Online Supplementary Appendix

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eTable 1. Potential applications of probabilistic bias analysis in pharmacoepidemiologic and comparative effectiveness research.

Type of bias	Application	Example*
Unmeasured confounding	Studies using claims data are likely missing information on potentially important confounders (e.g. lifestyle or severity of symptoms). Probabilistic bias analysis can be used to simulate unmeasured confounders.	Bannister-Tyrell et al. used expert judgement and prior studies to simulate the effects of severe labor pain on the association between epidural labor analgesia and Cesarean delivery.[31]
Misclassification	Many exposures, outcomes, and covariates in pharmacoepidemiologic studies are measured with error. Probabilistic bias analysis can be used to simulate the effects of misclassification on study results.	Huybrechts et al. used an internal validation study (comparing outcome defined using claims data to hospital reports) to examine the effects of nondifferential outcome misclassification on the association between specific antidepressant use during pregnancy and cardiac malformations in newborns.[39]
Selection bias – differential selection probabilities	Probabilistic bias analysis can be applied to scenarios in which there is concern that selection into the study was affected by both exposure and outcome.	Our systematic review found no example. However, one could imagine being concerned of unequal selection probabilities in a case-control study where more cases participated than controls.
Selection bias – differential loss to follow-up	Probabilistic bias analysis can be used to simulate the effects of differential loss to follow-up – a common concern in cohort studies	Our systematic review found no examples. However, Lash and Fink simulated the effects of differential loss to follow-up on the association between less-than-definitive therapy (vs. definitive therapy) on breast cancer mortality.[18]
Multiple biases	Probabilistic bias analysis can incorporate multiple forms of bias.	We found no examples applying probabilistic bias analysis to multiple sources. However, one could imagine implementing such an approach to

	examine both outcome misclassification and an unmeasured confounder in a retrospective cohort study using claims data, for example.

*We used examples from studies in our systematic review when available. For some scenarios, we were unavailable to provide examples from included studies, and we used earlier examples from the literature or hypothetical scenarios to illustrate how probabilistic bias analysis could be implemented.

eTable 2. Examples of simple bias analysis formulas that can be applied to crude effect estimates[2]*†

Type of bias simulated	Simple bias formulas	Notation
Unmeasured confounder (no effect measure modification)	$RR_{adj} = RR_{obs}\frac{RR_{CD}p_0 + (1-p_0)}{RR_{CD}p_1 + (1-p_1)}$	RR_{adj}: bias-adjusted risk ratio RR_{obs}: crude risk ratio $RR_{CD:}$ strength of confounder-outcome association $p_{1:}$ Prevalence of confounder in exposed group p_0: Prevalence of confounder in unexposed group
Exposure misclassification	$RR_{adj} = \frac{\frac{[a(PPV_{D+}) + b(1-NPV_{D+})]}{[(a(PPV_{D+}) + b(1-NPV_{D+})) + (c(PPV_{D-} + d(1-NPV_{D-}))]}}{\frac{D_{+total} - [a(PPV_{D+}) + b(1-NPV_{D+})]}{[(D_{+total} - [a(PPV_{D+}) + b(1-NPV_{D+})]) + (D_{-total} - (c(PPV_{D-} + d(1-NPV_{D-}))))]}}$	RR_{adj}: bias-adjusted risk ratio a : observed exposed persons with outcome b : observed unexposed persons with outcome c : observed exposed persons without outcome d : observed unexposed persons without outcome D_{+total} : total persons with outcome D_{-total} : total persons without outcome PPV_{D+}:positive predictive value of exposure in persons with outcome PPV_{D-}: Positive predictive value of exposure in persons without outcome NPV_{D+}: negative predictive value of exposure in persons with outcome NPV_{D-}: negative predictive value in persons without outcome
Outcome misclassification	$RR_{adj} = \frac{\frac{[a - E_{1total}(1-SP_{e1})]}{([SE_{E1} - (1-SP_{E1})]} / (\frac{[a - E_{1total}(1-SP_{e1})]}{[SE_{E1} - (1-SP_{E1})]} + \left(E_{1total} - \frac{[a - E_{1total}(1-SP_{e1})]}{([SE_{E1} - (1-SP_{E1})]}\right))}{\frac{[b - E_{0total}(1-SP_{E0})]}{[SE_{E0} - (1-SP_{E0})]} / (\frac{[b - E_{0total}(1-SP_{E0})]}{[SE_{E0} - (1-SP_{E0})]} + \left(E_{0total} - \frac{[b - E_{0total}(1-SP_{E0})]}{[SE_{E0} - (1-SP_{E0})]}\right))}$	RR_{adj}: bias-adjusted risk ratio a : observed exposed persons with outcome b : observed unexposed persons with outcome c : observed exposed persons without outcome d : observed unexposed persons without outcome E_{1total} : total exposed persons E_{0total} : total unexposed persons SE_{E1} : outcome sensitivity in exposed SE_{E0}: outcome sensitivity in unexposed SP_{E1}: outcome specificity in exposed SP_{0-}: outcome specificity in unexposed

