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Special Contribution

Basic Epidemiology
—Methods and their Application to Epidemiology on Cancer and Radiation (6)

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XIV. Non-differential miss-classification

2. Case ascertainment

Let us consider a follow-up study of 150,000 exposed men who were born in 1930 and exposed to a radiation dose of 20 mGy at age 30, and the same number of unexposed men belonging to the same birth cohort. Suppose that there are 10,000 solid cancer cases diagnosed at age 70 each in the two groups. If the expected number of cases is 10,000 for both groups, the ratio between the observed and the expected is 10,000/10,000 = 1 in both groups. The relative risk comparing the solid cancer risk in the exposed and unexposed groups can be obtained by dividing those two ratios, and is 1. If 80% of cases are ascertained in the exposed and unexposed groups, the corresponding RR is still 1 as long as the proportions of ascertained cases are the same in both groups. As shown in this example, non-differential case ascertainment is not expected to produce a biased estimate of RR or ERR. However, this is merely a theoretical expectation. In reality, the magnitude of case ascertainment among the exposed and unexposed groups can differ by chance even if the proportions of ascertained cases are expected to be the same in the exposed and unexposed groups. Suppose that the proportions of case ascertainment happened to be 80.2% and 79.8% in the exposed and the unexposed, respectively, the RR will be 1.005 (= 0.802/0.798). The probability of obtaining such ascertainment rates is approximately 10% (The following is the R commands to obtaining this probability: (1 - pbinom(8,020, size = 10,000, prob = 0.80))*pbinom (7,980, size = 10,000, prob = 0.80)). This RR corresponds to the ERR of 0.25 per gray since the dose of the exposed group was 20 mGy. This value is not much different from the ERR per gray of 0.35 for men reported by the LSS of atomic bomb survivors[54]. In the case of cancer mortality study, case ascertainment can be as low as 80%, considering the accuracy of cause of death. If cancer mortality is regarded as a surrogate indicator of cancer incidence, the proportion of case "ascertainment is even lower since mortality survey covers only deceased cases. Therefore, it does not seem a good idea to examine the cancer mortality associated with radiation dose as low as 20 mGy.

Incomplete ascertainment of out-migrated subjects from the fixed cohort inflates person-years. In cancer incidence studies, incomplete ascertainment of deaths from causes other than cancer has a similar effect on person-year calculations. Because the person-years are the denominator of the cancer incidence rate, essentially the same discussion as for case ascertainment can be applied to these problems. Non-differential misclassification in the person-year calculation affects the absolute risk in a manner similar to that for non-differential case ascertainment (the absolute risk is underestimated when person-years are overestimated).

Biased case ascertainment is suspected in the study of Carl J Johnson reporting an excess cancer incidence among Mormon families in southwestern Utah.

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The study area had radioactive fallout from nuclear detonations in the Nevada Test Site (NTS). In the NTS, atmospheric detonations were conducted during the period 1951-1962; and underground detonations, during the period 1962-1979[61]. There were 109 more cases of cancer than expected (288 observed/179 expected) in the 1951 cohort (N = 4,125) when compared with that of all Utah Mormons during the period 1967-75). However, it is suspected his study tended to identify cancer cases having lived during the period 1951-1962 more completely and tended to miss the cases without such residential history.

3. Exposure assessment

Indoor radon exposure is considered to increase lung cancer risk[62, 63]. The free fraction or unattached fraction of radon progeny gives significant dose to larger airways. Some houses in thoron-prone areas or houses built with thoron emitting materials have relatively high indoor thoron gas concentrations. In those houses, thoron contamination in radon gas measurements using air-based devices cannot be ignored if the devices sensitive to thoron are placed closely to the wall or floor. Actually, RadTrak, an air-based radon measuring device, which were used in many epidemiological studies to evaluate the association between lung cancer risk and indoor radon exposure, is known to be affected by the presence of thoron[64]. Since indoor radon and thoron gas concentrations do not show any predictable correlation, it is difficult to tell to which direction an ERR per unit radon concentration will be biased by thoron contamination.

