Identification of Hepatitis B Virus-infected Pregnant Women and Infants through Birth Estimates and Laboratory Reporting of Pregnancy Status

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Background

- Hepatitis B is an infection of the liver caused by Hepatitis B Virus
- Hepatitis B is transmitted by percutaneous or mucosal exposure to infectious blood or body fluids
- 700,000-1.4 million persons estimated to be infected with Hepatitis B in the U.S.

- MMWR 2005
- 2012 CDC Surveillance Data
Chronic Hepatitis B

- Chronic infection develops in
  - 90% of infected infants
  - 30% of infected children aged <5 years
  - <5% of infected persons aged ≥5 years

- Persons with chronic Hepatitis B have a 25% risk of premature death from cirrhosis/liver cancer

Mast et al. MMWR 2005
Perinatal Hepatitis B Infection

- An infant can acquire Hepatitis B from
  - Mother-to-child transmission (perinatal)
    - Annually, an estimated 25,000 infants are born to HBsAg positive women in the United States
  - An infected household member
Identifying Infants Born to HBsAg Positive Mothers

- 47% of the expected number of infants born to HBsAg positive mothers were identified in 2012 (U.S. Perinatal Hepatitis B Prevention Program)
  - Among states, this figure ranged from 0% to 104%

- Estimates based on
  - Natality data
  - HBsAg seroprevalence among women of child-bearing age, by race and ethnicity

HBsAg = Hepatitis B surface antigen
Smith et al. *Pediatrics* 2012
Risk for Perinatal Infection

- Without post-exposure prophylaxis, perinatal Hepatitis B infection occurs in
  - 70-90% of infants born to mothers who are HBsAg positive/HBeAg positive
  - <10% of infants born to mothers who are HBsAg positive/HBeAg negative

HBsAg = Hepatitis B surface antigen
HBeAg = Hepatitis B e antigen
MMWR2005
Session Overview

This session will include discussion of ways CDC helps optimize identification of hepatitis B virus (HBV)-infected* pregnant women and their infants through:

1) Annual estimates of infants born to HBV-infected women
   - Current and proposed methodologies

2) Improving laboratory reporting of pregnant women testing positive for HBV infection

*Hepatitis B virus infection is defined as positivity for hepatitis B surface antigen (HBsAg).
PART 1:

Estimating Annual Births to Hepatitis B Virus-Infected Women in the United States
Why is estimating births important?

A Comprehensive Immunization Strategy to Eliminate Transmission of Hepatitis B Virus Infection in the United States

Recommendations of the Advisory Committee on Immunization Practices (ACIP)
Part 1: Immunization of Infants, Children, and Adolescents

CDC established the Perinatal Hepatitis B Prevention Program to reduce mother-to-child transmission of hepatitis B virus infection by case-management of infants for:

- post-exposure prophylaxis (PEP)
- post-vaccination serologic testing (PVST)

Identify HBsAg+ Pregnant Women

Give PEP to their infants within 12 hours of birth + complete hepatitis B vaccine series

Prevent up to 95% of mother-to-child transmission of hepatitis B virus infection

Current Method for Estimating Births to HBsAg+ Pregnant Women – 1994 to Present

Estimated Births to HBsAg+ Women =
(# Infants in Subcategory) X (HBsAg prevalence from *NHANES or †Literature)

HBV Endemic Regions & Immigration to the US

FIGURE 3. Geographic distribution of chronic hepatitis B virus (HBV) infection — worldwide, 2006*

HBsAg Prevalence

- ≥8% = High
- 2%-7% = Intermediate
- <2% = Low

* For multiple countries, estimates of prevalence of hepatitis B surface antigen (HBsAg), a marker of chronic HBV infection, are based on limited data and might not reflect current prevalence in countries that have implemented childhood hepatitis B vaccination. In addition, HBsAg prevalence might vary within countries by subpopulation and locality.