Selection bias – unequal selection probabilities‡	$OR_{adj} = OR_{obs} \times \frac{S_{case,0}S_{control,1}}{S_{case,1}S_{control,0}}$	OR_{adj}:bias-adjusted odds ratio OR_{obs}:crude odds ratio $S_{case,1}$: selection probability for exposed cases $S_{case,0}$: selection probability for unexposed cases $S_{control,1}$:selection probability for exposed controls $S_{control,0}$: selection probability for unexposed control
Selection bias – loss to follow-up	$IRR_{adj} = \frac{Incidence_{obs,1} + Incidence_{LTF,1}}{\frac{Personyears_{obs,1} + Personyears_{LTF,1}}{Incidence_{obs,0} + Incidence_{LTF,0}}}{Personyears_{obs,0} + Personyears_{LTF,0}}$	IRR_{adj}: bias-adjusted incidence rate ratio $Incidence_{obs,1}$: number of observed exposed persons who developed outcome $Personyears_{obs,1}$: person-years of follow-up for observed exposed persons $Incidence_{LTF,1}$: hypothesized number of exposed persons lost to follow-up who developed outcome $Personyears_{LTF,1}$: hypothesized person-years of follow-up for exposed persons who were lost to follow-up $Incidence_{obs,0}$: number of observed unexposed persons who developed outcome $Personyears_{obs,0}$: person-years of follow-up for observed unexposed persons $Incidence_{LTF,0}$: hypothesized number of exposed persons lost to follow-up who developed outcome $Personyears_{LTF,0}$: hypothesized person-years of follow-up for unexposed persons who were lost to follow-up

*The formula notation is heavily adapted is from Lash, Fox, and Fink 2009.[2] This table provides examples of simple bias analysis formulas that can be applied to crude effect estimates using probabilistic bias analysis; it is not meant to be a comprehensive list of all plausible bias-adjustment formulas. Extensive discussions on simple bias analysis are provided elsewhere.[2,7,11]

† All variables are assumed to be binary in the formulas provided. All formulas assume a cohort study design unless otherwise noted.

‡Notation assumes a case-control study design; the formula can be easily adapted to a cohort study design.

eTable 3. General description of eligible pharmacoepidemiologic in 2010-2015 and included in the systematic review, sorted by bias addressed