Let us consider this problem with an example. Suppose that lung cancer incidence per 100,000 is 10 for the control group with a radon concentration of 10 Bq/m^3, and 100 for the exposed group (110 Bq/m^3). In this case, the RR comparing the exposed and control groups is 10, and the ERR per 100 Bq/m^3 is 9. Suppose also that thoron gas contamination increases measured indoor radon concentrations. However, it is difficult to tell whether the radon measurement in the control group (with a small amount of radon exposure), the radon-exposed group, or both groups is affected more evidently or not, since there is no correlation between radon and thoron gas concentrations. Therefore, it is difficult to tell whether the ERR estimate per unit dose will be decreased, increased, or unchanged by the contamination.

In this scenario, thoron exposure is assumed not to increase lung cancer risk. Indeed, it is considered that thoron progeny do not give significant dose to bronchial mucosa (2). It is because most thoron progeny are attached to aerosol particles in the air since thoron progeny have relatively long half-lives when compared with radon progeny. However, we cannot deny the possibility that ^{216}Po, a thoron progeny with the half-life of 0.15 second emitting alpha radiation, gives significant dose to the bronchial mucosa. Note that such a short half-life progeny can be present in the unattached form in the air is yet unclear[65]. If thoron progeny exposure is associated with lung cancer risk, the problem of thoron contamination in radon measurements is more serious when examining the association of radon and radon progeny exposure with lung cancer risk.

XV. Biases affecting the association between risk and radiation exposure

There are many different kinds of biases as shown in a catalogue of biases summarized by Sackett (1979)[66]. To date, methodologists identified more than 100 of biases (with different names). However, you do not need to remember all of them. All you have to do is to understand the underlying mechanisms causing them. Actually, most of the biases are caused by several common mechanisms. In this chapter, several important examples of such biases in radiation epidemiology are described.

1. Detection bias

The detection bias is "due to systematic error(s) in methods of ascertainment, diagnosis, or verification of cases in an epidemiologic study." (DE-IV)[2]. Typically, the detection bias is observed in a situation where special diagnostic procedures detect asymptomatic diseases. If the magnitude of case ascertainment is affected by the exposure status of study subjects, the association between the disease risk of interest and the exposure under survey will be distorted. In radiation epidemiology, a detection bias caused by screening (screening bias) observed in thyroid cancer survey is well-known. After Chernobyl accident, thyroid cancer risk increased among those who were under age 15 years at the time of the accident. However, an excess among older residents was / still is unclear. A study conducted in Bryansk, which is one of the most heavily contaminated area in Russia, found that the frequency of thyroid cancer among residents aged 15-69 in this area was evidently higher than that in the general population of the entire Russia[67]. However, since the inverse dose-response was observed, the observed excess is unlikely be due to radiation exposure. Another possible explanation is that medical attention to thyroid cancer in the contaminated areas resulted in a substantial screening bias, particularly in the 1990s, following the discovery of excess thyroid cancer among children. UNSCEAR 2008 report pointed out that those observations can be affected by the screening effect mainly due the use of ultrasonography[68]. A study conducted in the 1990s has

shown that physical examinations found only 21% of nodules detected by high-resolution ultrasonography[69]. In the case of the Fukushima Thyroid Survey, more advance ultrasonography techniques are used, and Peter Jacob and his colleagues predicted that the ultrasonography survey will increase baseline thyroid cancer incidence by a factor of 7.4 (95% CI 0.95; 17.3)[70].

Another famous example of detection bias is also about thyroid cancer. In 1974, US newspapers reported a thyroid cancer among those who had head and neck radiation. After this report, Michael Reese Hospital in Chicago started the examination in response to the public concern caused by the media. As a result, the frequency of thyroid diseases among those people jumped from 1.4/1000 before 1974 to 16.9/1000 during the period 1974-79 even though those people received radiation doses below 500 mGy[71].

2. Recall bias

Recall bias is a "systematic error due to differences in accuracy or completeness of recall to memory of past events or experiences."(DE-IV)[2] An interesting example of a recall bias was reported by WJ Schull and S Cobb. In their study, rheumatic patients and their siblings were interviewed and their parents' history of rheumatism was asked. In this study, 73% of rheumatic patients answered that their parents had rheumatism while only 50% of patients' siblings answered so[72] even though they had the same parents.

A recall bias is suspected in the case-control study of leukemia in the neighborhood of La Hague nuclear reprocessing plant in France[34] (this study conducted by Pobel and Viel was already mentioned in chapter IV). In this study, investigators obtained a RR of 4.5 (95% CI: 1.5 - 15.2) for those who used the local beach once or more in a month when compared to those who never used the beach. The observed association can be explained, at least partially, by a recall bias. For example, parents of controls might have forgotten the fact that their children played in the beach more frequently than the parents of cases.

