

Ready

B6 | fx | 0.2

2. Array approach

Example: HIV infection and religion

$$RR_{adj.} = \frac{ARR}{\left[\frac{P_{C1}(RR_{CD}-1)+1}{P_{C0}(RR_{CD}-1)+1}\right]}$$

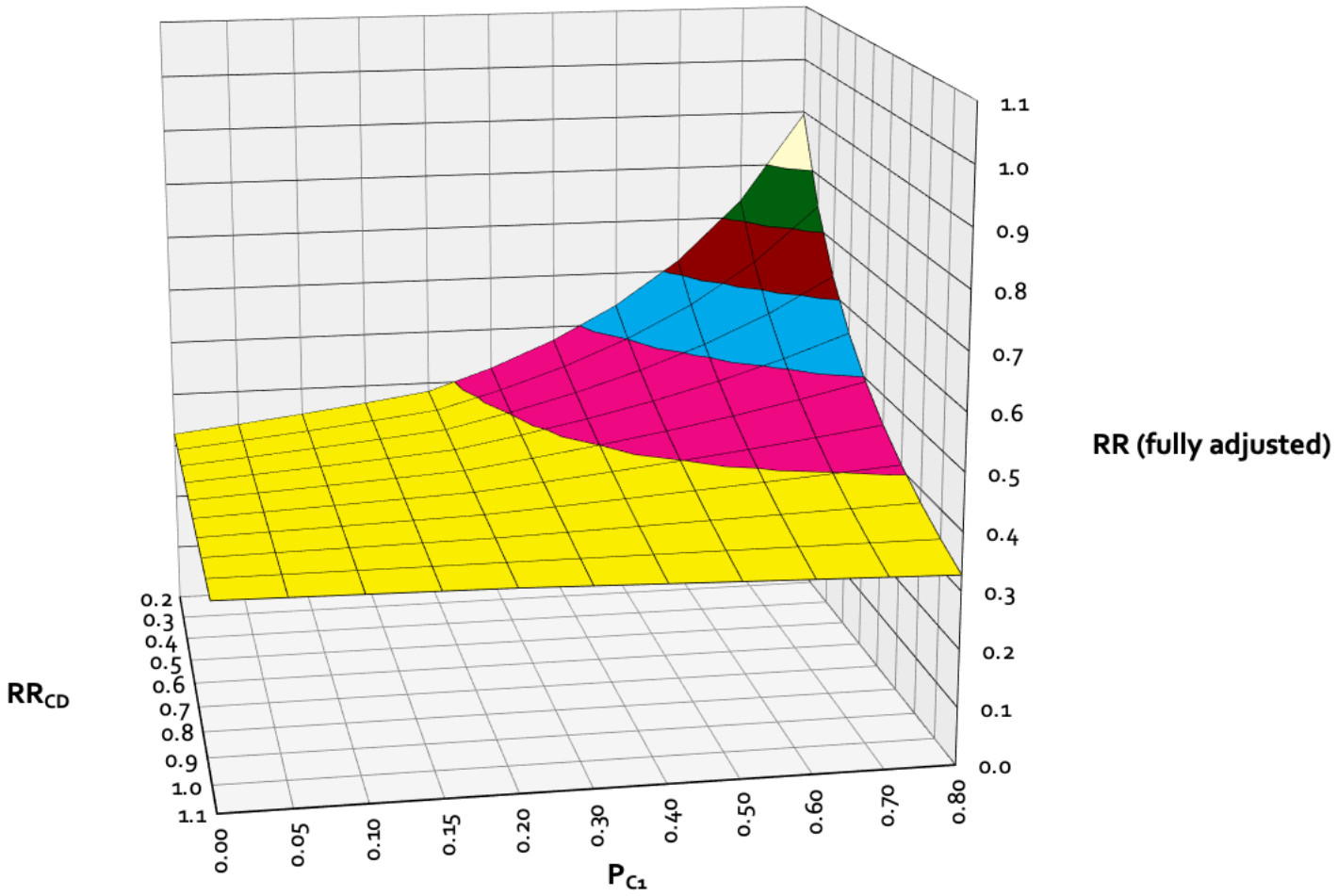
	A	B	C	D	E	F
4	fix	X	Y	fix	Z2	Z1
5	ARR	RR_{CD}	P_{C1}	P_{C0}	$RR_{adjusted}$	% Bias
6	0.35	0.2	0.00	0.100	0.32	8.70
7	0.35	0.3	0.00	0.100	0.33	7.53
8	0.35	0.4	0.00	0.100	0.33	6.38
9	0.35	0.5	0.00	0.100	0.33	5.26
10	0.35	0.6	0.00	0.100	0.34	4.17
11	0.35	0.7	0.00	0.100	0.34	3.09
12	0.35	0.8	0.00	0.100	0.34	2.04
13	0.35	0.9	0.00	0.100	0.35	1.01
14	0.35	1.0	0.00	0.100	0.35	0.00
15	0.35	1.1	0.00	0.100	0.35	-0.99
16	0.35	0.2	0.05	0.100	0.34	4.35
17	0.35	0.3	0.05	0.100	0.34	3.76
18	0.35	0.4	0.05	0.100	0.34	3.19
19	0.35	0.5	0.05	0.100	0.34	2.63
20	0.35	0.6	0.05	0.100	0.34	2.08
21	0.35	0.7	0.05	0.100	0.34	1.55
22	0.35	0.8	0.05	0.100	0.35	1.02
23	0.35	0.9	0.05	0.100	0.35	0.51
24	0.35	1.0	0.05	0.100	0.35	0.00
25	0.35	1.1	0.05	0.100	0.35	-0.50
26	0.35	0.2	0.10	0.100	0.35	0.00