Reference (Year)	Study design	Data Source	Exposure contrast	Outcome
Unmeasured Confounding				
Albert et al. (2012)[30]	Cohort	Surveillance, Epidemiology, and End Results-Medicare Data, diagnoses 1999-2002 and follow-up through 2007	Radiation therapy versus no treatment within the first 9 months of diagnosis	Mastectomy (Binary)
Bannister-Tyrell et al. (2014)[31]	Cohort	New South Wales Perinatal Collection and Admitted Patients Data Collection, 2007-2010	Epidural labor analgesia versus no treatment	Cesarean delivery (Binary)
Corrao et al. (2011)[32]	Cohort	National Health Service data (diagnosis on hospital discharge and outpatient drug claims) Lombardy, Italy,2000-2007	High versus very low adherence to blood pressure medication	First hospitalization for coronary or cerebrovascular events (Time to event)
Corrao et al. (2014)[33]	Cohort	National Health Service data (diagnosis on hospital discharge, outpatient visits and outpatient drug claims) Lombardy, Italy,2003-2010	High versus very low adherence to statins	First diabetes hospitalization or anti-diabetic medication dispensation (Time to event)
Corrao et al. (2014)[34]	Cohort	National Health Service data (diagnosis on hospital discharge, outpatient visits and outpatient drug claims) Lombardy, Italy,2008-2011	Generic versus brand-name simvastatin use	Discontinuation of simvastatin; first hospitalization for coronary or cerebrovascular events (Time to event)
Corrao et al.	Case-control	National Health Service data	Initial blood pressure	Hospitalization for

(2011)[29*]		(diagnosis on hospital discharge and outpatient drug claims) Lombardy, Italy,2000-2007	medication combination therapy versus monotherapy	coronary or cerebrovascular events (Binary)
Corrao et al. (2013)[35]	Case-control	National Health Service data (diagnosis on hospital discharge and outpatient drug claims) Lombardy, Italy,2003-2010	Long-term statin use versus statin use between two and six months	Dementia hospitalization (Binary)
Ghirardi et al. (2014)[36]	Case-control	National Health Service data (hospitalization and outpatient drug claims) from 13 Italian territorial units in the Bisphosphonates Effectiveness-Safety Tradeoff Project	3 exposure groups: ≥2 years bisphosphonate use versus 1-2 years use,<1 year use	Hospitalization for osteoporotic fracture (Binary)
Schmidt et al. (2010)[37]	Case-control	Danish National Patient Registry /Danish Civil Registration System, Northern Jutland and Aarhus County, 1997-2008	Four exposure groups: Low dose acetylsalicylic acid use; dipyridamole use; use of both versus never use	Hospitalization for sub-arachnoid hemorrhage (Binary)
Misclassification				
Ahrens et al. (2012)[38]	Cohort	Slone Birth Defects Study, 2006-2011	Influenza vaccination during pregnancy versus no vaccination during pregnancy	Preterm birth (Time to event)
Brunet et al. (2015)[43]	Cohort	Canadian Co-Infection Cohort Study, 2003-2013	Self-reported prescribed or illicit use of opioids versus no use	Time to progression to liver fibrosis (Time to event)
Huybrechts et al. (2014)[39]	Cohort	Medicaid Analytic eXtract excluding Arizona, Connecticut,	Specific antidepressant types versus no use in	Inpatient or outpatient claim for

		Michigan, and Montana, includes hospitalization and outpatient physician services and prescription claims, 2000-2007	first trimester only	specific types of cardiac malformations (Binary)
Palmsten et al. (2013)[40]	Cohort	Medicaid Analytic eXtract, includes hospitalization and outpatient physician services and prescription claims, 2000-2007	Antidepressant dispensed between 90-225 gestational days versus no antidepressant claim between last menstrual period and 225 gestational day	Inpatient or outpatient claim for preeclampsia or eclampsia (Binary)
Barron et al. (2013)[41]	Case-control	National Cancer Registry Ireland linked to prescription dispensing data from Primary Care Reimbursement Services, 2002-2007	Non-persistence to hormonal therapy versus persistent; non-compliant hormonal therapy versus compliant, low-cumulative hormonal therapy versus high cumulative Tertiles of proportion of days covered	Early local or distant breast cancer recurrence (within 4 years of initiating hormonal therapy) (Binary)
Mahmud et al. (2011)[42]	Case-control	Saskatchewan Ministry of Health databases and Saskatchewan Cancer Registry, 1985-2000	Specific non-steroidal anti-inflammatory drug use versus never users	Prostate cancer (Binary)

*We selected the first of two articles using probabilistic bias analysis on the same study sample [Excluded: Corrao G, Nicotra F, Parodi A, Zambon A, Soranna D, Heiman F, Merlino L, Mancia G. External adjustment for unmeasured confounders improved drug-outcome association estimates based on health care utilization data. J Clin Epidemiol 2012;65:1190-199.]

