7.2 McIsaac Score and Rapid Antigen Detection Test

Tanz et al.[1] investigated whether the sensitivity and specificity of a rapid antigen detection test for group A streptococcal infection ("strep") depended on the prior probability of strep. They did rapid antigen detection tests (RADT) on 1848 children 3 to 18 years of age with sore throats using a laboratory throat culture as the gold standard. They estimated the prior probability of strep throat using the McIsaac Score, which gives 1 point for each of the following items:[1]

- history of temperature of >38°C
- absence of cough
- tender anterior cervical lymph nodes
- tonsillar swelling or exudates
- age <15 years

a. For this part, ignore the RADT and consider the McIssac Score as a single test for strep (as determined by the gold standard throat culture). If clinicians used some of the items in the McIsaac score to decide which children to enroll in the study, what bias would this cause, and how would it affect the apparent sensitivity and specificity of a McIsaac score ≥ 3 as a test for strep throat? [2]

Preferential inclusion of subjects who have a positive test or finding in a study leads to partial verification (or referral) bias, which inflates sensitivity and reduces specificity (see Chapter 4).

The study found that the sensitivity and specificity of the RADT varied with the McIsaac clinical symptom score. In other words, the sensitivity and specificity were different depending on the estimated prior probability of strep.

b. Using terminology from Chapter 7, how can we describe the relationship between the McIsaac Score and rapid antigen detection as tests for strep throat? [2]

They are not independent, conditional on disease state. For example, if sensitivity of the RADT is higher in patients with high McIsaac score, then among D+ patients, a high McIsaac Score makes a (true) positive RADT more likely. This could be because D+ patients with high McIsaac scores have more severe disease that is easier for the RADT to detect (perhaps due to a larger number of strep bacteria in the throat.

c. The authors reported that (in their entire sample of children) McIsaac scores >2 were significantly associated with a positive result on the rapid antigen detection test (compared with scores of 0 to 2): odds ratio 3.44, 95% CI: 2.66–4.44, P < 0.001.

[1] You may notice that the McIssac score uses the 4 Centor criteria you met in problem 2.6, and adds an additional point for Age < 15 years.

i. Explain in words what the odds ratio of 3.44 reported above means.[2]

The odds of a positive rapid antigen test if the McIsaac score is > 2 are 3.44 times higher than the odds of a positive RADT if the McIsaac score is ≤ 2.

ii. The term "spectrum bias" is sometimes used to describe non-independence (conditional on disease status) between two tests, where one test is a clinical assessment like the McIsaac score and the other test is a laboratory test like the rapid antigen test. Does the odds ratio of 3.44 show that the McIsaac Score and the rapid antigen test are not conditionally independent? Explain your answer. [3]

ii) No, in order to know whether the McIsaac score and rapid antigen test are conditionally independent, we would need to stratify ("condition") on disease status. Sensitivity and specificity (part b) are calculated conditional on disease status, so the fact that the sensitivity and specificity of the rapid test vary with the McIsaac score shows that the rapid test and McIsaac score are not independent.

But all that one can conclude from the odds ratio of 3.44 is that the RADT test is more likely to be positive for McIsaac scores > 2. This is no surprise because if the McIsaac is > 2 you are more likely to have strep!

d) Treat the McIsaac Score as a dichotomous test for strep throat with scores of 3, 4, and 5 considered "positive" and scores of 0, 1, and 2 as "negative." Assume that the sensitivity and the specificity of this dichotomous test are 80% and 70%. In a population with a pretest probability) of strep throat of 25%, what is the probability of a "positive" McIsaac Score? What is the positive predictive value of the McIsaac Score? (Hint: It may help to use the 2x2 table method with 1000 total patients of whom 250 have strep.)

P(McIsaac+) = 25% × 80% + 75% × 30% = 42.5%

LR(McIsaac+) = 80%/30% = 8/3 or 2.67

P(D+|McIsaac+): 25% → 1:3 × 8/3 = 8:9 → 8/17 = 47%

	Strep		
McIsaac	**D+**	**D–**	
Pos	200	225	**425**
Neg	50	525	**575**
	250	**750**	**1000**

P(McIsaac+) =425/1000 = 42.5%
P(D+|McIsaac+) = 200/425 = 47%

e) Assume that the sensitivity and specificity of the RADT are 60% and 90% and that they are independent of the McIsaac Score. This means that you can assume that the 60% sensitivity applies to D+ patients with a positive McIsaac Score and the 90% specificity applies to D– patients with a positive McIsaac Score. Take all the patients in the population above with a positive McIsaac Score and apply the RADT test. What is the probability that the RADT test will be positive? (Hint: If you used the 2x2 table for Part (d), you can use the top row (cells a & b) as the totals of D+ and D- for your new 2x2 table.)

47% * 60% + 53% * 10% = 34%

RADT	D+	D –	
Pos	120	22.5	**142.5**
Neg	80	202.5	**282.5**
	200	**225**	**425**

P(RADT+) = 142.5/425 = 34%

f) You can also assume that the 60% sensitivity applies to D+ patients with a **negative** McIsaac Score and the 90% specificity applies to D– patients with a **negative** McIsaac Score. Take all the patients in the population above with a **negative** McIsaac Score and apply the RADT test. What is the probability that the RADT test is positive? (Hint: If you used the 2x2 table for Part (d), you can use the bottom row (Cells c & d) as the totals of D+ and D- for your new 2x2 table.)

For this you need 1 – NPV

LR(McIsaac–) = 20%/70% = 2/7 or 0.286

P(D+|McIsaac–) 25% → 1:3 × 2/7 = 2:21 → 2/23 = 8.7%

P(RADT+|McIsaac-) = 8.7% × 0.6 + 91.3% × 0.1 = 14%

RADT	D+	D-	
Pos	30	52.5	**82.5**
Neg	20	472.5	**492.5**
	50	**525**	**575**

P(RADT+|McIsaac-) = 82.5/575 = 14.3%

g) In order to get the odds ratio calculated by the authors, you have to convert your answers in (e) and (f) above to odds and take the ratio. Do so now.

(34%/66%)/(14%/86%) = 3

h) The calculations that you have done in (e), (f), and (g) assumed that the McIsaac Score and the RADT are conditionally independent, i.e. that you can multiply their LRs. Answer c (iii) again.

Despite assuming McIsaac and RADT are independent, you still got an odds ratio of 3, so the authors' implication that the OR of 3.4 shows evidence of non-independence is incorrect. A positive McIsaac score increases the probability of strep, which increases the probability of a positive RADT.

1. Tanz RR, Gerber MA, Kabat W, Rippe J, Seshadri R, Shulman ST. Performance of a rapid antigen-detection test and throat culture in community pediatric offices: implications for management of pharyngitis. Pediatrics. 2009;123(2):437-44.