Dear Author,

Attached for your review are the typeset pages of the article, etc. you have written for *Biological Theory*. Please check for accuracy and consistency, placement of illustrations, and answer any queries noted at the end of the pages.

Within three days of receipt, please return these pages to Dan Bouchard at the MIT Press.

You may return your corrected proofs using an overnight delivery service, fax, or email. If you send corrections by email, please list the corrections in the body of the email. Send to:

Dan Bouchard
The MIT Press Journals
238 Main Street, Suite 500
Cambridge, MA 02142

Fax: 617-258-5028
Email: bouchard@mit.edu

If you notice the letters "FPO" on your figure art, this indicates that the figure is either in color or will be shot as a halftone by the printer to capture shades of gray. The FPO marker will not appear on the printed figure. If you want figure art to be printed in color, you must send a check for the printing costs (**$1,200** ***for the first page;*** **$600** ***for each subsequent page***, as noted in the "Information for Contributors") to The MIT Press. If you cannot procure a check within three days, you must acknowledge in writing (e.g. cover letter or email) your agreement to pay for the costs. Figure art lacking either of these two things will be printed in black and white by default.

You can leave phone messages at (617) 258-0588, or feel free to contact me by e-mail at bouchard@mit.edu.

We depend upon your prompt attention to the proof to ensure timely delivery of the journal. If your corrections are not received by the deadline, your article may be published as is.

Thank you very much for your help.

Sincerely,
Dan Bouchard

OFFPRINT ORDERS FOR *Biological Theory*

Prior to publication of your paper, offprints may be purchased at the prices listed below. All orders must be **prepaid**, and payment may be made **only** in the following forms: a check drawn on a U.S. bank, an international money order, VISA, MasterCard, or American Express **(no other credit cards can be accepted).** The MIT Press cannot guarantee that late orders will be placed; to ensure production of your offprints, this form and payment must be returned within 14 days of receipt to:

MIT Press Journals
Attn: Billing Department
238 Main Street, Suite 500
Cambridge, MA 02142-1046
Fax: 617-577-1545

Please print or type, and fill out all items completely.

1) Your name _____

Article name _____

2) How many copies do you want? (Number cannot be smaller than 100, and must be a multiple of 100.) _____

3) Total number of pages in article: _____ . My article runs from pages _____ to _____ .

4) Please refer to the price chart below to calculate the cost of your order.

- for articles over 32 pages, please add the 32-page price to the price for the number of pages over 32 (i.e., for 38 pages, add the 32-page price and the 6-page price).

	.	
pages in article	first 100 offprints	each add'l 100 offprints
1-4	$ 37.00	$ 13.00
5-8	$ 58.00	$ 21.00
9-12	$ 78.00	$ 34.00
13-16	$108.00	$ 42.00
17-20	$128.00	$ 56.00
21-24	$148.00	$ 65.00
25-28	$173.00	$ 76.00
29-32	$202.00	$ 84.00

Total cost of offprints: $_____

Canadian orders please add 5% GST: $_____

TOTAL: $_____

PAYMENT (please print or type):

Amount of check enclosed: _____ made payable to The MIT Press.

¨ VISA # _____

¨ MasterCard # _____

¨ American Express # _____

Expiration date: _____ Signature: _____

SHIP TO:

Name _____

Address _____

_____

_____

Relative Risk and Methodological Rules for Causal Inferences

Kristin Shrader-Frechette
AQ1 Department of Biological Sciences, Department of Philosophy
University of Notre Dame, IN, USA
kshrader@nd.edu

One of the most troubling questions in disciplines from conservation biology and vector ecology to toxicology and epidemiology is how to resolve disagreements over interpreting evidence for causal claims about risk. These disagreements include *whether* or not something is a risk factor for a given biological population and *how* best to explain that population risk. Biologists disagree on the "whether" question, for instance, when they accept (e.g., Moffett et al. 2007), or reject (e.g., Snow et al. 1998), the claim that human population density, not the vector species' niche, is the critical factor determining malaria risk. They disagree on the "how" question, for instance, when they accept (e.g., Maehr and Deason 2002), or reject (e.g., Comiskey et al. 2004; Shrader-Frechette 2004) the claim that the Panther Habitat Evaluation Model, premised on requiring forest habitat patches larger than 500 ha, is a good predictor of Florida panthers' risk of extinction.