eTable 4. Comparison of original results with probabilistic bias analysis results when simulating an unmeasured confounder, sorted by study design.*

Reference (Year)	Simulation presentation†	Type of probability distribution assigned‡	Estimate of confounder prevalence in exposed and unexposed	Associations between confounder and outcome	Conventional results	Bias analysis results	% Change in estimate from conventional analysis§	% Change in interval width from conventional analysis**
Cohort studies								
Albert et al. (2012)[30]	Multiple scenarios	Not reported	**Least biased**: P_1=5% (range: 0–10%) P_0=50% (range: 40–60%) **Most biased**: P_1=15% (range:10–20%) P_0=85% (range:80–90%)	**Least biased**: HR=1.75 **Most biased**: HR=3.32	HR=0.33 95% CI: 0.22–0.48	**Least biased**: HR=0.32 95% SI: 0.20–0.54 **Most biased**: HR=0.86 95% SI: 0.43–1.60	**Least biased**: 3.0 **Most biased**: -160.6	**Least biased**: 30.8 **Most biased**: 350.0
Bannister-Tyrell et al. (2014)[31]	Single scenario	Trapezoidal	P_1: Min=5%, $Mode_1$=15% $Mode_2$= 25%, Max= 35% P_0: Min= 2%, $Mode_1$= 4%, $Mode_2$=6%, Max=10%	RR: Min=4,$Mode_1$=7, $Mode_2$=10, Max=12	RR=2.5 95% CI: 2.5–2.6	RR=1.54 95% SI: 1.03–2.22	-38.4	1090.0
Corrao et al. (2011)[32]	Multiple scenarios††	Not reported	P_1=1% P_0=20%	RR=1.71	HR=0.75 95% CI: 0.71–0.80	HR=0.84 95% SI: 0.77–0.92	-12.0	66.7
Corrao et al. (2014)[33]	Continuous interval††	Not reported	Overall prevalence of 37.5%; OR_{CE} ranging 0.5-2.0.	RR-3.0	HR=1.32 95% CI: 1.26–1.39	HR=1.13 95% SI: 1.00–1.28	-14.4	115.0
Corrao et al. (2014)[34]	Continuous interval††	Not reported	**Least biased:** Overall prevalence of 35%; OR_{CE} ranging 1.0-10.0 **Most biased:** Overall prevalence of 35%; OR_{CE} ranging 1.0-10.0	**Least biased:** RR=1.21 **Most biased:** RR=1.21	HR=1.06 95% CI: 0.83–1.34	**Least biased:** HR=1.05 95% SI: 0.81–1.33 **Most biased:** HR=1.09 95% SI: 0.85-1.40	**Least biased:** -0.9 **Most biased:** 2.8	**Least biased:** 2.0 **Most biased:** 7.8
Case-control studies								
Corrao et al. (2011)[29]	Multiple scenarios‡‡	Normal (association only) §§	**Least biased:** P_1=17.3 P_0=11.9 **Most biased:** P_1=17.3 P_0=11.9	**Least biased:** RR=1.5§§ **Most biased:** RR=5.0§§	OR=0.89 95% CI: 0.84–0.95	**Least biased:** OR=0.88 95% SI: 0.83–0.93 **Most biased:** OR=0.81 95% SI: 0.76–0.86	**Least biased:** 1.0 **Most biased:** 9.0	**Least biased:** -0.1 **Most biased:** -0.1
Corrao et al. (2013)[35]	Multiple scenarios	Not reported	**Least biased:** Overall prevalence of 35%; OR_{CE}=1.5 **Most biased:** Overall prevalence of 35%; OR_{CE}=5.0	**Least biased:** RR=1.5 **Most biased:** RR=1.5	OR=0.75 95% CI: 0.61–0.94	**Least biased:** OR=0.69 95% SI: 0.55–0.88 **Most biased:** OR=0.54 95% SI: 0.43–0.68	**Least biased:** 8.0 **Most biased:** 28.0	**Least biased:** 0.0 **Most biased:** -24.2
Ghirardi et al. (2014)[36]	Multiple scenarios	Not reported	**Least biased**: P_1=40%, P_0=20 **Most biased**:	**Least biased:** RR=1.5 **Most biased:**	OR=0.79 95% CI: 0.67-0.93	**Least biased**: OR=0.72 95% SI: 0.64–0.82 **Most biased**:	**Least biased**: 8.9 **Most biased**:	**Least biased**: -30.8 **Most biased**:

