Malaria. A prospective cohort study sought to determine the association between P. vivax and severe malaria (SM).[1] Data from this study are reproduced below and are accompanied by questions.

		Severe Malaria?	
		Yes	No
Age	0 to < 2 years	173	846
	2 to < 5 years	207	2216

1. Can prevalence be calculated using these data? Why or why not?
   Yes, it is a cohort study.

2. What is the prevalence of Severe Malaria among children aged 0 to < 5 years?
   $\frac{173+207}{3442} = 0.11$ or 11%

3. What is the relative risk of Severe Malaria for participants under 2 years of age compared with those aged between 2 and 5?
   $$\frac{173/(173+846)}{207/(207+2216)} = 1.99$$

[1] Genton B, D'Acremont V, Rare L, et al. Plasmodium vivax and Mixed Infections Are Associated with Severe Malaria in Children: A Prospective Cohort Study from Papua New Guinea. Rogerson S, ed. *PLoS Med*. 2008;5(6):e127. doi:10.1371/journal.pmed.0050127

		Severe Malaria?	
		Yes	No
Age	0 to < 2 years	173	846
	2 to < 5 years	207	2216

4. Can the odds ratio be calculated using these data? Why or why not?
    Yes, odds ratio can always be calculated from a 2x2 table.

5. What is the odds ratio for Severe Malaria for participants under 2 years of age compared with those aged between 2 and 5?
    $$\frac{173 \cdot 2216}{207 \cdot 846} = 2.19$$

6. Compare the relative risk to the odds ratio.
    1.99 vs. 2.19: they are similar values, which is why the odds ratio is often used (to estimate relative risk).

7. Interpret the Relative Risk from #3.
    Children aged 0 to < 2 have a 1.99 times greater chance of having SM compared with those aged 2 to < 5 years.
    Children aged 0 to < 2 have a 99% greater chance of having SM compared with those aged to 2 < 5 years.
    Or, if taking reciprocal ($\frac{1}{1.99}$ = .503): Children aged 2 to < 5 years have a 49.7% lower chance of having SM compared with those aged 0 to < 2 years.

8. Interpret the Odds Ratio from #5.
    The odds of having SM are 2.19 times greater for children aged 0 to < 2 compared with those aged 2 to < 5 years.

Cytokines. A case-control study was undertaken to illuminate the relationship between venous thrombosis (VT) and different cytokines (IL-1β, IL-6, IL-8, IL-10, IL12p70).[2] From a larger national study, 506 participants with VT were identified. Another sample of 1,464 participants without VT was randomly-selected. Excerpts from the article follow, accompanied by questions.

		IL-1β	
		Detected	Undetected
Group	Cases	289	217
	Controls	850	614

1. Can prevalence be calculated using these data? Why or why not?
   No, case-control studies cannot be used to estimate prevalence. The 506 cases were selected *because* they had VT and the 1464 were selected because they *did not* have VT separately. The ratio 506/1464 is meaningless: the researchers picked the group sizes. If a single group of people had been selected and then VT status evaluated within this group an estimate of prevalence would be possible.

2. What is the odds ratio comparing cases to controls?
$$\frac{289 \times 614}{850 \times 271} = 0.96$$

3. A 95% confidence interval for odds ratio was calculated to be [0.8, 1.2]. Do you think the Cases and Controls groups differ in the presence of IL-1β?
   No difference in odds is represented by the value 1. The confidence interval includes 1, so 1 is a plausible value for the true odds ratio. Therefore, it is plausible that the Cases and Controls groups have the same odds for presence of the cytokine.

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[2] Christiansen SC, Næss IA, Cannegieter SC, Hammerstrøm J, Rosendaal FR, Reitsma PH. Inflammatory Cytokines as Risk Factors for a First Venous Thrombosis: A Prospective Population-Based Study. Greaves M, ed. *PLoS Med*. 2006;3(8):e334. doi:10.1371/journal.pmed.0030334

Cytokines, Part 2. The table below is from the same study as that in *Cytokines*.

		IL-6	
		Detected	Undetected
Group	Cases	194	312
	Controls	547	917

1. Can prevalence be calculated using these data? Why or why not?
   (See previous page #1)

2. What is the odds ratio comparing cases to controls?
$$\frac{194 \times 917}{547 \times 312} = 1.04$$

3. A 95% confidence interval for odds ratio was calculated to be [0.9, 1.3]. Do you think the Cases and Controls groups differ in the presence of IL-6?
   No difference in odds is represented by the value 1. The confidence interval includes 1, so 1 is a plausible value for the true odds ratio. Therefore, it is plausible that the Cases and Controls groups have the same odds for presence of the cytokine.

Leptospirosis. A study was conducted to evaluate the performance of a Rapid Diagnostic Test (RDT) for leptospirosis in French tropical territories.[3] PCR was used as a gold standard to classify patients as either having Leptospirosis or being Controls. Germane results are reproduced below, and questions follow.