Many disagreements about risks to biological populations can be illuminated by more attention to case-specific empirical details. For instance, in the case of the Florida panther, examining nocturnal (e.g., Beier et al. 2003), not merely daytime (Maehr and Deason 2002), habitats has helped to resolve conflicts over extinction risk. In the case of malarial infection, examining average age in mosquito populations and distribution of larval habitat, not merely human population density, has helped resolve conflicts over malaria risk (Smith et al. 2004).

Other conflicts over population risks arise when biologists agree about the relevant empirical data, but disagree about the methodological rules *m* that are used for causal inferences about those data. What are such methodological rules, and why do scientists often disagree about them?

Disagreement about Methodological Rules and the Relative Risk Rule

According to one prominent account, methodological rules dictate means to cognitive ends, as in the following rule *m*: "If you want theories likely to stand up successfully to subsequent testing, then accept only theories that have successfully made surprising predictions, in addition to explaining what is already known, over those which explain only what is already known" (Laudan 1987: 19–26; Doppelt 1990: 12; Schaffner 1993: 390–391). On Laudan's account—as amended by Schmaus (1996), so as to respond to Laudan's critics (e.g., Doppelt 1990)—many methodological rules *m* can be construed as having this form: *If one's goal is to achieve* g*, in an empirical world with characteristics* c*, one ought to do m.*

How might some biological controversies be understood as conflicts over methodological rules, as just defined? Given the same or equivalent data, but different methodological rules for interpreting those data, scientists may draw different conclusions. For instance, when epidemiologists Wynder and Harris (1989) assessed the association between breast cancer and alcohol consumption, they used the methodological rule *m* (that I call) "the relative risk rule" (RRR). According to RRR, alleging that some factor/agent has caused a given harm requires evidence that RR = at least 2, where RR is defined as incidence of harm in a population exposed to some agent, divided by that incidence in a non-exposed population. RR = 1 means the null hypothesis is the case. RR $<$ 1 means the event is less likely to occur in the experimental than in the control group. RR $>$ 1 means the event is more likely to occur in the experimental than in the control group. Higher RR thus indicates stronger statistical associations, as when pack-a-day smokers, compared to nonsmokers, have RR = 10 for developing lung cancer (Foster et al. 1993: 4).

Requiring RRR, Wynder and Harris (1989) denied that moderate alcohol consumption is a causally important risk factor for breast cancer because, for alcohol consumption, 1 $<$ RR $<$ 2. Yet Hiatt (1990) rejected RRR and thus affirmed the

November 21, 2007; accepted December 11, 2007
Biological Theory 2(4) 2007, 1–5.

alcohol-breast cancer association. Instead of RRR, Hiatt used another methodological rule (the external-consistency rule according to which one can make a causal inference if other studies replicate the association). As a consequence, Hiatt claimed there is a small but detectable increased breast-cancer risk associated with alcohol consumption. In other words, he concluded that moderate alcohol consumption is a causally important risk factor for breast cancer, even though he agreed with Wynder and Harris that, for alcohol consumption, $1 < \text{RR} < 2$. Thus he advised women with breast-cancer risk factors to limit their alcohol consumption (see Weed 1997).

Which scientists (Wynder and Harris, or Hiatt) seem more correct regarding the methodological rule RRR? Given weak associations and the impossibility of conclusive statistical findings, either could be correct. If the preceding account of methodological rules *m* is correct, however, the answer also could depend on each study's goals *g*, and on characteristics *c* of the empirical world.

The Wynder-Harris–Hiatt conflict over *m* thus might be explained by their differing *g* and *c*. When Wynder and Harris required RRR and rejected alcohol as a risk factor for breast cancer, their *g* might have been "to discover only major risk factors for breast cancer, those with very strong associations with disease," and their postulated *c* might have been "only a few empirical factors are responsible for increased incidence of breast cancer." Given this *g* and *c*, a reasonable *m* could have been "count only RR = at least 2 as evidence of empirical factors that are causally associated with breast cancer." However, when Hiatt (1990) rejected RRR and accepted alcohol as a risk factor for breast cancer, his *g* might have been "to discover even very small risk factors for breast cancer," and his *c* might have been "many different empirical factors each contribute slightly to increased incidence of breast cancer." Given this *g* and *c*, a reasonable *m* could have been "count even small RRs ($1 < \text{RR} < 2$) as important, if they have been repeatedly replicated."