			P_1=40%, P_0=20	RR=2.5		OR =0.64 95% SI: 0.56-0.74	19.0	-30.8
Schmidt et al. (2010)[37]	Single scenario***	Not reported	Not reported	**Least biased***:** RR ranging: 2-3	**Least biased***:** OR=2.52 95% CI: 1.37-4.62	**Least biased***:** OR=2.47 (SI not reported)	**Least biased***:** -2	**Least biased***:** N/A[§§]
				Most biased*:** RR ranging 2-3	**Most biased***:** OR =2.09 95%: 1.04–4.23	**Most biased***:** OR =1.88 (SI not reported)	**Most biased***:** -10	**Most biased***:** N/A[§§]

CI, confidence interval; HR, hazard ratio; P_1, prevalence of the confounder in the exposed ; OR_{CE}, exposure-confounder odds ratio; P_0, prevalence of the unmeasured confounder in the unexposed; RR, relative risk; SI, simulation interval.

*When multiple scenarios were simulated, we tried to present the least and most extreme bias simulations (defined by looking at changes in the effect estimate). In some studies, many scenarios were visually displayed but the exact values of the effect estimate and interval were not available; in this case, we have presented the corrected estimates and intervals discussed in the text.

[†]Simulation results were presented as single discrete scenarios, multiple discrete scenarios, or applied over a continuous interval of plausible bias parameters. See Methods for further description.

[‡]See eFigure1 for further description of probability distribution types.

[§]When conventional effect estimate was <1,estimated as [Effect estimate$_{conventional}$ – Effect estimate$_{probabilistic}$) / Effect estimate$_{conventional}$]*100.
When conventional effect estimate was ≥1, estimated as[Effect estimate$_{probabilistic}$ – Effect estimate$_{conventional}$) / Effect estimate$_{conventional}$]*100.

**Estimated as [SI width$_{probabilistic}$ - CI width$_{conventional}$)/ CI width$_{conventional}$]. Interval width calculated as the upper interval bound – lower interval bound

[††]Although multiple scenarios or a range of plausible bias-adjusted estimates were generated, they were visually displayed. The estimates provided are for the example(s) discussed in the text .

[‡‡]Three separate unmeasured confounders were simulated using similar methods. Only one is presented for brevity (severity of hypertension).

[§§]Probability distribution type was provided for exposure-outcome association only. Investigators sampled the relative risk from a distribution with mean of ln(RR) and a variance of 0.04

***This study applied a single bias scenario to two exposure-outcome associations. The least biased scenario was new use of low dose aspirin vs. no use and the most biased scenario was long-term use of dipyridamole vs. no use.

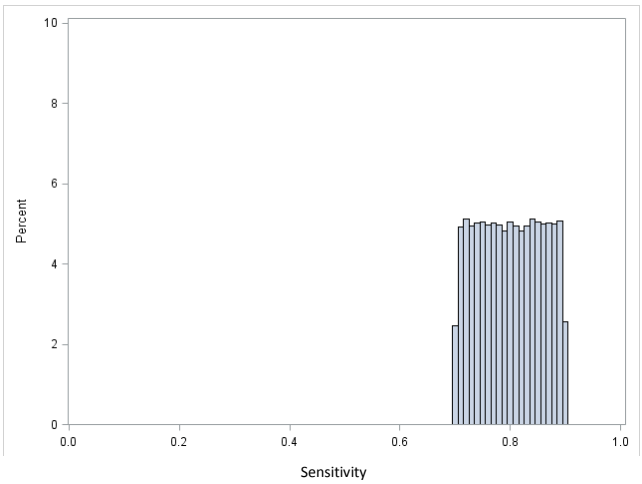
eTable 5. Comparison of original results with probabilistic bias analysis results when simulating misclassification, sorted by study design.*