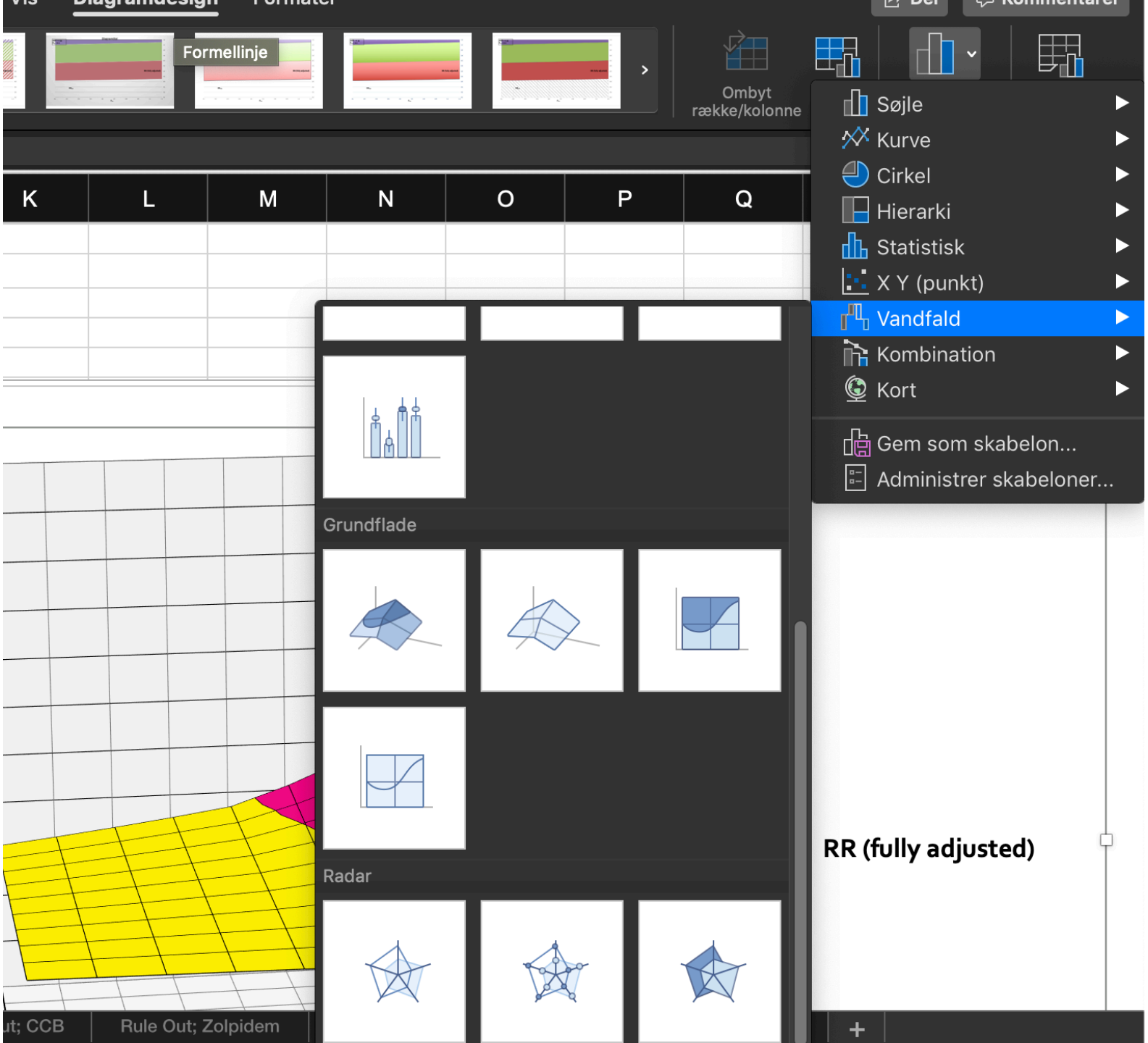
% Bias = [(ARR-RRadj.)/RRadj.]*100

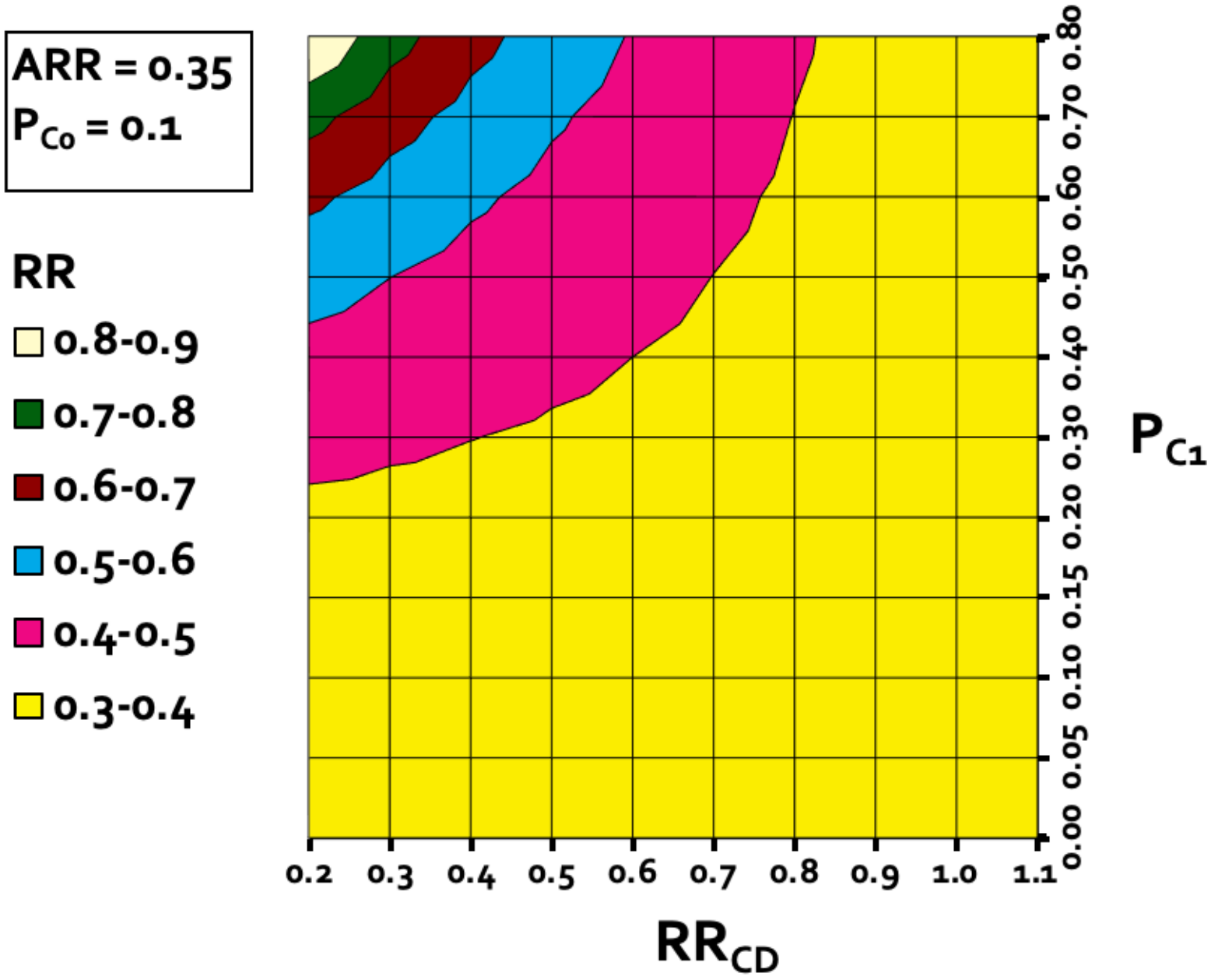
ARR = 0.35
P_{Co} = 0.1

Start | Notation | Array; TNFa | Array; COX2 | Rule Out; CCB | Rule Out; Zolpidem | External adjus

ARR = 0.35
P_{C0} = 0.1




Diagramdesign
Formellinje
Ombyt række/kolonne
Søjle
Kurve
Cirkel
Hierarki
Statistisk
X Y (punkt)
Vandfald
Kombination
Kort
Gem som skabelon...
Administrer skabeloner...
Grundflade
Radar
K
L
M
N
O
P
Q
RR (fully adjusted)
Rule Out; Zolpidem


ARR = 0.35
P_{Co} = 0.1
RR
0.8-0.9
0.7-0.8
0.6-0.7
0.5-0.6
0.4-0.5
0.3-0.4
0.00 0.05 0.10 0.15 0.20 0.30 0.40 0.50 0.60 0.70 0.80
P_{C1}
0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0 1.1
RR_{CD}

1. Given confounding by an unmeasured variable, what effect estimate would remain if we were able to adjust for this confounder?

2. How strong would an unknown confounder have to be to fully explain the observed effect?

2. How strong would an unknown confounder have to be in order to fully explain the observed effect?

RR_{CD}

RR_{EC}

Bias parameters

Example

How strong would confounding be to explain the effect of smoking on lung cancer?

RR 10.73, 95% CI 8.02 to 14.36

The E-value is the minimum strength of association on the relative risk scale that a confounder would need to have with both the treatment and outcome to explain away the observed association

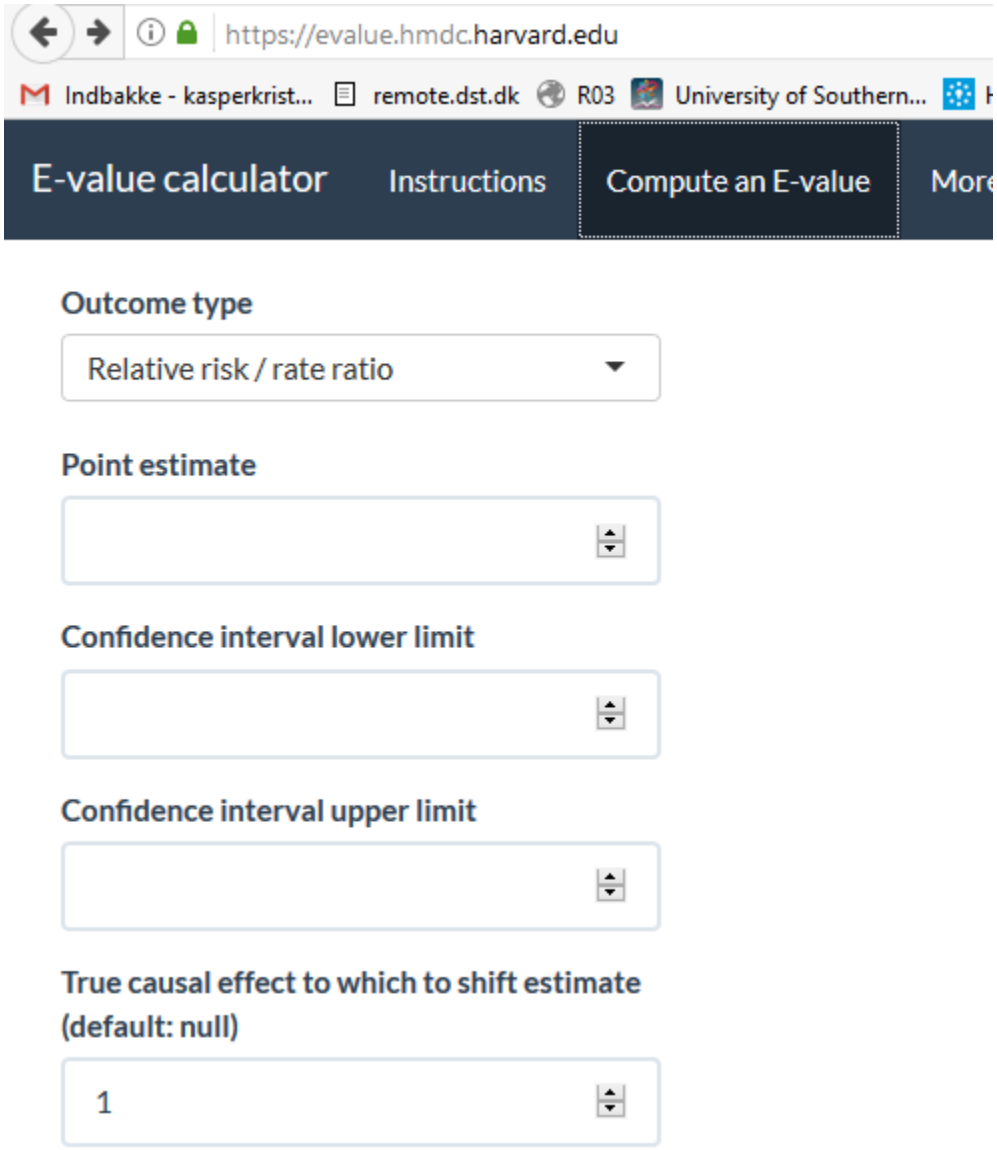
E-value calculations are straightforward. For an observed risk ratio of *RR*:

