Comparing the Costs Associated with Two Different Approaches to Screening for Hepatocellular Carcinoma in Persons with Chronic Hepatitis B Virus Infection

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Hepatitis B Virus (HBV) Infection and Liver Cancer

- ~360 million people with chronic HBV infection worldwide
- 15-40% lifetime risk for hepatocellular carcinoma (liver cancer)
Management of Liver Cancer

- Depends on a combination of factors such as tumor size, number of tumors, and liver functional reserve
- Liver transplant is preferred treatment
  - Removes tumor and diseased liver
  - Not readily available
- Alternatives
  - Surgical resection or ablation if early stage
  - Embolization or chemotherapy if late stage
Early-Stage Tumors

- Definition (Milan Criteria)
  - Single tumor $\leq 5$ cm in diameter
  - $\leq 3$ tumors with largest $\leq 3$ cm diameter
- Associated with improved prognosis in series of liver transplant patients
- Liver cancer screening could improve survival by identifying tumors at an early-stage
Screening for Liver Cancer

- Guidelines recommend screening for liver cancer every 6 months
- Screening indicated for
  - Males aged >40 years
  - Females aged >50 years
  - Cirrhosis (scarring of the liver)
  - Family history of liver cancer
- Ultrasound only recommended screening method
Alaska Native Health System Patient Referral Patterns

- 45% of Alaska Native persons live in remote villages accessible only by air
- Many villages lack ultrasound capability so residents need referral to regional health facility
Alaska Native Health System Liver Cancer Screening Program

- Alpha-fetoprotein (AFP)
  - Blood test that can be used to screen for liver cancer
  - Not recommended by guidelines because less accurate than ultrasound
  - First Alaska Native person with liver cancer was diagnosed with an elevated AFP
- HBV infected persons mailed a reminder to have blood drawn for AFP every 6 months
- Ultrasound for persons with an elevated AFP, cirrhosis, family history of liver cancer
Objectives

- Compare the cost of liver cancer screening in persons with HBV infection by
  - Ultrasound-alone (as recommended by guidelines)
  - AFP initially and converting to ultrasound (AFP → US as done in Alaska Tribal Health System)
Methods
Study Population

- Included persons for whom liver cancer screening indicated during 1983–2012
  - Men aged >40 years
  - Women aged >50 years
  - Excluded persons who died or were diagnosed with liver cancer <6 months after cohort entry (unlikely to have benefited from screening)

- Data source: Registry of HBV infected Alaska Native persons
Estimating Number of Tumors Identified at an Early-Stage by Two Hypothetical Approaches

- Obtained data for the actual screening program from HBV registry
- Classified early-stage tumors according to Milan criteria
- Assumed AFP→US identified same number of early-stage tumors as the actual screening program
  - AFP→US approach resembled actual Alaska Native Health System screening method
- Assumed US-alone approach detected 33% more tumors at an early-stage that the actual screening program
  - Based on difference in sensitivity between AFP and US for detecting liver cancer
Data Analysis

- Excel spreadsheet based model
- Total Years-of-Life-Gained (YLG) – additional years of survival attributable to screening
- Cost estimates based on 2012 Medicare reimbursement rates for AFP and ultrasound
- Adjusted costs and YLG to 2012 by discounting at 3% per year
- Incorporated cost of transportation
  - Assumed 60% of study participants required transportation to an US facility
  - Assumed cost per roundtrip visit to an US facility = $200
Results
Characteristics of Study Participants

- 839 persons from HBV registry received liver cancer screening under actual screening program during study period
  - 67% male
- 21 persons had liver cancer
  - 10 had early-stage tumor
- Median survival of persons with liver cancer
  - Early-stage tumor = 3.1 years
  - Late-stage tumor = 0.2 years
Excel Spreadsheet Model Inputs

- Number of tumors hypothetically detected at an early-stage by
  - AFP $\rightarrow$ US = 10
  - US-alone = 14

- Direct costs per test
  - AFP = $26.76
  - US = $109.94
Total Cost of Screening Program Over 30-Year Period

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<th>With travel costs</th>
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- **AFP--US**
- **US-alone**
Cost of Screening Program per Early-Stage Tumor Detected

Cost ($)/Early-stage tumor detected

- Without travel costs
- With travel costs

- AFP--US
- US-alone
Cost per Years-of-Life-Gained (YLG) at Median Survival

Without travel costs

With travel costs

Cost ($)/YLG

AFP--US

US-alone
Cost/Early-Stage Tumor Detected by Varying the Sensitivity of Ultrasound

Base case assumption
Conclusion
Summary

- Liver cancer screening by US-alone might detect more tumors at an early stage but the overall cost of the screening program would be approximately 2-times more than AFP→US.

- The cost/year-of-life-gained and cost/tumor detected by AFP→US is less than with ultrasound alone.
Discussion

- AFP not as good as ultrasound but it can diagnose many tumors at an early-stage
  - Alaska Native Health System obtains AFP for all age groups
  - Children with genotype F at highest risk for liver cancer can benefit from AFP screening (data not shown)
- In areas with limited access to ultrasound similar to Alaska, the AFP→US approach should be considered as an alternative to ultrasound alone
- Better screening tests needed to identify liver cancer for persons living in remote communities
Questions?

For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.