Reference (Year)	Misclassification simulated	Type of probability distribution assigned†	Sensitivity or PPV	Specificity or NPV	Conventional results	Bias analysis results	% Change in estimate from conventional analysis‡	% Change in interval width from conventional analysis§
Cohort studies								
Ahrens et al. (2012)[38]	Differential exposure misclassification	Beta	Outcome: PPV=0.88, 95% SI: 0.82–0.93 No outcome: PPV=0.85, 95% SI: 0.79–0.90	Not reported**	HR=1.00 95% CI: 0.71–1.41	HR=1.04 95% SI: 0.70–1.52	4	17.1
Brunet et al. (2015)[43]	Nondifferential exposure misclassification	Trapezoidal	Sensitivity: Min=45%, $Mode_1$=50%,$Mode_2$=60%, Max=99%	Specificity: Min=70%, $Mode_1$=80%,$Mode_2$=90%, Max=100%	HOR=1.20 95% CI: 0.73-1.67	HOR=1.11 95% SI: 0.62–1.98	-7.5	44.7
Huybrechts et al. (2014)[39]	Nondifferential outcome misclassification	Triangular	Sensitivity: Min=50%, Mode=75%,Max=100%	Specificity: Min=99.85%, Mode=99.875%,Max=99.9%	**Least biased:** RR=0.66 90% CI: 0.39–1.13 **Most biased:** RR=1.13 90% CI: 0.83–1.52	**Least biased:** RR=0.65 90% SI: 0.36–1.20 **Most biased:** RR=1.24 90% CI: 0.89–1.73	**Least biased:** 1.5 **Most biased:** 9.7	**Least biased:** 13.5 **Most biased:** 53.6
Palmsten et al. (2013)[40]	Nondifferential misclassification	Not reported	Not reported††	Not reported††	**Least biased:** RR= 1.00 95% CI: 0.93–1.07 **Most biased:** RR=1.52 95% CI: 1.26–1.83	**Least biased:** RR=1.00 95% SI: 0.91–1.09 **Most biased:** RR= 2.16 95% SI: 1.38–3.37	**Least biased:** 0.0 **Most biased:** 42.1	**Least biased:** 28.6 **Most biased:** 249.1
Case-control studies								
Barron et al. (2013)[41]	Nondifferential outcome misclassification; differential outcome misclassification	Trapezoidal	*Nondifferential*: Sensitivity: Min=70%, $Mode_1$=75%, $Mode_2$=85%, Max=90% *Differential*: Exposed, sensitivity: Min=70%, $Mode_1$=75%, $Mode_2$=85%, Max=90% Unexposed: sensitivity: Min=80%, $Mode_1$=85%, $Mode_2$=95%, Max=100%	*Nondifferential*: Specificity: Min=94%, $Mode_1$=96%, $Mode_2$=98%, Max=100% *Differential*: Exposed, specificity: Min=94%, $Mode_1$=96%, $Mode_2$=98%, Max=100% Unexposed, specificity: Min=95%, $Mode_1$=97%, $Mode_2$=99%, Max=100%	**Least biased**: OR= 1.30 95% CI: 0.74–2.30 **Most biased**: OR= 2.88 95% CI: 1.11–7.46	*Nondifferential***:** **Least biased**: OR=1.35 95% SI: 0.73–2.60 **Most biased:** OR=4.0 95% SI: 1.39–12.30 *Differential*: **Least biased:** OR=1.46 95% SI: 0.77–2.81 **Most biased:** OR=4.29 95% SI: 1.51–12.79	*Nondifferential*: **Least biased:** 3.8 **Most biased:** 38.9 *Differential*: **Least biased:** 12.3 **Most biased:** **4**9.0	*Nondifferential*: **Least biased:** 19.9 **Most biased:** 71.8 *Differential*: **Least biased:** 30.8 **Most biased:** 77.6
Mahmud et al. (2011)[42]	Nondifferential exposure misclassification	Not reported	Not reported	Not reported	**Scenario 1**‡‡*:* OR=0.90 95% CI: 0.84-0.95 **Scenario 2**‡‡**:** OR=1.01 95% CI: 0.95-1.07	Not reported‡‡	N/A‡‡	N/A‡‡