Why does the preceding account of the Wynder-Harris–Hiatt conflict seem plausible? Although the *m* in question, RRR, requires RR = at least 2 before accepting evidence as adequate for a causal inference about risk, this *m* does not specify either the *g* or *c* on which requiring or not requiring RRR might be conditional. This gap (in the formulation of *m*) suggests at least two hypotheses whose investigation might clarify both *m* and causal inferences about risk. These hypotheses are that (1) by presupposing different *g* or *c*, *m* can be more or less appropriate, and (2) by using meta-analysis both to discover implicit *g* or *c,* and to make them explicit, philosophers of science might help clarify methodological rules *m*. That is, they might help make disagreement over one type of *m* (those that govern causal inferences about population risk) more transparent. For instance, when *g* and *c* are not made explicit, one easily can think of some *g* (e.g., avoiding false positives) and *c* (e.g., the relevant risk is not seriously harmful) for which requiring RRR might be reasonable. Likewise, one easily can think of some *g* (e.g., avoiding false negatives) and *c* (e.g., the relevant risk is catastrophic) for which requiring RRR might not be reasonable. In the absence of case-specific information about *g* and *c*, however, should the *prima facie* requirement of RRR be the default *m* position? To answer this question, consider first what can be said on behalf of requiring RRR.

The *Prima Facie* Case for Requiring RRR for Risk Inferences

Authors like Foster et al. (1993: 5) and Breslow (2003) require RRR because their *g* (although they explicitly use neither "goal" language nor this symbol) is to avoid postulating causes on the basis of apparently weak associations. They argue that although scientists might report RRs just above 1, because the margin of sampling error might include RR = 1, these RRs are likely only "phantom risks." They also say that the benefits of requiring RRR (the various *g* that it achieves) are the transparency of its grounds for causal inferences about population risks, and RRR's limiting the latitude of judgments that experts can use to interpret alleged causal effects.

Requiring methodological rules *m* (for causal inferences about population risk) that are at least as strong as RRR was apparent, 12 years ago, when *Science* editors interviewed top epidemiologists and biologists—e.g., Philip Cole, Richard Doll, Alvin Feinstein, Joe Fraumeni, Sander Greenland, Richard Peto, Charles Poole, Ross Prentice, Jamie Robins, Ken Rothman, David Sackett, David Savitz, David Thomas, Dimitrios Thomas, Lewis Thomas, Robert Temple, Michael Thun, Noel Weiss, and Walter Willett (Taubes 1995). Virtually all those interviewed (except for John Bailar) said they required RR = 2, 3, 4, or more, before they were willing to make a causal inference about risk. "As a general rule of thumb," Marcia Angell (then coeditor of the *New England Journal of Medicine*, along with Jerome Kassirer), said the journal would publish epidemiology articles only when RR = 3 or higher (Taubes 1995: 168). Robert Temple, evaluation director for the US Food and Drug Administration, likewise claimed his agency wanted RR = 3, 4, or more before supporting a causal inference (Taubes 1995: 168). Presenting a list of 25 alleged associations (e.g., between vasectomy and prostate cancer), for most of which RRs were small ($1 < \text{RRs} < 2$), the *Science* authors said that, because most of these alleged associations had not been replicated, requiring RRR was needed to achieve a particular *g* (although they did not explicitly use "goal" language), namely, avoiding spurious associations (Taubes 1995: 165). Consistent with such epidemiological and biological support for requiring *m* at least as strong as RRR, roughly half of the courts that discuss RR require RRR (RR = at least 2) for proof of causation in toxic-tort cases (Cranor 2006: 233).

The *Prima Facie* Case against Requiring RRR

Are these many scientists correct to require either RRR or RR = 3 or more? As already mentioned, while requiring RRR is *ultima facie* reasonable given some *g* (e.g., avoiding false positives) and *c* (e.g., only trivial risks are involved), at least eleven considerations—six epistemic, three ethical, and two practical—suggest one should be wary of *prima facie* requiring RRR as a default rule *m* for interpreting evidence about risks to populations.

On the *epistemic* side, those who require RRR (for causal inferences about risks) appear to confuse two different things: certainty of causation and frequency of adverse effects. While RR measures only the latter, many proponents who require RRR (e.g., Foster et al. 1993; Breslow 2003) do so on grounds that it provides greater certainty about causation. This is a noble goal, but one not precisely tied to RR. In confusing certainty of causation and frequency of adverse effects, proponents who require RRR forget that great *uncertainty* about causation is compatible with *high frequency* of adverse effects, like RR $>$ 5, while near-*certainty* about causation is compatible with a *low frequency* of adverse effects, like $1 <$ RR < 2. Proponents who require RRR often erroneously suggest that frequent adverse effects, alone, provide greater certainty about causation.

