2. 8 Biliary Atresia

Biliary atresia is a disorder that leads to the bile ducts closing off in the first few months after birth and (if untreated) eventual liver failure. It is the leading reason for liver transplantation in children. There is evidence that the prognosis improves if it is detected early.

Harpavat et al[1] reported preliminary results of screening for biliary atresia using direct bilirubin measurements in newborns. An excerpt from the abstract is pasted below:

"Of 124,385 newborns in the screening study, 49.2% were female, 87.6% were of term gestational age, 70.0% were white, and 48.1% were Hispanic. Screening identified the 7 known infants with biliary atresia with a sensitivity of 100% (95% CI, 56.1%-100.0%), a specificity of 99.9% (95% CI, 99.9%-99.9%), a positive predictive value of 5.9% (95% CI, 2.6%-12.2%), and a negative predictive value of 100.0% (95% CI, 100.0%-100.0%)."

A. Assume that all of the numbers in the abstract are correct. Create a 2×2 table for the results above. *(2 points)*

	BA	**No BA**	**total**
Test+	**7**	**112**	**119**
Test-	**0**	**124266**	**124266**
Total	**7**	**124378**	**124385**
	Sens	**100.0%**	
	Spec	**99.9%**	

Note the 119 in the "total" column 7/5.9% = 118.6. 119 – 7 = 112. If you do it this way, then specificity is 124266/124378 = 99.90995% which rounds to 99.9%
If you did it using 1- specificity, you would get 124378 *0.1% = 124. So, the number in cell c could be 112 or 124. If you use 124, then the positive predictive value =7 /131 = 5.3%, which is different from the 5.9% in the answer.
We prefer 112 to 124 in Cell C, but either one gets full credit.

B. What was the prevalence of biliary atresia in this population? *(2 points)*
There were 7 newborns with biliary atresia out of 124,385, so the prevalence was 7/124385 = 5.6 per 100,000. This means 5.6 babies with biliary atresia per 100,000 live newborns or 56 babies with biliary atresia per 1,000,000 live newborns.

C. The 100.0% negative predictive value looks really good! But the 95% CI (100.0%-100.0%) for NPV looks suspicious, since the lower 95% CI limit for the sensitivity is only 56%. If the false-negative rate could be as high as 44%, can we really be confident that the negative predictive value is very close (within rounding error of) 100%? Explain. *(2 points: 1 pt for correct yes/no, 1 pt for explanation)*

Yes, we can be confident that the NPV is very high. The high NPV is due to the very low pretest probability (7/124,385). Even if sensitivity were ZERO, the NPV would still be (124266-7)/124385 = 99.9%!

1. Harpavat S, Garcia-Prats JA, Anaya C, Brandt ML, Lupo PJ, Finegold MJ, et al. Diagnostic Yield of Newborn Screening for Biliary Atresia Using Direct or Conjugated Bilirubin Measurements. JAMA. 2020;323(12):1141-50.