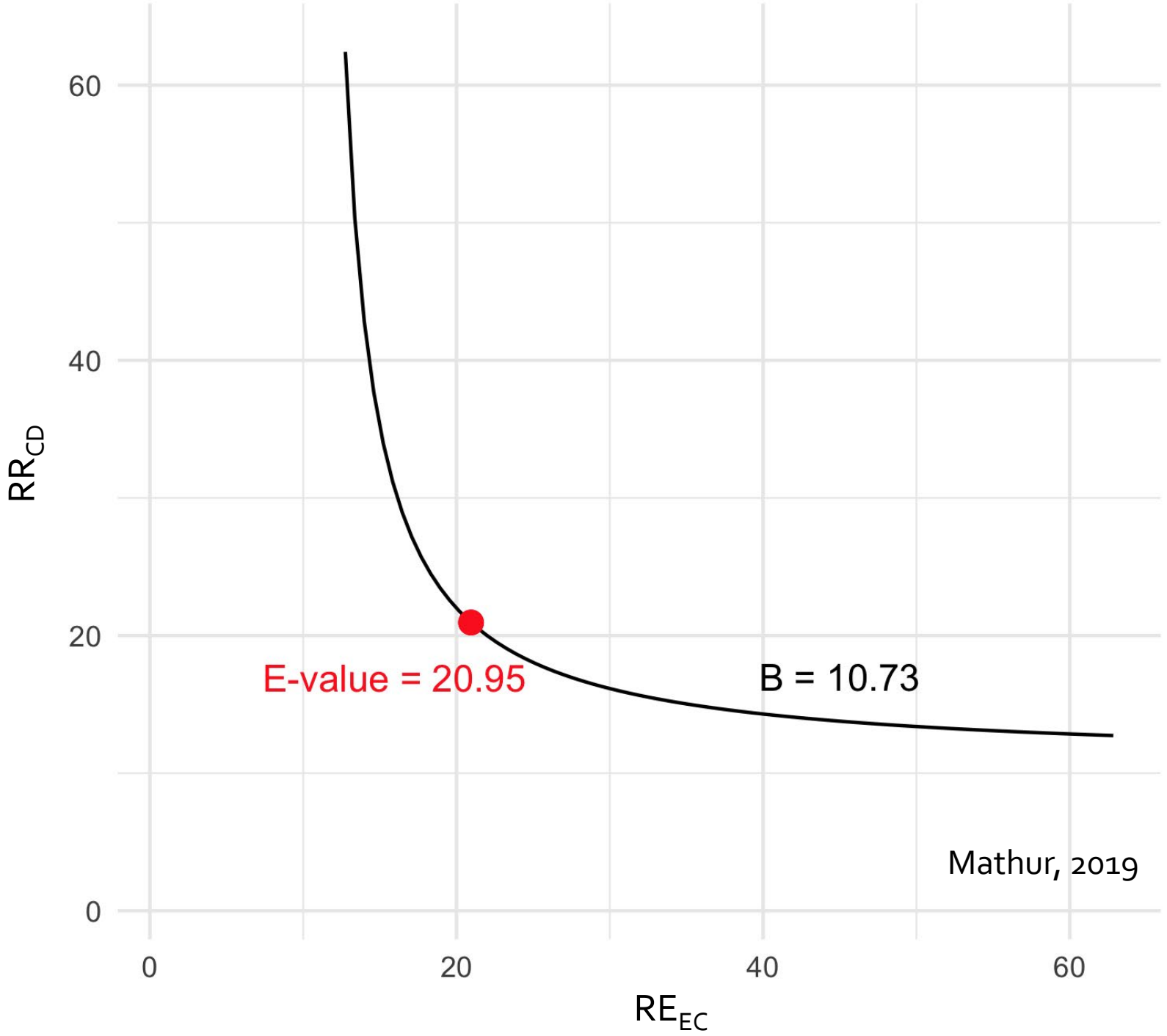
$$\text{E-value} = RR + \text{sqrt}\{RR \times (RR - 1)\}.$$

The proof appears elsewhere (37). The formula applies to a risk ratio greater than 1; for a risk ratio less than 1, one first takes the inverse of the observed risk ratio and then applies the formula.

VanderWeele and Ding, 2017

https://evalue.hmdc.harvard.edu/




60
40
20
0
RR_{CD}
E-value = 20.95
B = 10.73
Mathur, 2019
0
20
40
60
RE_{EC}

Hydrochlorothiazide use and risk of nonmelanoma skin cancer: A nationwide case-control study from Denmark

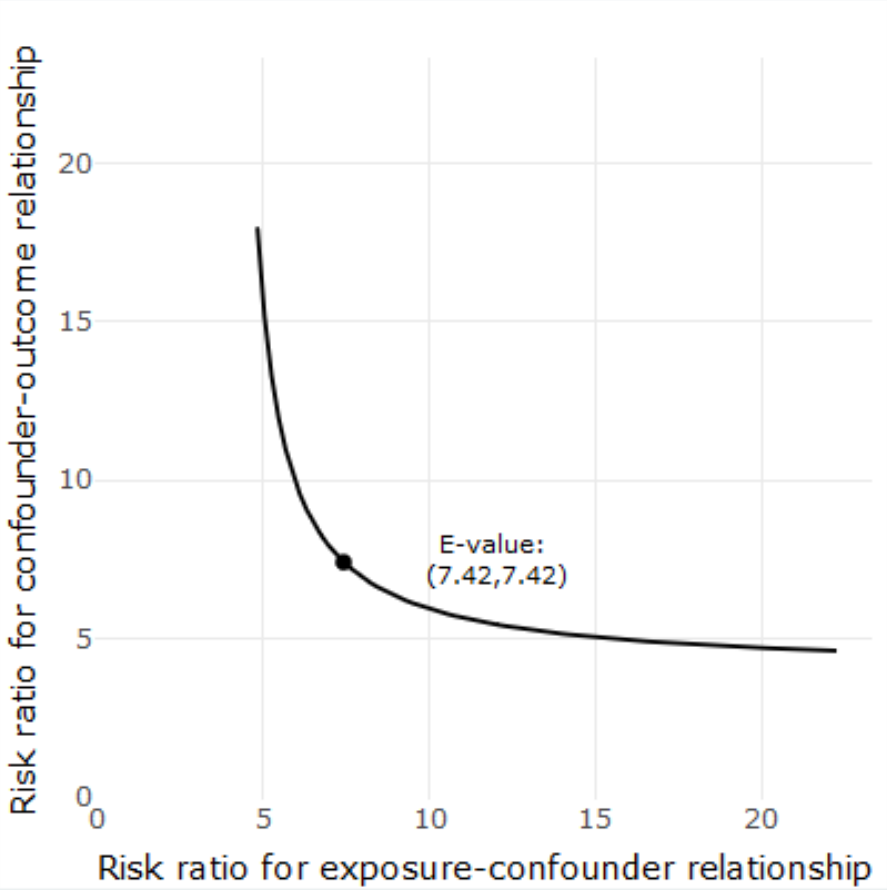
Sidsel Arnspang Pedersen, MD,[a,b,c] David Gaist, PhD,[a,b] Sigrun Alba Johannesdottir Schmidt, PhD,[d] Lisbet Rosenkrantz Hölmich, DMSc,[e] Søren Friis, MD,[d,f,g] and Anton Pottegård, PhD[c]
Odense, Aarhus, Herlev, and Copenhagen, Denmark

Background: Hydrochlorothiazide, one of the most frequently used diuretic and antihypertensive drugs in the United States and Western Europe, is photosensitizing and has previously been linked to lip cancer.