A second epistemic consideration against requiring RRR is that, because any RR $>$ 1 can support causal evidence of increased harm, those who require RRR specify an arbitrary cut-off for when causal evidence is compelling. There are no clear grounds for requiring RR = 2, 3, 4, or more (as the preceding *Science* discussion suggests)—especially if higher RRs indicate greater frequency, rather than greater certainty, of adverse effects.

A third epistemic problem with requiring RRR is that doing so is inconsistent with current scientific findings. For instance, radiation biologists have long known that for the roughly 20 radiation-induced cancers (like those of the bone, esophagus, stomach, colon, lung, lymph nodes), all except four (leukemia, multiple myeloma, urinary-tract, and colon cancer) have small RRs ($1 <$ RR < 2); yet radiation is accepted as one of the factors able to induce these 16 cancers (NRC 2005; Jones and Southwood 1987). If radiation biologists had required RRR before making causal inferences about radiation risk for these 16 cancers, they would have missed identifying an important carcinogen and erroneously encouraged weaker regulatory standards for ionizing radiation.

A fourth epistemic point is that requiring RRR may be unnecessary, if one's goal is to achieve greater causal certainty and to avoid false positives, false assertions of causal links between some risk factor and harm. Because scientists require virtually all research results to be replicated, before they are accepted, this *m* (replication), rather than requiring RRR, could help avoid false positives and ensure greater confirmation of results.

A fifth epistemic consideration, against requiring RRR, is premised on the observation that biological sciences like vector biology and epidemiology often involve more initial conditions and auxiliary hypotheses than do most physical sciences (Schaffner 1993: 139–142). For instance, one auxiliary hypothesis of epidemiologists might be that avoiding some risk is necessary to protect public health. These initial conditions and hypotheses might complicate studies about population risks and might require scientists to assess not only epistemic concerns and pure science, but also welfare consequences, possible harms or benefits. As a consequence, the frequent need to assess welfare consequences provides population-risk studies with *prima facie* reasons for avoiding *m* (e.g., requiring RRR, minimizing false positives) that are more applicable to purer and purely-physical sciences (see Shrader-Frechette and McCoy 1993). Facing statistical uncertainty and welfare concerns, scientists studying population risks must "weigh carefully the value of what is to be won or lost, against the odds of winning or losing ... If a lot might be lost if we are wrong, we want higher probabilities that we are right before we act" (Clouser 1985: 44). Thus, although Neyman-Pearson suggests that minimizing false positives is a more important *g* for pure scientists (Schaffner 1993: 253), whenever biologists studying population risks have *g* that require them to minimize false negatives, it is reasonable to reject RRR as required for causal inferences (see Clouser 1985).

A final epistemic consideration against *prima facie* requiring RRR, as a default rule *m* in population-risk studies, is that doing so appears contrary to demarcation criteria often used in practical sciences like conservation biology and epidemiology. Although researchers in such sciences realize that they bear the burden of proof for inferring risk (see Amsterdamska 2005), their disciplinary demarcation criteria often are not purely epistemic. For instance, they say (1) their discipline focuses on minimizing harm (Burney 1959; Amsterdamska 2005), not merely falsehoods (Rothman 1998; Matthews 1995); and (2) their discipline focuses on positing causal inferences that require merely a preponderance of evidence (Hammond 1955; Wynder 1961), not merely confirmation beyond a reasonable doubt (Little 1961). For two reasons, using demarcation criteria like (1) and (2) argues against requiring RRR for causal inferences about population risks. One reason is that requiring RRR is less likely (than requiring *m* such as replication and RR $>$ 1) to meet (1), as radiation-induced cancer illustrates. The second reason is that requiring RRR is much stricter than demarcation criteria like (2) specify.

On the *ethics* side, requiring RRR (rather than *m* like replication and RR $>$ 1) for causal inferences would allow greater imposition of population risks, because fewer risks would be identified as such. Moreover, requiring RRR falsely suggests

that risk impositions in which $1 < RR < 2$ are ethically acceptable. For large populations, $1 < RR < 2$ could cause many additional deaths, as from alcohol-induced breast cancer, or cancer from US nuclear-weapons testing—estimated to have caused from hundreds of thousands (IOM 1998), to a million, additional cancers (Makhijani et al. 1995). Requiring RRR, thus ignoring possible risks when $1 < RR < 2$, is like allowing people to play Russian roulette, provided it does not double their chances of death. Such considerations suggest that scientists ought to use less demanding *m* (than requiring RRR) for assessing potential risks that are undesirable, catastrophic, or violate rights e.g., pollution-induced extinction risks, or cancer risks to victims who neither consent to, nor benefit from, the risks.

