Reviewer’s report

Title: Cholelithiasis and the risk of intrahepatic cholangiocarcinoma: a meta-analysis of observational studies

Version: 2 Date: 20 July 2015

Reviewer: Geoffrey R Weiss

Reviewer’s report:

The authors have conducted a meta-analysis of 6 published studies of intrahepatic cholangiocarcinoma and the presence of prior intrahepatic cholelithiasis, choledocholithiasis, and cholecystolithiasis. Three national studies and three hospital-based studies comprised of >4700 cases of intrahepatic cholangiocarcinoma, and matched controls of >118,000 normal subjects. The authors applied rigorous statistical analysis indicating significant risk of intrahepatic cholangiocarcinoma associated with both intrahepatic and extrahepatic cholangiocarcinoma. Substantially lesser risk of intrahepatic cholangiocarcinoma was associated with cholecystolithiasis. The authors offer conjecture about the etiological relationship between intrahepatic cholangiocarcinoma and the presence of bile duct or gall bladder stones. This report has interest for generation of hypotheses about cause of stone-related malignancy.

Major compulsory revisions: The statistical methods and results should be reviewed by a biostatistical reviewer selected by the editors.

Minor essential revisions: None

Discretionary revisions: None

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.

Geoffrey Weiss, M.D.