Source: Centers for Disease Control and Prevention. Recommendations for Identification and Public Health Management of Persons with Chronic Hepatitis B Virus Infection. MMWR 2008;57(No. RR-8)
Global Vaccine Campaigns

Global 3-dose hepatitis B vaccine coverage among infants

1% 1990

81% 2013

Evolving Hepatitis B Prevalences Worldwide

Source:
WHO Global Immunization Data, 2013: http://www.who.int/immunization/monitoring_surveillance/global_immunization_data.pdf?ua=1
Proposed Method for Estimating Births to HBsAg+ Pregnant Women

Estimated Births to HBsAg+ Women = 
(# Infants in Subcategory) X (HBsAg prevalence from *NHANES 07-12 or †PHBPP data)

Results – US Births and Estimated Births to HBsAg+ Women, 2013

Overall Births by Mother's Country of Birth, 2013
- US-Born: 77%
- Foreign-Born: 20%
- US Territory-Born: 2%
- Other/Unknown Origin: 1%

n = 3,932,181

Estimated Births to HBV-infected Mothers, 2013
- US-Born: 33%
- Foreign-Born: 8%
- US Territory-Born: 59%
- Other/Unknown Origin: 0%

n = 18,017
Results – Estimated Births to US-Born HBsAg+ Women by Race/Ethnicity (n=6,008), 2013

Number of Births

White, Non-Hispanic | Black, Non-Hispanic | Hispanic | Asian/Pacific Islander | Other/Unknown
Results — Estimated Births to Foreign-born HBsAg+ Women by Region of Birth (n=10,617), 2013

Number of Births

<table>
<thead>
<tr>
<th>Region</th>
<th>Number of Births</th>
</tr>
</thead>
<tbody>
<tr>
<td>East Asia</td>
<td>5000</td>
</tr>
<tr>
<td>Southeast Asia</td>
<td>4000</td>
</tr>
<tr>
<td>West/Central Asia</td>
<td>3000</td>
</tr>
<tr>
<td>Australia/Oceania</td>
<td>2000</td>
</tr>
<tr>
<td>Caribbean (except Haiti)</td>
<td>1000</td>
</tr>
<tr>
<td>Mexico and Central...</td>
<td>500</td>
</tr>
<tr>
<td>Middle East</td>
<td>500</td>
</tr>
<tr>
<td>North America</td>
<td>500</td>
</tr>
<tr>
<td>Pacific Islands</td>
<td>500</td>
</tr>
<tr>
<td>South Asia</td>
<td>500</td>
</tr>
<tr>
<td>Haiti</td>
<td>500</td>
</tr>
<tr>
<td>Eastern Europe</td>
<td>500</td>
</tr>
<tr>
<td>Southern Europe</td>
<td>500</td>
</tr>
<tr>
<td>Africa</td>
<td>500</td>
</tr>
<tr>
<td>Total</td>
<td>10,617</td>
</tr>
</tbody>
</table>
## Results – Comparison of Methodologies, 2013

<table>
<thead>
<tr>
<th></th>
<th>Current Method (race/ethnicity)</th>
<th>Proposed Method (country of birth)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated Births, Point Estimate</td>
<td>25,268</td>
<td>18,017</td>
</tr>
<tr>
<td>Estimated Births, Lower Limit</td>
<td>18,003</td>
<td>13,204</td>
</tr>
<tr>
<td>Percent of Overall Births</td>
<td>0.64%</td>
<td>0.46%</td>
</tr>
</tbody>
</table>
In 2013, 10,902 infants were identified and enrolled into PHBPPs across the United States.

- Texas* PHBPP: 562

**Infants Identified by PHBPPs, 2013**

<table>
<thead>
<tr>
<th></th>
<th>Current n = 25,268</th>
<th>Proposed n = 18,017</th>
</tr>
</thead>
<tbody>
<tr>
<td>National, % Identified</td>
<td>43%</td>
<td>61%</td>
</tr>
<tr>
<td>Texas, % Identified</td>
<td>38%</td>
<td>60%</td>
</tr>
</tbody>
</table>

* Texas values do not include values from San Antonio or Houston.
Advantages of Proposed Method

- The proposed method for estimating the number of births to pregnant women with chronic hepatitis B infection by using mother’s country of birth and updated hepatitis B prevalences accounts for the changing demographics of the US as well as evolving global HBsAg prevalences.