3. Selection bias – a systematic error

More than two thousand years ago, Marcus Tullius Cicero presented the following story: One Diagoras, a nonbeliever in the gods, was shown painted tablets bearing the portraits of some worshippers who prayed, then survived a subsequent shipwreck. The implication was that praying protects you from drowning. Diagoras asked, "Where were the pictures of those who prayed, then drowned?"(cited from Black Swan written by Nassim Nicholas Taleb)[73]. This episode can be regarded as an example of selection bias.

John M Last defined the selection bias as follows: "It is an error due to systematic differences in characteristics between those who take part in a study and those who do not." (DE-IV)[2] He pointed out that "selection bias invalidates conclusions and generalizations that might otherwise be drawn from such studies." (DE-IV)[2]

Rothman and Greenland (ME-II)[8] gives the definition of selection bias as follows: "Selection biases are distorted results from procedures used to select subjects and from factors that influence study participation. The common element of such biases is that the relation between exposure and disease is different for those who participate and those who should be theoretically eligible for study, including those who do not participate. The result is that the associations observed in the study represent a mix of forces determining participation, as well as forces determining disease." "it is sometimes (but not always) possible to disentangle the effects of participation determinant from those disease determinants using analytic methods for the control of confounding."

Note that the definition by John M Last includes the lack of generalization. Rothman and other epidemiologists deemphasize the importance of the lack of generalizability in epidemiological studies evaluating causal relationships. Here, we use Rothman's definition. The selection biases distort the relationship between the exposure and the disease. Note that this kind of selection bias cannot be eliminated by statistical analysis of the data obtained. However, the selection bias introduced by matching can be remedied in the analysis via control of the matching factors.

A famous example of the selection bias is the one pointed out by Joseph Berkson, Mayo Clinic statistician. He criticized the first hospital-based case-control study on smoking and lung cancer, in which cases and controls were selected from hospital patients. He argued that smokers with lung cancer being more likely to be hospitalized than smokers without cancer[14].

The case–control study of Pobel and Viel is also suspected to have a selection bias. Parents of cases who were concerned about the possible exposure to radiation from La Hague might have been more likely to be included in the study than controls.

In a retrospective cohort study, living subjects and workers with higher-level exposure can be more easily ascertained. For example, in a study of nuclear workers in Japan, the cohort was established using the workers who were identified through address records[28]. There were a number of workers who had left the job many years ago. In this study, workers with a shorter period of employment and those deceased long time ago were more difficult to find.

Another interesting example is given by Rothman and

Greenland (ME-II. P119). This textbook cited the study by Caldwell *et al*[74]. They wrote as follows: "When Center for Disease Control investigated subsequent leukemia incidence among troops who had been present at the Smoky Atomic Test in Nevada, 76% of the troops identified as members of that cohort had known outcomes. Of this 76%, 82% were traced by the investigators, but the other 18% contacted the investigators on their own initiative in response to publicity about the investigation." Citing a paper by Criqui *et al*.[75], Rothman and Greenland made the following comment: "This self-referral of subjects is ordinarily considered a threat to validity, since the reasons for self-referral may be associated with the outcome understudy".