Objective: To examine the association between hydrochlorothiazide use and the risk of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC).

Methods: From the Danish Cancer Registry, we identified patients (cases) with nonmelanoma skin cancer (NMSC) during 2004-2012. Controls were matched 1:20 by age and sex. Cumulative hydrochlorothiazide use (in 1995-2012) was assessed from the Danish Prescription Registry. Using conditional logistic regression, we calculated odds ratios (ORs) for BCC and SCC associated with hydrochlorothiazide use.

Results: High use of hydrochlorothiazide (≥50,000 mg) was associated with ORs of 1.29 (95% confidence interval [CI], 1.23-1.35) for BCC and 3.98 (95% CI, 3.68-4.31) for SCC. We found clear dose-response relationships between hydrochlorothiazide use and both BCC and SCC; the highest cumulative dose category (≥200,000 mg of HCTZ) had ORs of 1.54 (95% CI, 1.38-1.71) and 7.38 (95% CI, 6.32-8.60) for BCC and SCC, respectively. Use of other diuretics and antihypertensives was not associated with NMSC.



E-value for point estimate: 7.4

E-value for lower limit of CI: 6.8

’The observed risk ratio could be explained away by an unmeasured confounder that was associated with both hydrochlorothiazide and skin cancer by a risk ratio of 7.4-fold each.
The confidence interval could be moved to the null by an unmeasured confounder associated with both hydrochlorothiazide and skin cancer by a risk-ratio of 6.8-fold’

Quantitative bias analysis

1. Simple bias analysis
2. Probabilistic bias analysis

1. Given confounding by an unmeasured variable, what effect estimate would remain if we were able to adjust for this confounder?

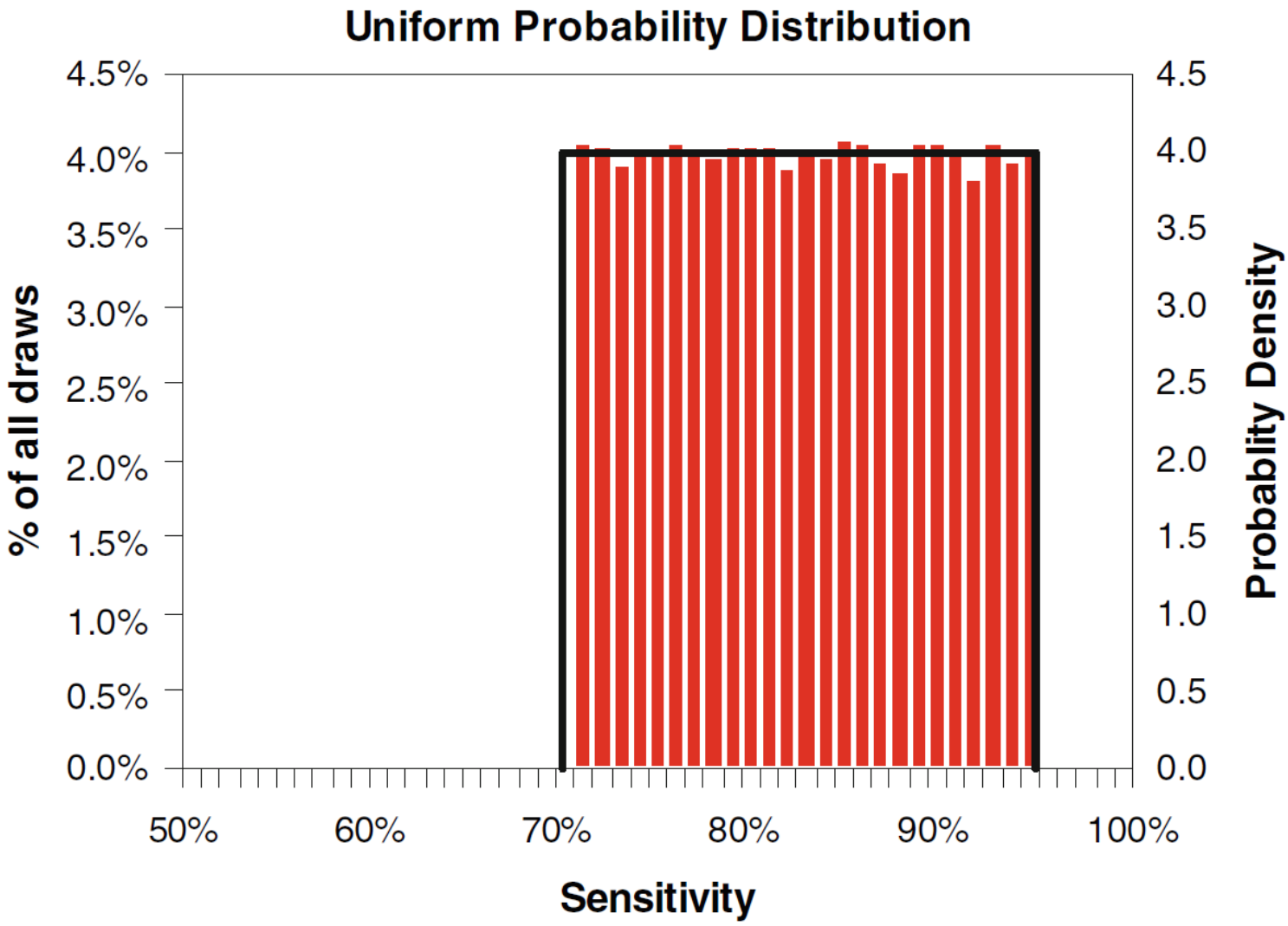
2. How strong would an unknown confounder have to be to fully explain the observed effect?