Another ethics worry is that requiring RRR, which is based on average RR, would not protect sensitive subpopulations who could be harmed seriously and at great frequency, even if $1 < RR < 2$ (see Perera 1996). As already mentioned, most radiation-induced cancers do not satisfy RRR, yet for identical exposures when all other things are equal, radiation-induced cancers are more likely in women than men, and many times more likely in children than adults (Jones and Southwood 1987; IOM 1998; NRC 2005). Therefore, *m* that are more lenient (than requiring RRR) seem needed to protect vulnerable groups. A third ethics worry focuses on rights to equal protection. All other things being equal, people harmed by risks (whose $1 < RR < 2$) do not suffer less harm, simply because the set of those harmed is smaller than the set of those harmed by agents whose $RR > 2$. If not, requiring RRR, for causal inferences about population risk, is ethically questionable on grounds of inadequately protecting individual rights (see Rothman and Greenland 2005).

On the practical side, a *prima facie* requirement for using more risk-sensitive *m* (such as requiring replication and $RR > 1$), rather than RRR, may be needed to counterbalance pressures from special interests. When biologists confirm exposure-harm associations (e.g., lung cancer from tobacco smoke, species extinction from habitat development), special interests often subject these scientists to professional defamation and harassment (Parascandola 1998). Trying to discredit causal inferences whose identification could harm their profits, special interests frequently do "private-interest science," flawed science designed to achieve extraneous ends, rather than reliable conclusions (Shrader-Frechette 2007). Requiring RRR makes it easier for special interests to use private-interest science and to deny the harms they cause.

Other practically relevant *c* also argue *against* requiring RRR and *for* requiring more risk-sensitive *m* that might help to counterbalance special-interest pressures. For instance, the American Association for the Advancement of Science confirms that three-fourths of all US science is funded by special interests, often anti-regulatory interests (Barnes and Bero 1998; Koizumi 2005). As Krimsky (2003) showed, one consequence (of such disproportionate special-interest funding of science) is false-negative biases in most pharmaceutical-industry studies of drug risks. The Science Advisory Board of the US Environmental Protection Agency (EPA) found similar false-negative biases in all pesticide-industry studies of chemical risks (submitted to EPA for use in setting pesticide regulations); all the industry studies used too-small sample sizes, mostly under 50 (EPA 2000). If such cases are typical, and if special interests routinely use *m* (that have false-negative biases) to assess the risks of their products, requiring RRR would further contribute to such biases. Not requiring RRR for causal inferences thus might help counterbalance these biases.

Conclusion

Given the preceding account of methodological rules *m*, some disagreements over *m* can be explained in terms of conflicts over *g* or *c*, as in the case of RRR. For some *g* or *c*, requiring RRR is reasonable. However, for most biological studies of risks to populations, requiring RRR is not a reasonable *prima facie* rule *m* because of epistemic, ethical, and practical problems often associated with risk-related *g* or *c*.

Acknowledgment

The author thanks the US National Science Foundation (NSF) for the History and Philosophy of Science research grant, "Three Methodological Rules in Risk Assessment," 2007–2009, through which work on this project was done. All opinions and errors are those of the author, not the US NSF.

References

Amsterdamska O (2005) Demarcating epidemiology. Science, Technology, and Human Values 30(1): 17–51.

Barnes D, Bero L (1998) Why review articles on the health effects of passive smoking reach different conclusions. Journal of the American Medical Association 279: 1566–1570.

Beier P, Vaughan MR, Conroy MJ, Quigley H (2003) An analysis of scientific literature related to the Florida panther. Submitted as final report for Project NG01-105. Tallahassee, FL: Florida Fish and Wildlife Conservation Commission.

Breslow N (2003) Are statistical contributions to medicine undervalued? Biometrics 59(1): 1–8.

Burney L (1955) Smoking and lung cancer. Journal of the American Medical Association 171: 1829–1836.

Clouser K (1985) Approaching the logic of diagnosis. In: Logic of Discovery and Diagnosis in Medicine (Schaffner KF, ed), 35–55. Berkeley: University of California Press.

Comiskey EJ, Eller AC, Perkins DW (2004) Evaluating impacts to Florida panther habitat: How porous is the umbrella? Southeastern Naturalist 3: 51–74.

Cranor C (2006) Toxic Torts. New York: Cambridge University Press.