References

1. WHO. Health topics: Epidemiology [homepage on the internet.] Available from: http://www.who.int/topics/epidemiology/en/
2. Last J. A Dictionary of Epidemiology, 4th ed. International Epidemiological Association. Oxford: Oxford University Press; 2001.
3. Porta M. A Dictionary of Epidemiology, 5th ed. International Epidemiological Association. Oxford: Oxford University Press; 2008.
4. National Cancer Institute. NCI Dictionary of Cancer Terms: observational study [Internet]. Available from: http://www.cancer.gov/dictionary
5. Brown JR and Thornton JL. Percivall Pott (1714–1788) and Chimney Sweepers' Cancer of the Scrotum. Br J Ind Med.1957;14(1):68–70.
6. Lind J. A Treatise of the Scurvy in Three Parts. Containing an inquiry into the Nature, Causes and Cure of that Disease, together with a Critical and Chronological View of what has been published on the subject. London: Millar; 1753.
7. Hempel S. John Snow. The Lancet [serial online]. 381(9874):1269–70. Available from:http://www.thelancet.com/journals/lancet/article/PIIS0140–6736(13)60830–2/fulltext
8. Rothman KJ, Greenland S. Modern Epidemiology 2nd ed. Philadelphia: Lippincott Williams and Wilkins; 1998.
9. Gardner MJ, Winter PD. Mortality in Cumberland during 1959–78 with reference to cancer in young people around Windscale. Lancet 1984;1(8370):216–7.
10. Gardner MJ, Hall AJ, Downes S, Terrell JD. Follow up study of children born to mothers resident in Seascale, West Cumbria (birth cohort). BM J. 1987;295:822–7.
11. Gardner MJ, Hall AJ, Downes S, Terrell JD. Follow up study of children born elsewhere but attending schools in Seascale, West Cumbria (schools cohort): BMJ. 1987;295:819–22.
12. Lagakos SW, Mosteller F. Assigned shares in compensation for radiation-related cancers. Risk Anal. 1986;6:345–57.
13. Kreyszig E. Introductory mathematical statistics. Principles and methods. New York: John Wiley & Sons. Inc.; 1970.
14. Miettinen OS. Theoretical Epidemiology. New York: Wiley; 1985.
15. Rothman KJ, Greenland S. Modern Epidemiology 3rd ed. Philadelphia: Lippincott Williams and Wilkins; 2008.
16. Beebe G, Usagawa M. The major ABCC samples. TR12–68. Hiroshima: Atomic Bomb Casualty Commission; 1968.
17. Radiation Effects Research Foundation. Active Research Protocols [Internet]. Hiroshima: Radiation Effects Research Foundation. Available from: http://www.rerf.or.jp/programs/rp_e/index.html.
18. Nair MK, Nambi KS, Amma NS. Gangadharan P, Jayalekshmi P, Jayadevan S et al. Population study in the high natural background radiation area in Kerala, India. Radiat Res. 1999;152:S145–8.
19. Azizova TV, Muirhead CR, Druzhinina MB, Grigoryeva ES, Vlasenko EV, Sumina MV et al. Cerebrovascular diseases in the cohort of workers first employed at Mayak PA in 1948–1958. Radiat Res. 2010;174:851–64.
20. Krestinina LY, Davis F, Ostroumova E, Epifanova S, Degteva M, Preston D et al. Solid cancer incidence and low-dose-rate radiation exposures in the Techa River cohort: 1956–2002. Int J Epidemiol. 2007;36:1038–46.
21. Bauer S, Gusev BI, Pivina LM, Apsalikov KN, Grosche B. Radiation exposure due to local fallout from Soviet atmospheric nuclear weapons testing in Kazakhstan: solid cancer mortality in the Semipalatinsk historical cohort, 1960–1999. Radiat Res. 2005;164:409–19.
22. Tung CJ, Chao TC, Chen TR, Hsu FY, Lee IT, Chang SL et al. Dose reconstruction for residents living in ^{60}Co-contaminated rebar buildings. Health Phys. 1998;74:707–13.
23. Chen, WL. Radiation surveys and dose equivalent assessments for 60Co-contaminated rebar buildings. Appl Radiat Isot. 2002;56:901–6.
24. Hwang SL, Guo HR, Hsieh WA, Hwang JS, Lee SD, Tang JL et al. Cancer risks in a population with prolonged low dose-rate gamma-radiation exposure in radiocontaminated buildings, 1983–2002. Int J Radiat Biol 2006;82:849–58.
25. Azizova TV, Muirhead CR, Druzhinina MB, Grigoryeva ES, Vlasenko EV, Sumina MV et al. Cardiovascular diseases in the cohort of workers first employed at Mayak PA in 1948–1958. Radiat Res. 2010;174:155–68.
26. Ivanov VK, Maksioutov MA, Chekin SYu, Kruglova ZG, Petrov AV, Tsyb AF et al. Radiation-epidemiological analysis of incidence of non-cancer diseases among the Chernobyl liquidators. Health Phys. 2000;78:495–501.
27. http://www.nrer.ru/rgmdr_eng.html.
28. Hosoda Y, Kuba M, Miyake T, Kudo S, Matsudaira H, Kaneko M et al. First Analysis of Mortality of Nuclear Industry Workers in Japan,1986–1992. J Health Phys 1997;32:173–84.
29. United Nations Scientific Committee on the Effects of Atomic Radiation. Effects of Ionizing Radiation. Annex A: Epidemiological studies of radiation carcinogenesis.Vienna. United Nations; 2006. 322p. Report No.: I.
30. Clark GN, Briggs A, Cooke AM. A history of the Royal College of Physicians of London. Oxford: Oxford University Press; 2005.
31. Gardner MJ, Snee MP, Hall AJ, Powell CA, Downes S, Terrell JD. Results of case-control study of leukemia and lymphoma among young people near Sellafield nuclear plant in West Cumbria. BMJ. 1990;300:423–9.
32. Doll R, Evans J, Darby SC. Paternal exposure not to blame, Commentary Nature. 1994;367:678–80.
33. HSE investigation of leukemia and other cancers in the children of male workers at Sellafield. HSE Books 1994.
34. Pobel D, Viel JF. Case-control study of leukaemia among young people near La Hague nuclear reprocessing plant: the environmental hypothesis revisited. BMJ. 1997;314:101–6.
35. Miettinen O. Estimability and estimation in case-referent studies. Am J Epidemiol. 1976;103:226–335.
36. Kendall GM, Little MP, Wakeford R, Bunch KJ, Miles JC, Vincent TJ, et al. A record-based case-control study of natural background