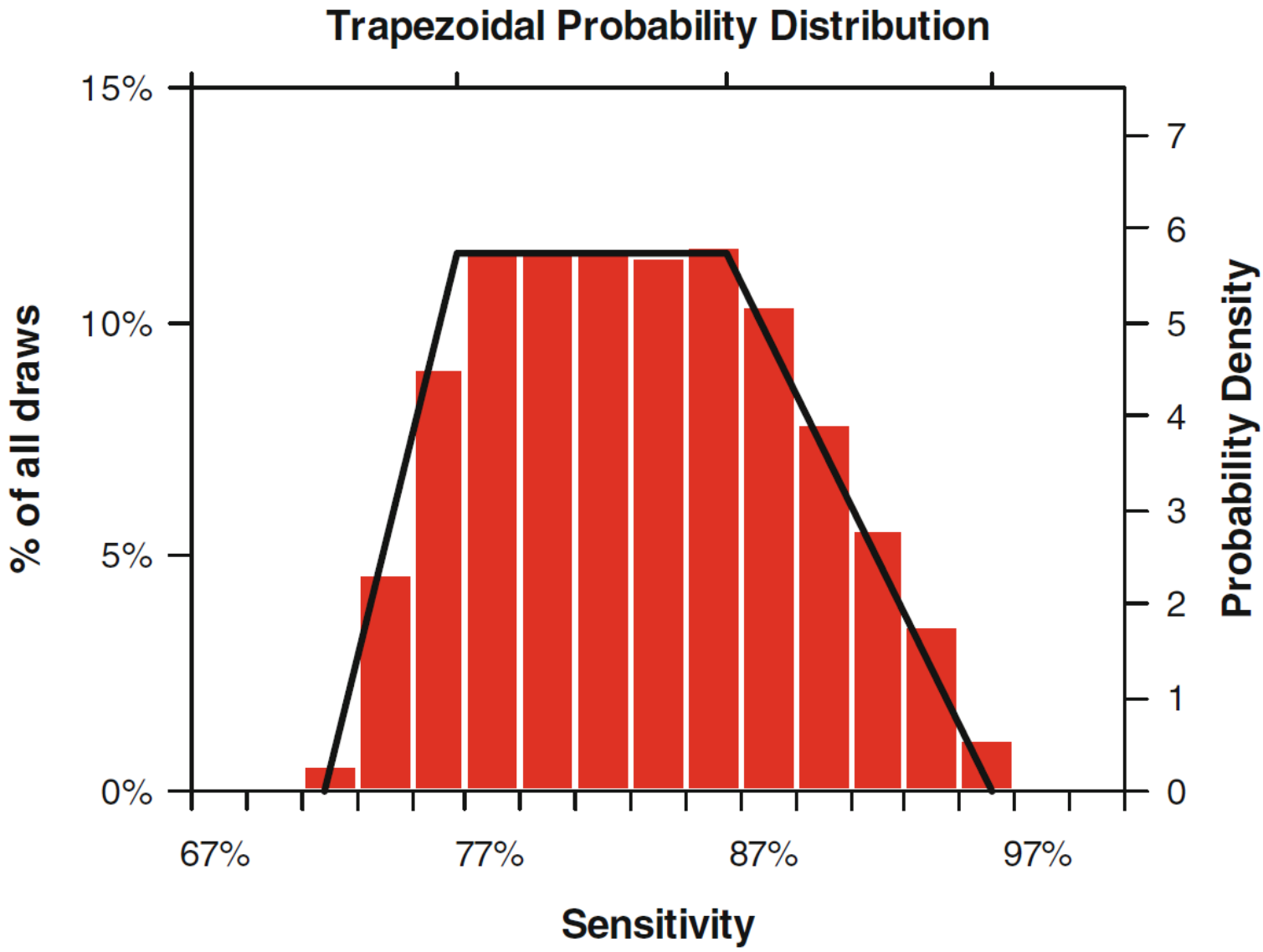
~~Bias parameters~~

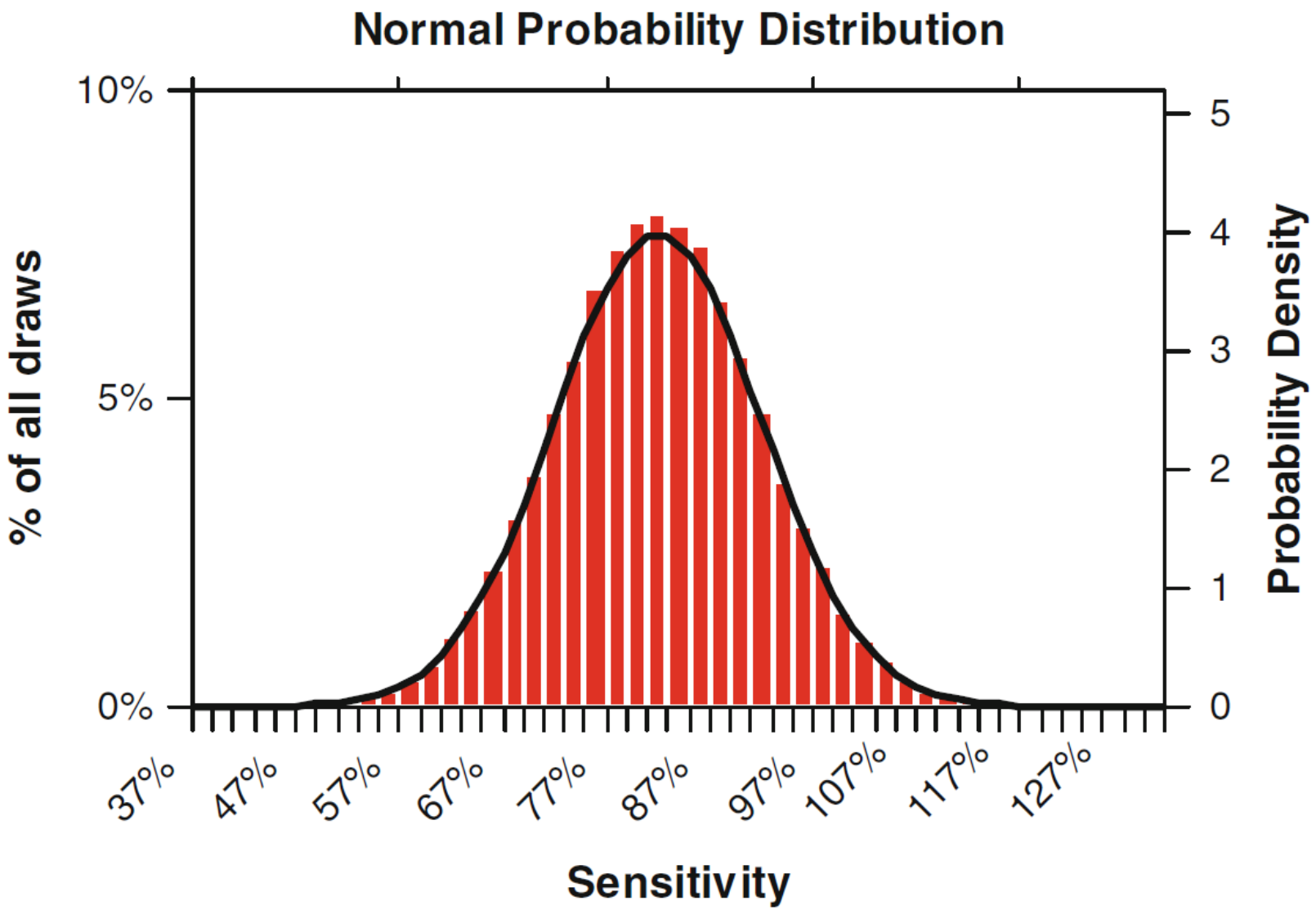
→

Probability distribution of bias parameters

1. Assign probability distributions to each bias parameter
2. Randomly sample from the bias parameter distributions
3. Use simple bias analysis to correct for the bias
4. Resample, save, and summarize


Uniform Probability Distribution
4.5%
4.0%
3.5%
3.0%
2.5%
2.0%
1.5%
1.0%
0.5%
0.0%
% of all draws
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Probablity Density
50%
60%
70%
80%
90%
100%
Sensitivity


Trapezoidal Probability Distribution
15%
10%
5%
0%
% of all draws
7
6
5
4
3
2
1
0
Probability Density
67%
77%
87%
97%
Sensitivity


Normal Probability Distribution
10%
5%
0%
% of all draws
5
4
3
2
1
0
Probability Density
37%
47%
57%
67%
77%
87%
97%
107%
117%
127%
Sensitivity

Ressoruces for probabilistic bias analysis in Excel and SAS: https://sites.google.com/site/biasanalysis/

Stata

The Stata Journal (2008)
8, Number 1, pp. 29–48

A tool for deterministic and probabilistic sensitivity analysis of epidemiologic studies

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Los Angeles, CA

Abstract. Classification errors, selection bias, and uncontrolled confounders are likely to be present in most epidemiologic studies, but the uncertainty introduced by these types of biases is seldom quantified. The authors present a simple yet easy-to-use Stata command to adjust the relative risk for exposure misclassification, selection bias, and an unmeasured confounder. This command implements both deterministic and probabilistic sensitivity analysis. It allows the user to specify a variety of probability distributions for the bias parameters, which are used to simulate distributions for the bias-adjusted exposure–disease relative risk. We illustrate the command by applying it to a case–control study of occupational resin exposure and lung-cancer deaths. By using plausible probability distributions

Example

Does circumcision protect against HIV infection?

Possible confounder: being muslim

Table 8.8 Observed data on the association between male circumcision (E) and HIV (D) (Tyndall et al, 1996)

	Total	
	E_1	E_0
D_+	105	85
D_-	527	93
Total	632	178
	RR	0.35

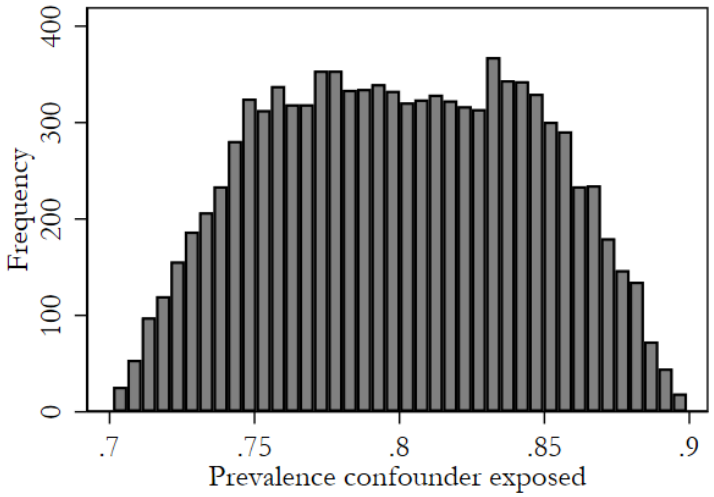
RR not adjusted for religion: 0.35 (95% CI 0.28 to 0.44)