Doppelt G (1990) The naturalist conception of methodological standards in science. Philosophy of Science 57: 1–19.

Environmental Protection Agency (EPA), Science Advisory Board (2000) Comments on the Use of Data from the Testing of Human Subjects, EPA-SAB-EC-00-017. Washington, DC: US EPA.

Foster KR, Bernstein DE, and Huber PW (1993) Phantom Risk. Cambridge, MA: MIT Press.

Hammond E (1955) Cause and effect. In: The Biologic Effects of Tobacco (Wynder E, ed), 193–194. Boston: Little, Brown.

Hiatt RA (1990) Alcohol consumption and breast cancer. Medical Oncology Tumor Pharmacotherapy 7: 143–51.

Institute of Medicine (IOM) (1998) Exposure of the American People to Iodine-131 from Nevada Nuclear-Bomb Tests. Washington, DC: National Academy Press.

Jones R, Southwood R, eds (1987) Radiation and Health. Chichester: Wiley.

Koizumi K (2005) AAAS Report XXIX: R&D Trends and Special Analyses. Washington, DC: AAAS.

Krimsky S (2003) Science in the Private Interest. Lanham, MD: Rowman and Littlefield.

Laudan L (1987) Progress or rationality. American Philosophical Quarterly 24: 19–32.

Little C (1961) Some phases of the problem of smoking and lung cancer. New England Journal of Medicine 264: 1241–1245.

Maehr DS, Deason JP (2002) Wide-ranging carnivores and development permits. Clean Technologies and Environmental Policy 3: 398–406.

Makhijani A, Hu H, Yih K, eds (1995) Nuclear Wastelands. Cambridge, MA: MIT Press.

Matthews J (1995) Major Greenwood versus Almroth Wright: Contrasting visions of "scientific" medicine in Edwardian Britain. Bulletin of the History of Medicine 69: 30–43.

Moffett A, Shackelford N, Sarkar S (2007) Malaria in Africa: Vector species' niche models and relative-risk maps. PLoS ONE 2(9). www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pubmed&pubmedic =17786196

National Research Council (NRC) (2005) Health Risks from Exposure to Low Levels of Ionizing Radiation, BEIR VII. Washington, DC: National Academy Press.

Parascandola M (1998) Epidemiology: Second-rate science? Public Health Reports 113: 312–320.

Perera F (1996) Molecular epidemiology. Journal of the National Cancer Institute 88: 496–509.

Rothman KJ (1998) Should the mission of epidemiology include the eradication of poverty? The Lancet 352: 810–813.

Rothman KJ, Greenland S (2005) Causation and causal inference in epidemiology. American Journal of Public Health 95: S144–S150.

Schaffner KF (1993) Discovery and Explanation in Biology and Medicine. Chicago: University of Chicago Press.

Schmaus W (1996) The empirical character of methodological rules. Philosophy of Science 63: S98–106.

Shrader-Frechette KS (2004) Measurement problems and Florida panther models. Southeastern Naturalist 3: 37–50.

Shrader-Frechette KS (2007) Taking Action, Saving Lives: Our Duties to Protect Public and Environmental Health. New York: Oxford University Press.

Shrader-Frechette KS, McCoy ED (1993) Method in Ecology: Strategies for Conservation. New York: Cambridge University Press.

Smith DL, Dushoff J, McKenzie FE (2004) The risk of a mosquito-borne infection in a heterogeneous environment. PLoS Biology 2(11). http://biology.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pbio.0020368

Snow RW, Peshu N, Forster D, Bomu G, Mitsanze E, Ngumbao E, Chisengwa R, Armstrong Schellenberg JRM, Hayes RJ, Newbold CI, Marsh K (1998) Environmental and entomological risk factors for the development of clinical malaria among children on the Kenyan coast. Transactions of the Royal Society of Tropical Medicine and Hygiene 92: 381–385.

Taubes G (1995) Epidemiology faces its limits. Science 268: 164–169.

Weed D (1997) Underdetermination and incommensurability in contemporary epidemiology. Kennedy Institute of Ethics Journal 7(2): 107–124.

Wynder EL (1961) An appraisal of the smoking-lung-cancer issue. New England Journal of Medicine 264: 1235–1240.

Wynder EL, Higgins IT, Harris RE (1989) The wish bias. Journal of Clinical Epidemiology 43: 619–621.

Queries

AQ1. Au: Please confirm whether you want to retain this or deleted in AFF.
AQ2. AU: Please update the reference.