radiation and the incidence of childhood leukaemia and other cancers in Great Britain during 1980–2006. Leukemia. 2013;27:3–9.

37. Sato Y, Akiba S, Kubo O, Yamaguchi N. A case-case study of mobile phone use and acoustic neuroma risk in Japan. Bioelectromagnetics 2011;32:85–93.

38. Walker AM. Anamorphic analysis: sampling and estimation for covariate effects when both exposure and disease are known. Biometrics 1982;38:1025–32.

39. White JE. A two stage design for the study of the relationship between a rare exposure and a rare disease. Am J Epidemiol. 1982;115:119–28.

40. Langholz B, Clayton D. Sampling strategies in nested case-control studies. Environ Health Perspect. 1994;102 (Suppl. 8):47–51.

41. Ebi KL, Zaffanella LE and Greenland S. Application of the case-specular method to two studies of wire codes and childhood cancers. Epidemiology. 1999;10:398–404.

42. Cohen BL. Test of the linear no-threshold theory of radiation carcinogenesis for inhaled radon decay products. Health Phys. 1995;68:157–74.

43. Darby S and Doll R. Reply to 'Explaining the lung cancer versus radon exposure data for USA counties'. J Radiol Prot. 2000;20:221–2.

44. Ahmad OB, Boschi-Pinto C, Lopez AD, Murray CJL,Lozano R, Inoue M. et al. Age standardization of rates: a new WHO standard. GPE Discussion Paper Series: No.31 EIP/GPE/EBD. Geneva: World Health Organization; 2001.

45. Brenner AV, Tronko MD, Hatch M, Bogdanova TI, Oliynik VA, Lubin JH et al. I-131 dose response for incident thyroid cancers in Ukraine related to the Chornobyl accident. Environ Health Perspect. 2011;119:933–9.

46. Tao Z, Akiba S, Zha Y, Sun Q, Zou J, Li J et al. Cancer and non-cancer mortality among Inhabitants in the high background radiation area of Yangjiang, China (1979–1998). Health Phys. 2012;102:173–81.

47. Iwasaki T, Murata M, Ohshima S, Miyake T, Kudo S, Inoue Y et al. Second analysis of mortality of nuclear industry workers in Japan, 1986–1997. Radiat Res. 2003;159:228–38.

48. Boice JD Jr, Marano DE, Cohen SS Mumma MT, Blot WJ, Brill AB et al. Mortality among Rocketdyne workers who tested rocket engines, 1948–1999. J Occup Environ Med. 2006;48:1070–92.

49. Lai MS. Cancer monitoring and control planning in Taiwan. JACR Monograph No 16. Tokyo: Japanese Association of Cancer Registries; 2010.

50. Cornfield, J. A method for estimating comparative rates from clinical data. Applications to cancer of the lung, breast and cervix. J Nat Cancer Inst. 1951;11:1269–75.

51. Prentice RL. A case-cohort design for epidemiologic cohort studies and disease prevention trials. Biometrika. 1986;73 (1):1–11.

52. Blot WJ and Day NE Synergism and interaction: are they equivalent? [letter] American J Epidemiol. 1979;110:99–100.

53. Rothman KJ, Greenland S, Walker AM. Concepts of interaction. Am J Epidemiol. 1980;112:467–70.

54. Preston DL, Ron E, Tokuoka S, Funamoto S, Nishi N, Soda M et al. Solid cancer incidence in atomic bomb survivors: 1958–1998. Radiat Res. 2007;168:1–64.