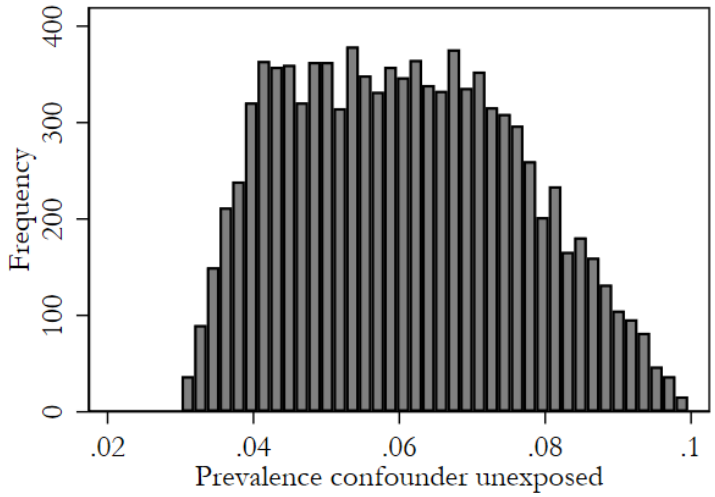
Example

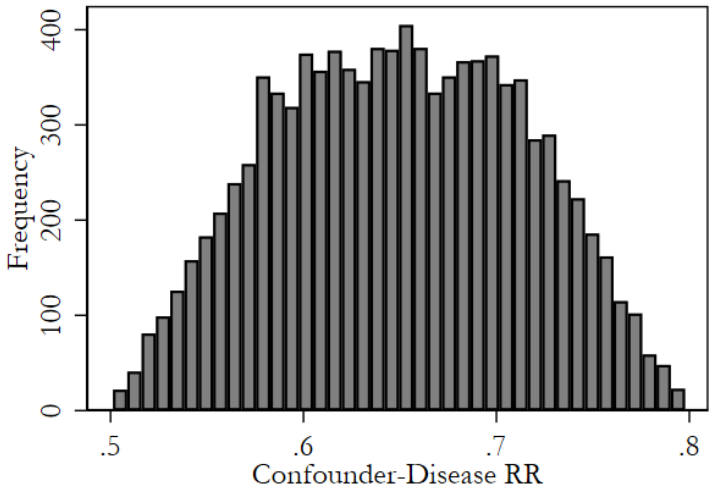
1. Assign probability distributions to each bias parameter
2. Randomly sample from the bias parameter distributions
3. Use simple bias analysis to correct for the bias
4. Resample, save, and summarize

Table 8.9 Bias parameter distributions for a probabilistic bias analysis of the relationship between male circumcision and HIV stratified by an unmeasured confounder (religion)

Bias parameter	Description	Min	Mod_{low}	Mod_{up}	Max
p_1 (%)	Prevalence of being Muslim among circumcised	70	75	85	90
p_0 (%)	Prevalence of being Muslim among uncircumcised	3	4	7	10
RR_{CD}	Association between being Muslim and HIV acquisition	0.5	0.6	0.7	0.8


Frequency
0
100
200
300
400
.7
.75
.8
.85
.9
Prevalence confounder exposed


Frequency
0
100
200
300
400
.02
.04
.06
.08
.1
Prevalence confounder unexposed


Frequency
0
100
200
300
400
.5
.6
.7
.8
Confounder-Disease RR

Example

1. Assign probability distributions to each bias parameter
2. Randomly sample from the bias parameter distributions
3. Use simple bias analysis to correct for the bias
4. Resample, save, and summarize

Stata/IC 15.1

File Edit Data Graphics Statistics User Window Help

Review

Filter commands here

#	Command	_rc
1	findit episens	

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  ___  ____  ____  ____  ____ (R)
 /__    /   ____/   /   ____/
___/   /   /___/   /   /___/   15.1   Copyright 1985-2017 StataCorp LLC
  Statistics/Data Analysis            StataCorp
                                      4905 Lakeway Drive
                                      College Station, Texas 77845 USA
                                      800-STATA-PC        http://www.stata.com
                                      979-696-4600        stata@stata.com
                                      979-696-4601 (fax)

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       Serial number:  301509002998
         Licensed to:  IT service
                       SDU

Notes:
      1.  Unicode is supported; see help unicode_advice.

. findit episens

.
```

Command

Variables

Filter variables here

Name	Label

There are no items to show.

Properties

Variables	
Name	
Label	
Type	
Format	
Value label	
Notes	
Data	
Filename	
Label	
Notes	
Variables	0
Observations	0
Size	0
Memory	32M
Sorted by	

Viewer - search episens, all

File Edit History Help

search episens, all

net sj 8-1 st0138 | search episens, all ×

Dialog | Also see | Jump to

search for **episens** (manual: **[R] search**)

Search of official help files, FAQs, Examples, SJs, and STBs

SJ-8-1 st0138 . . . . . Deterministic and probabilistic sensitivity analysis
. . . . . N. Orsini, R. Bellocco, M. Bottai, A. Wolk, and S. Greenland
(help episens, episensi if installed)
Q1/08 SJ 8(1):29--48
A tool for deterministic and probabilistic sensitivity
analysis of epidemiologic studies that adjusts the
relative risk for exposure misclassification, selection
bias, and an unmeasured confounder

Web resources from Stata and other users

(contacting http://www.stata.com)

3 packages found (Stata Journal and STB listed first)
---

st0138 from http://www.stata-journal.com/software/sj8-1
SJ8-1 st0138. Deterministic and probabilistic sensitivity... /
Deterministic and probabilistic sensitivity analysis of / epidemiological
results / by N.Orsini and Alicja Wolk, Division of Nutritional
Epidemiology / Karolinska Institutet, Stockholm, Sweden / Rino Bellocco,

episens from http://fmwww.bc.edu/RePEc/bocode/e
'EPISENS': module for basic sensitivity analysis of epidemiological
results / episens provides basic sensitivity analysis of the observed /
relative risks adjusting for unmeasured confounding and /
misclassification of the exposure. episensi is the / immediate form of

episensrri from http://fmwww.bc.edu/RePEc/bocode/e
'EPISENSRRI': module for basic sensitivity analysis for unmeasured
confounders / episensrri provides basic sensitivity analysis of the
apparent or / observed relative risks according to specified plausible /

Viewer - net sj 8-1 st0138

File Edit History Help

net sj 8-1 st0138

net sj 8-1 st0138

Dialog Also see Jump to

---

package **st0138** from http://www.stata-journal.com/software/sj8-1

TITLE

SJ8-1 st0138. Deterministic and probabilistic sensitivity...

DESCRIPTION/AUTHOR(S)

Deterministic and probabilistic sensitivity analysis of
epidemiological results

by N.Orsini and Alicja Wolk, Division of Nutritional Epidemiology
Karolinska Institutet, Stockholm, Sweden
Rino Bellocco, Department of Statistics
University of Milano-Bicocca, Milano, Italy
Matteo Bottai, Department of Epidemiology and Biostatistics
University of South Carolina
Sander Greenland, Departments of Epidemiology and Statistics
University of California, Los Angeles

Support: nicola.orsini@ki.se

After installation, type help **episens**

INSTALLATION FILES (click here to install)

st0138/episens.ado
st0138/episensi.ado
st0138/episens.hlp
st0138/episensi.hlp
st0138/episens_mcsa_unc.ado
st0138/episens_mcsa_mie.ado
st0138/episens_mcsa_sel.ado
st0138/episens_mcsa_all.ado

ANCILLARY FILES (click here to get)

st0138/sj_paper_examples.do

(click here to return to the previous screen)