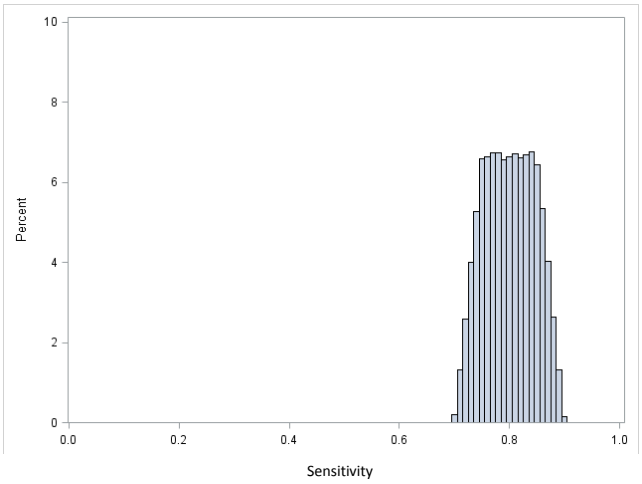
CI, confidence interval; HOR, hazard odds ratio; HR, hazard ratio; NPV, negative predictive value; PPV, positive predictive value; RR, relative risk; SI, simulation interval.
*When misclassification was simulated for multiple exposure-outcome associations, we presented the least and most extreme bias simulations (defined by looking at changes in the effect estimate).
†See eFigure1 for further description of probability distribution types.
‡When conventional effect estimate was <1,estimated as [Effect estimate$_{conventional}$ – Effect estimate$_{probabilistic}$) / Effect estimate$_{conventional}$]*100.
When conventional effect estimate was ≥1, estimated as[Effect estimate$_{probabilistic}$ – Effect estimate$_{conventional}$) / Effect estimate$_{conventional}$]*100.
§Estimated as [SI width$_{probabilistic}$ - CI width$_{conventional}$)/ CI width$_{conventional}$]. Interval width calculated as the upper interval bound – lower interval bound
**Sensitivity and specificity point estimates for calculating negative predictive value were provided (Sensitivity=95%, Specificity=90%)
††Investigators reported that they “used plausible estimates” of sensitivity and specificity based on positive predictive values from internal validation study
‡‡Investigators did not report any quantitative results from bias analysis; they only discussed findings qualitatively. Scenario 1 compares any use of propionates vs. never users. Scenario 2 compares any aspirin use vs. never users.

eFigure 1. Common probability distributions assigned to bias parameters – simulating sensitivity as an example.