55. Ron E, Carter R, Jablon S, Mabuchi K. Agreement between death certificate and autopsy diagnoses among atomic bomb survivors. Epidemiology. 1994;5:48–56.

56. Richardson DB, Cardis E, Daniels RD, Gillies M, O'Hagan JA, Hamra GB et al. Risk of cancer from occupational exposure to ionising radiation: retrospective cohort study of workers in France, the United Kingdom, and the United States (INWORKS). BMJ. 2015;351:h5359. doi: 10.1136/bmj.h5359.

57. Engel LW, Strauchen JA, Chiazze L Jr, Heid M. Accuracy of death certification in an autopsied population with specific attention to malignant neoplasms and vascular diseases. Am J Epidemiol. 1980;111:99–112.

58. Mollo F, Bertoldo E, Grandi G, Cavallo F. Reliability of death certifications for different types of cancer. An autopsy survey. Pathol Res Pract. 1986;181:442–7.

59. Delaigle A, Hall P. Estimation of a regression function when the observations contain measurement errors: Berkson vs classical errors. Statistica Sinica. 2011;21:1023–63.

60. Dosemeci M, Wacholder S and Lubin JH. Does nondifferential misclassification of exposure always bias a true effect toward the null value? Am J Epidemiol. 1990;132:746–8.

61. Johnson CJ. Cancer incidence in an area of radioactive fallout downwind from the Nevada Test Site. JAMA 1984;251(2):230–6.

62. Darby S, Hill D, Auvinen A, Barros-Dios JM Baysson H, Bochicchio F et al. Radon in homes and risk of lung cancer: collaborative analysis of individual data from 13 European case-control studies. BMJ. 2005;330(7485):223.

63. Krewski D, Lubin JH, Zielinski JM, Alavanja M, Catalan VS, Field RW et al. Residential radon and risk of lung cancer: a combined analysis of 7 North American case-control studies. Epidemiology 2005;16(2):137–45.

64. Tokonami S. Thoron in the environment and its related issues. Indian J Phys. 2009;83:777–85.

65. Akiba S, Tokonami S, Bochicchio F, McLaughlin J, Tommasino L, Harley N. Thoron: its metrology, health effects and implication for radon epidemiology: a summary of roundtable discussions. Radiat Prot Dosimetry. 2010;141:477–81.

66. Sackett DL. Bias in analytic research. J Chronic Dis. 1979;32:51–63.

67. Ivanov VK, Gorski AI, Maksioutov MA Vlasov OK, Godko AM, Tsyb AF et al. Thyroid cancer incidence among adolescents and adults in the Bryansk region of Russia following the Chernobyl accident. Health Phys. 2003;84(1):46–60.

68. United Nations Scientific Committee on the Effects of Atomic Radiation. Sources and Effects of Ionizing Radiation. Annex D: Health effects due to radiation from the Chernobyl accident. Vienna, United Nations; 2008, 179p. Report No.: II.

69. Wiest PW, Hartshorne MF, Inskip PD, Crooks LA, Vela BS, Telepak RJ et al. Thyroid palpation versus high-resolution thyroid ultrasonography in the detection of nodules. J Ultrasound Med. 1998;17:487–96.

70. Jacob P, Kaiser JC, Ulanovsky A. Ultrasonography survey and thyroid cancer in the Fukushima Prefecture. Radiat Environ Biophys. 2014;53:391–401.

71. Ron E, Lubin J, Schneider AB. Thyroid cancer incidence. Nature. 1992;360:113.

72. Schull WJ Cobb S. The intrafamilial transmission of rheumatoid arthritis. J Chronic Dis. 1969;22:217–22.

73. Taleb NN. The black swan: The Impact of the Highly Improbable. Penguin Books; 2007. Chapter 8, Giacomo Casanova's unfailing luck: the problem of silent evidence.

74. Caldwell GG, Kelley DB, Heath CW Jr. Leukemia among participants in military maneuvers at a nuclear bomb test: A preliminary report. JAMA. 1980;244(14):1575–8.

75. Criqui MH, Austin M, Barrett-Connor E. The effect of non-response on risk ratios in a cardiovascular disease study. J Chronic Dis. 1979;32:633–8.