```
episensi 105 85 527 93, st(cs) reps(10000)
dpunexp(trapezoidal(0.03 0.04 0.07 0.10))
dpexp(trapezoidal(0.7 0.75 0.85 0.9))
drrcd(trapezoidal(0.5 0.6 0.7 0.8))
grarrtot grprior nodot
```

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dpexp(trapezoidal(0.7 0.75 0.85 0.9))
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drrcd(trapezoidal(0.5 0.6 0.7 0.8))
grarrtot grprior nodot
```
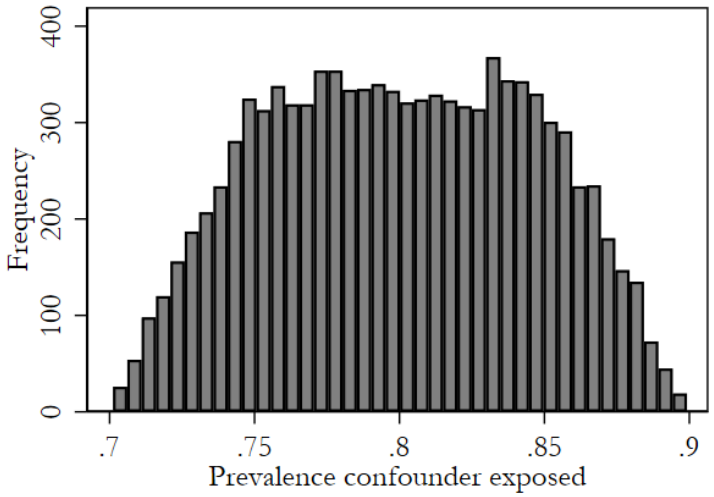
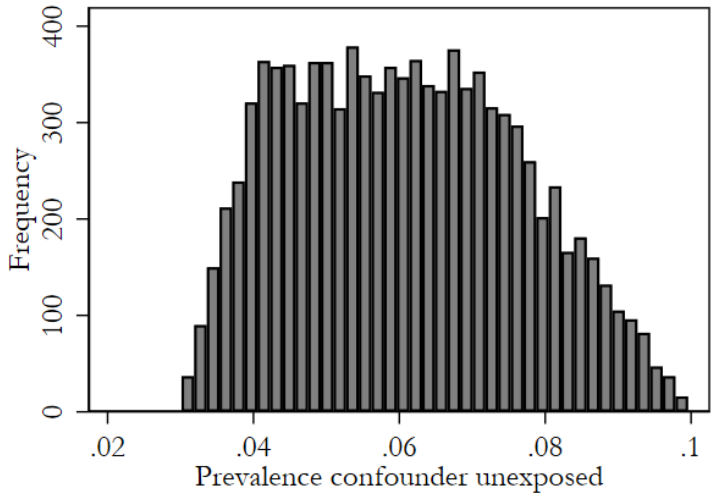
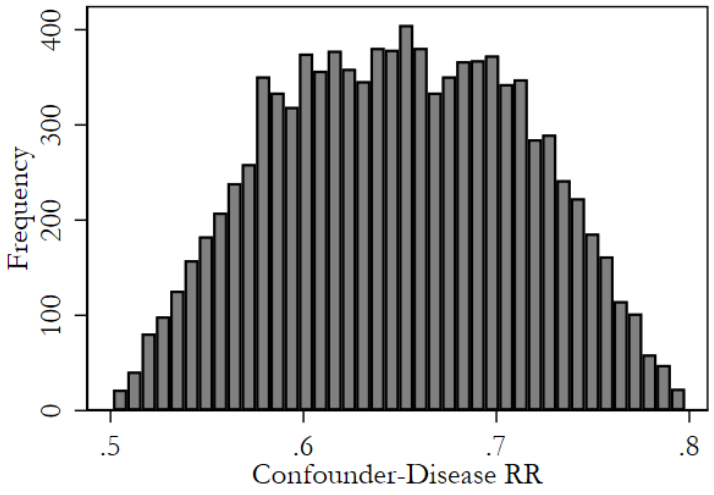
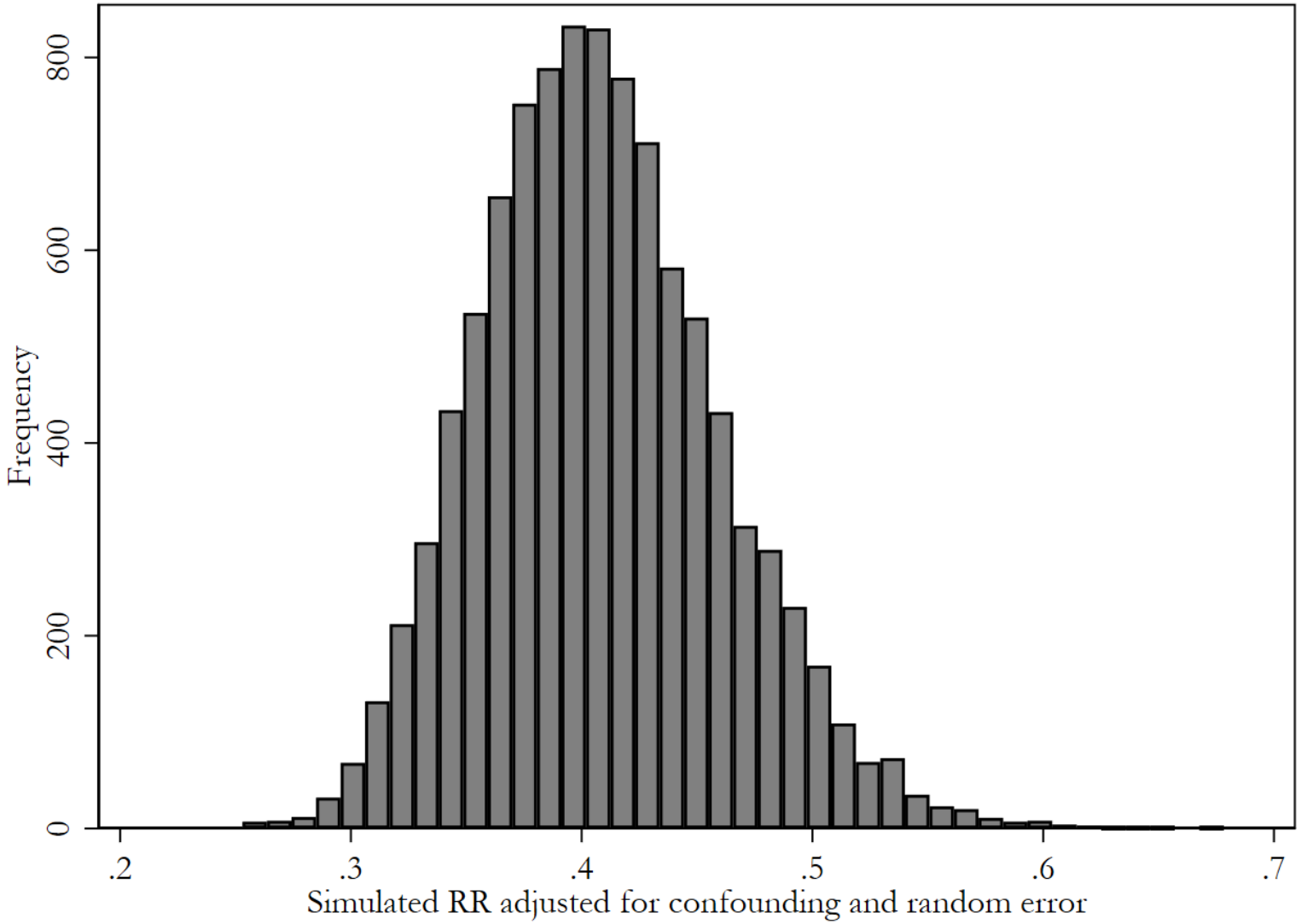


Frequency
0
100
200
300
400
.7
.75
.8
.85
.9
Prevalence confounder exposed


Frequency
0
100
200
300
400
.02
.04
.06
.08
.1
Prevalence confounder unexposed


Frequency
0
100
200
300
400
.5
.6
.7
.8
Confounder-Disease RR


Frequency
0
200
400
600
800
.2
.3
.4
.5
.6
.7
Simulated RR adjusted for confounding and random error

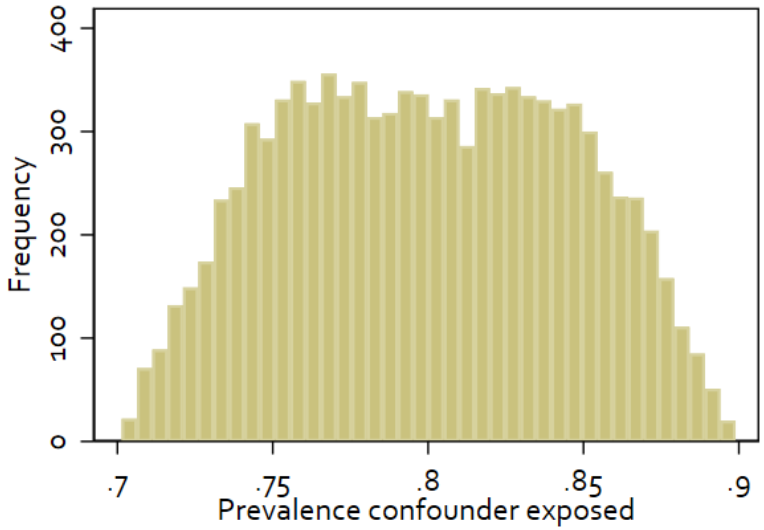
```
. episensi 105 85 527 93, st(cs) reps(1000) dpunexp(trapezoidal(0.03 0.04 0
> 5 0.85 0.9)) drrcd(trapezoidal(0.5 0.6 0.7 0.8)) grarrtot grprior nodot

Pr(c=1|e=1): Trapezoidal(.7,.75,.85,.9)
Pr(c=1|e=0): Trapezoidal(.03,.04,.07,.1)

Probabilistic sensitivity analysis for unmeasured confounding

                                          Percentiles          Ratio
                             2.5         50         97.5       97.5/2.5
                             ----------------------------------------
Conventional                 0.28        0.35       0.44       1.59
Systematic error             0.38        0.40       0.44       1.17
Systematic and random error  0.31        0.40       0.51       1.65

.
```