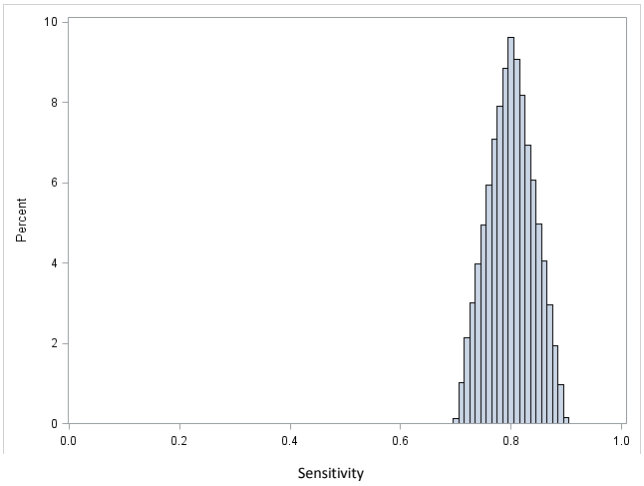
A. Uniform distribution



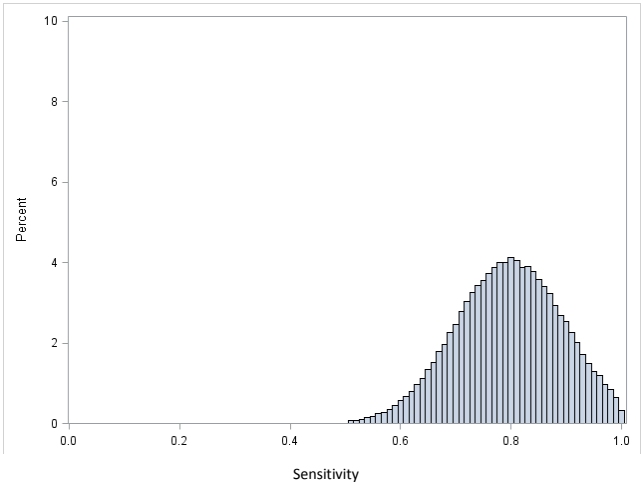
B. Trapezoidal distribution



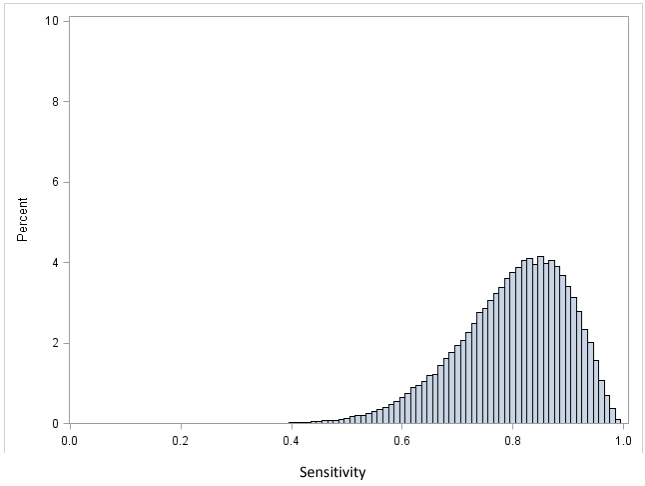
C. Triangular distribution



D. Truncated normal distribution



E. Beta distribution



eFigure 1 shows five commonly simulated probability distributions assigned to bias parameters (simulating plausible distributions for sensitivity as an example). Panel A simulates a uniform probability for sensitivity with a minimum=0.70 and a maximum=0.90. Uniform probability distributions assume that all values between the minimum and maximum are equally plausible. Panel B shows a trapezoidal probability distribution with minimum=0.70, $mode_1$=0.75, $mode_2$=0.85, and maximum=0.90. Trapezoidal distributions assume that values between $mode_1$ and $mode_2$ are equally plausible but assume linear decreases in the probability density between the modes and the tails of the distribution (the minimum and maximum). Panel C shows a triangular distribution with minimum=0.70, mode=0.80, maximum=0.90. Triangular distributions assume a linear decrease from the mode to the distribution tails. Panel D shows a truncated normal distribution with mean=0.8 and standard deviation=0.1; the distribution has been truncated at 1.0 because a sensitivity > 1.0 is impossible. Panel E shows a beta distribution with mean=0.8 and a standard deviation=0.1 simulated with two shape parameters (here: alpha=12; beta=3). Beta distributions are bound between 0 and 1.

Different distribution types (including shape and type of probability distribution assigned) make different assumptions about bias parameters. For example, the uniform and triangular distributions (panels A and C) assume the same range of plausible bias parameters (min=0.70, max=0.90), but the triangular distribution assumes that 0.80 is the most likely value whereas the uniform distribution assumes that all values between the minimum and maximum are equally plausible. Alternatively – when comparing the uniform and beta distribution (panels A and E) – the beta distribution assumes a wider range of plausible values than the uniform distribution (uniform: min=0.70, max=0.90; beta: min=0.26, max=1.0), but values at the tails of the distribution are less likely than the mean/mode of 0.80. Further description of simulating bias parameter distributions is provided elsewhere.[2]