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?
   $$\frac{289 \times 614}{850 \times 217} = 0.96$$

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.

[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.

		Leptospirosis	Control
IgM RDT assay	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 - $\frac{1-.347}{.752} = .869$

[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

Hemorrhage. Researchers wanted to compare the misoprostol and oxytocin for prevention of postpartum hemorrhage (PPH) for mothers in sub-Saharan Africa.[5] Excerpts from the journal article are below, followed by questions:

> Of 8,867 mothers screened for eligibility from 23 September 2012 to 9 September 2013, 4,314 were eligible. A total of 2,369 (55%) declined participation in the study, and 1,140 were enrolled, received a randomized treatment, and completed study procedures. [An equal number of mothers were assigned to each treatment.] Demographic and clinical characteristics were similar between the two treatment groups. Primary PPH occurred in 163 (__A__) participants in the misoprostol group and 99 (__B__) participants in the oxytocin group (RR __C__, 95% CI 1.32 to 2.05, p<0.001; absolute risk difference __D__, 95% CI 6.44 to 16.1), corresponding to a number needed to treat of __E__ (meaning that __E__women would need to be treated with __F__ instead of __G__ to prevent one case of PPH).

1. What is the risk for each group (A and B)?

Misoprostol: $\frac{163\ cases}{570\ people} = 0.285964912 \approx 0.286$ or 28.6%

Oxytocin: $\frac{99\ cases}{570\ people} = 0.173684211 \approx 0.174$ or 17.4%

2. Why is it appropriate to calculate relative risk for this study?

This randomized experiment began with a single group of patients and then randomly assigned them to groups. Because everyone begins in the same group, calculating relative risk is appropriate. (Compare this design with a cohort study and a case control study.)

3. What is the relative risk for participants in the misoprostol group relative to the oxytocin group (C)?

$$RR = \frac{0.286}{0.174} \approx 1.64$$

4. What is the absolute risk difference (D)?

$$0.286 - 0.174 = 0.112 = 11.2\%$$

5. What is the number needed to treat (E)?

$$NNT = \frac{1}{\text{Absolute Risk Difference}} = \frac{1}{0.112} \approx 8.92857 \rightarrow 9$$

6. What are F and G so that the interpretation is true?

F should be *misoprostol* and G should be *oxytocin* based on the order we have done the comparisons.

[5] Atukunda, E. C., Siedner, M. J., Obua, C., Mugyenyi, G. R., Twagirumukiza, M., & Agaba, A. G. (2014). Sublingual misoprostol versus intramuscular oxytocin for prevention of postpartum hemorrhage in Uganda: a double-blind randomized non-inferiority trial. *PLoS medicine*, *11*(11), e1001752. https://doi.org/10.1371/journal.pmed.1001752