IgM RDT assay		Leptospirosis	Control
	Positive	168	14
	Negative	19	207

1. Calculate the following:

    a. Sensitivity $\frac{168}{168+19} = .898$ or 89.8%

    b. Specificity $\frac{207}{207+14} = .937$ or 93.7%

    c. False Positive Error Rate $1 - .937 = 0.063$ or 6.3%

    d. False Negative Error Rate $1 - .898 = .102$ or 10.2%

    e. Positive Predictive Value $\frac{168}{168+14} = .923$ or 92.3%

    f. Negative Predictive Value $\frac{207}{207+19} = .916$ or 91.6%

    g. Likelihood Ratio + $\frac{.898}{1-.937} = 14.182$

    h. Likelihood Ratio - $\frac{1-.898}{.937} = .108$

[3] Goarant C, Bourhy P, D'Ortenzio E, et al. Sensitivity and Specificity of a New Vertical Flow Rapid Diagnostic Test for the Serodiagnosis of Human Leptospirosis. Büscher P, ed. *PLoS Negl Trop Dis*. 2013;7(6):e2289. doi:10.1371/journal.pntd.0002289

Schistosoma. A cross-sectional study was conducted to determine the diagnostic properties of urine microscopy for detecting *Schistosoma haematobium* infections in South African young women.[4] Table 3 from this article is reproduced below, followed by questions.

	Urine microscopy [b]		
Pseudo gold standard [a]	Negative	Positive	Total
Negative	203	67	**270**
Positive	303	161	**464**
Total	**506**	**228**	**734**

Sensitivity (95% CI): 34.7 (30.4 to 37.0)
Specificity (95% CI): 75.2 (69.6 to 80.2)

Missing data was not included in this analysis. CI: Confidence Interval
a. Sandy patches identified using clinical photocolposcopic examination or by computerised colourimetric image analysis [17, 26]
b. *Schistosoma haematobium* ova detected in a single urine sample by microscopy [27].

https://doi.org/10.1371/journal.pone.0191459.t003

1. Calculate the following:

   a. Sensitivity $\frac{161}{161+303} = .347$ or 34.7%

   b. Specificity $\frac{203}{203+67} = .752$ or 75.2%

   c. False Positive Error Rate $1 - .752 = 0.248$ or 24.8%

   d. False Negative Error Rate $1 - .347 = .653$ or 65.3%

   e. Positive Predictive Value $\frac{168}{168+67} = .706$ or 70.6%

   f. Negative Predictive Value $\frac{203}{203+303} = .401$ or 40.1%

   g. Likelihood Ratio + $\frac{.347}{1-.752} = 1.398$

   h. Likelihood Ratio - $\frac{1-.347}{.752} = .869$

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[4] Galappaththi-Arachchige HN, Holmen S, Koukounari A, et al. Evaluating diagnostic indicators of urogenital Schistosoma haematobium infection in young women: A cross sectional study in rural South Africa. Knight M, ed. *PLOS ONE*. 2018;13(2):e0191459. doi:10.1371/journal.pone.0191459

Neoplasms. A recent study examined the Surveillance, Epidemiology, and End Results (SEER) database to examine the occurrence of myeloid neoplasms (MN) among breast cancer survivors who had received radiotherapy (RT) and who did not receive chemotherapy.[5] Excerpts from the journal article and questions follow.

> In the unadjusted analysis, there was an increased risk of subsequent MN among breast cancer patients who received RT compared to those who underwent surgery alone … After 5 years of follow-up 5.0 (95% CI 2.1–12.2) of 1,000 who received RT and 3.7 (95% CI: 1.8–7.9) of 1,000 who did not receive RT had developed subsequent MN (absolute risk increase of __A__ per 1,000 patients); corresponding to a number needed to harm of __B__. After 8 years of follow-up, the absolute risk increase was 1.7 per 1,000 patients corresponding to a number needed to harm of __C__, consistent with an increase in risk over time and longer follow-up.

1. What is the absolute risk increase (A)?

$$\frac{5.0\ cases}{1000\ people} - \frac{3.7\ cases}{1000\ people} = \frac{1.3\ cases}{1000\ people} = 0.0013$$

2. What is the number needed to harm (NNH) after 5 years (B)?

$$\frac{1}{0.0013} = 769.23 \rightarrow 769\ people$$

3. What is the number needed to harm (NNH) after 8 years (C)?

$$\frac{1}{1.7/1000} = 588.24 \rightarrow 588\ people$$

4. Explain why a *lower* value for #3 represents an *increase* in risk.

Fewer patients need to receive RT (588 vs. 769) to result in an additional MN case.

[5] Zeidan AM, Long JB, Wang R, et al. Risk of myeloid neoplasms after radiotherapy among older women with localized breast cancer: A population-based study. Hills RK, ed. *PLOS ONE*. 2017;12(9):e0184747. doi:10.1371/journal.pone.0184747