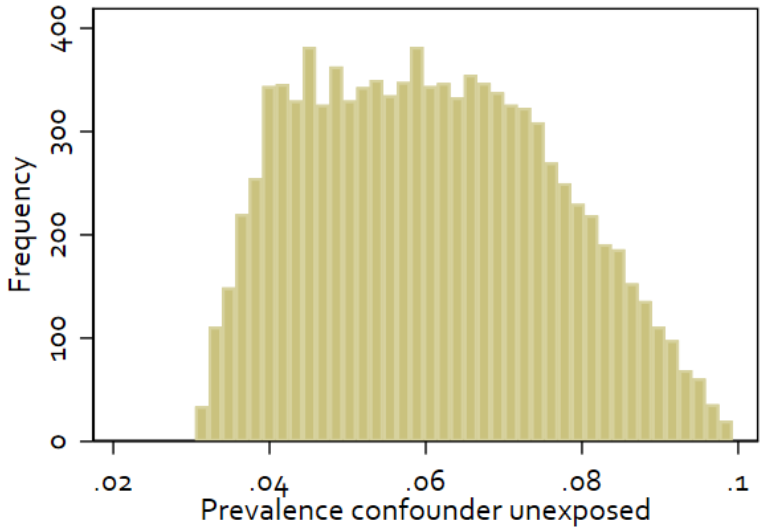
RR_{CD}: 0.65 (0.4–0.9)

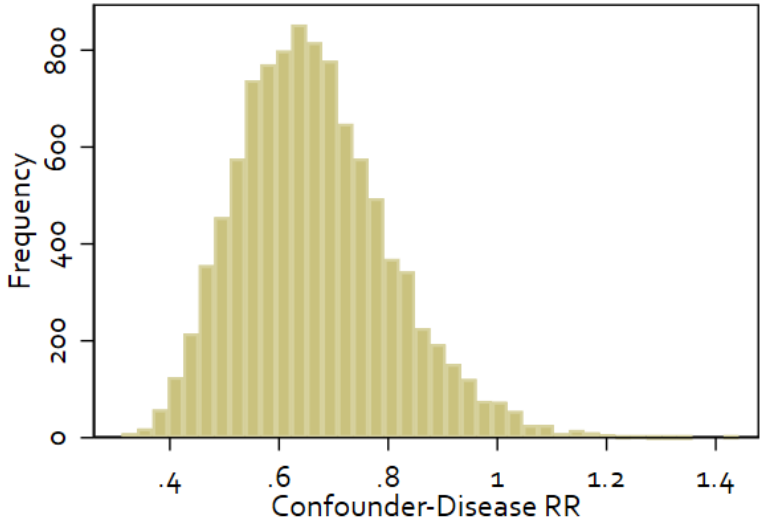
```
episensi 105 85 527 93, st(cc) reps(1000)
dpunexp(trapezoidal(0.03 0.04 0.07 0.10))
dpexp(trapezoidal(0.7 0.75 0.85 0.9))
drrcd(log-n(-0.43 0.21))
grarrtot grprior nodot
```

RRcd: ln(0.65) = -0.43

SD: (ln(0.9)-ln(0.4))/(2*1.96) = 0.21


Frequency
0
100
200
300
400
.7
.75
.8
.85
.9
Prevalence confounder exposed


Frequency
0
100
200
300
400
.02
.04
.06
.08
.1
Prevalence confounder unexposed


Frequency
0
200
400
600
800
.4
.6
.8
1
1.2
1.4
Confounder-Disease RR

```
. episensi 105 85 527 93, st(cc) reps(10000) dpunexp(trapezoidal(0.03 0.04
> 0.85 0.9)) drrcd(log-n(-0.43 0.21)) grarrtot grprior nodot

Pr(c=1|e=1): Trapezoidal(.7,.75,.85,.9)
Pr(c=1|e=0): Trapezoidal(.03,.04,.07,.1)
RR_cd      : Log-Normal(-0.43,0.21)

Probabilistic sensitivity analysis for unmeasured confounding

                                        Percentiles         Ratio
                                2.5         50         97.5      97.5/2.5
                                ----------------------------------------
Conventional                    0.15        0.22       0.31      2.06
Systematic error                0.22        0.30       0.39      1.77
Systematic and random error     0.19        0.30       0.47      2.52
```

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 2010; **19**: 638–644
Published online 5 April 2010 in Wiley InterScience (www.interscience.wiley.com) **DOI**: 10.1002/pds.1938

ORIGINAL REPORT

Methods to apply probabilistic bias analysis to summary estimates of association†

Timothy L. Lash DSc, MPH[1,2]*, Morten Schmidt MB[1],
Annette Østergaard Jensen MD, PhD[1] and Malene Cramer Engebjerg MSc[1]

[1]*Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark*
[2]*Department of Epidemiology, Boston University School of Public Health, Boston, MA, USA*

Quantitative bias analysis

1. Simple bias analysis
2. Probabilistic bias analysis
    - Confounding
    - Selection bias
    - Misclassification

Probabilistic bias analysis

- Confounding
- Selection bias
- Misclassification

Accounting for several biases at the same time: Multiple bias modeling

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 2006; **15**: 291–303
Published online 31 January 2006 in Wiley InterScience (www.interscience.wiley.com). **DOI**: 10.1002/pds.1200

ORIGINAL REPORT

Sensitivity analysis and external adjustment for unmeasured confounders in epidemiologic database studies of therapeutics†

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Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA

http://www.drugepi.org/dope-downloads

RESEARCH AND REPORTING METHODS Annals of Internal Medicine

Sensitivity Analysis in Observational Research: Introducing the E-Value

Tyler J. VanderWeele, PhD, and Peng Ding, PhD

Sensitivity analysis is useful in assessing how robust an association is to potential unmeasured or uncontrolled confounding. This article introduces a new measure called the "E-value," which is related to the evidence for causality in observational studies that are potentially subject to confounding. The E-value is defined as the minimum strength of association, on the risk ratio scale, that an unmeasured confounder would need to have with both the treatment and the outcome to fully explain away a specific treatment–outcome association, conditional on the measured covariates. A large E-value implies that considerable unmeasured confounding would be needed to explain away an effect estimate. A small E-value implies little unmeasured confounding would be needed to explain away an effect estimate. The authors propose that in all observational studies intended to produce evidence for causality, the E-value be reported or some other sensitivity analysis be used. They suggest calculating the E-value for both the observed association estimate (after adjustments for measured confounders) and the limit of the confidence interval closest to the null. If this were to become standard practice, the ability of the scientific community to assess evidence from observational studies would improve considerably, and ultimately, science would be strengthened.

Ann Intern Med. 2017;167:268-274. doi:10.7326/M16-2607 **Annals.org**
For author affiliations, see end of text.
This article was published at Annals.org on 11 July 2017.

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https://evalue.hmdc.harvard.edu/

Statistics for Biology and Health

Timothy L. Lash
Matthew P. Fox
Aliza K. Fink

Applying Quantitative Bias Analysis to Epidemiologic Data

Springer

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 2010; **19**: 638–644
Published online 5 April 2010 in Wiley InterScience (www.interscience.wiley.com) **DOI**: 10.1002/pds.1938

ORIGINAL REPORT

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[1]*Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark*
[2]*Department of Epidemiology, Boston University School of Public Health, Boston, MA, USA*

International Journal of Epidemiology, 2014, 1969–1985
doi: 10.1093/ije/dyu149
Advance Access Publication Date: 30 July 2014
Original article

Education Corner

Good practices for quantitative bias analysis

Timothy L Lash,[1]* Matthew P Fox,[2] Richard F MacLehose,[3] George Maldonado,[4] Lawrence C McCandless[5] and Sander Greenland[6]

[1]Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA, USA, [2]Department of Epidemiology and Center for Global Health & Development, Boston University School of Public Health, Boston, MA, USA, [3]Division of Epidemiology and Community Health and [4]Division of Environmental Health Sciences, University of Minnesota School of Public Health, Minneapolis, MN, USA, [5]Faculty of Health Sciences, Simon Fraser University, Burnaby, BC, Canada and [6]Department of Epidemiology and Department of Statistics, University of California Los Angeles, Los Angeles, CA, USA

*Corresponding author. Department of Epidemiology, Rollins School of Public Health, Emory University, 1518-002-3BB, 1518 Clifton Rd NE, Atlanta, GA 30322, USA. E-mail: tlash@emory.edu

Accepted 7 July 2014

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kaskristensen@health.sdu.dk