- This method provides targeted birth estimates for health jurisdictions by better taking into account demographics of their populations served
Limitations to Proposed Method

- The proposed model partly utilizes HBsAg prevalences determined from PHBPP, which likely do not identify all infected women, leading to probable underestimation.

- The model also partly uses NHANES data
  - NHANES is believed to underestimate overall HBV because high-risk groups (e.g. institutionalized, homeless) are not included.
  - Sample sizes for race/ethnicity groups were limited, possibly resulting in an overestimate of prevalence in these groups.

- Regional prevalences do not necessarily reflect local or cultural differences in prevalence of HBsAg.
PART 2:

Laboratory Reporting of HBV-infected Pregnant Women
Background

- The Laboratory Reporting of Pregnancy Status (LRPS) Working Group was formed to facilitate identification of HBsAg+ pregnant women.

- Members include representatives from:
  - CDC
  - Health Departments
  - Professional Medical Organizations
  - Public Health and Commercial Laboratories
Background, part II

- Four commercial labs report HBsAg+ women who are possibly pregnant to health departments by sending a Special Laboratory Report (SLR)

- These labs include:
  - ARUP Laboratories
  - LabCorp
  - Mayo Medical Laboratories
  - Quest Diagnostics
What is a Special Laboratory Report?

- A Special Laboratory Report (SLR) indicates the possible pregnancy status of an individual with an HBsAg+ laboratory test result.

- Each of these labs has a unique SLR that is sent by HL7/ELR, secure fax, or secure email.

*For more information on SLRs, please contact Alaya Koneru at xjq8@cdc.gov*
SLR Formats

If a health department has an electronic laboratory reporting (ELR) system, prenatal indicators from the following commercial labs are sent by:

- ARUP Laboratories
- LabCorp
- Mayo Medical Laboratories
- Quest Diagnostics*

* Quest Diagnostics is beta-testing sending SLR via ELR in some parts of the US. As of June 2015, the majority of health departments continue to receive SLR through a supplemental Excel report.
If a health department does not have an ELR system, prenatal indicators from the following commercial labs are sent by:

- ARUP Laboratories
- Mayo Medical Laboratories
- Quest Diagnostics

Please note: LabCorp does not send prenatal indicators via hardcopy reports.
### Screening Pregnant Women for Hepatitis B Virus (HBV) Infection:
*Ordering Prenatal Hepatitis B Surface Antigen (HBsAg) Tests from Major Commercial Laboratories*

<table>
<thead>
<tr>
<th>Laboratory</th>
<th>Test Option</th>
<th>Test Name</th>
<th>Reflex to Confirmation Test*</th>
<th>Test Code/ID</th>
<th>CPT Code</th>
<th>Web Link</th>
</tr>
</thead>
<tbody>
<tr>
<td>LabCorp</td>
<td>Panel</td>
<td>Prenatal Profile I with Hepatitis B Surface</td>
<td>✓</td>
<td>202945</td>
<td>80055</td>
<td><a href="https://www.labcorp.com/wps/portal/provider/testmenu/">https://www.labcorp.com/wps/portal/provider/testmenu/</a> (Enter test code or CPT code to search for test)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antigen</td>
<td></td>
<td></td>
<td></td>
<td><a href="https://www.labcorp.com/wps/portal/provider/testmenu/">https://www.labcorp.com/wps/portal/provider/testmenu/</a> (Enter test code or CPT code to search for test)</td>
</tr>
<tr>
<td></td>
<td>Panel</td>
<td>Hepatitis Profile XIII (HBV Prenatal Profile)</td>
<td>✓</td>
<td>265397</td>
<td>87340**</td>
<td><a href="https://www.labcorp.com/wps/portal/provider/testmenu/">https://www.labcorp.com/wps/portal/provider/testmenu/</a> (Enter test code or CPT code to search for test)</td>
</tr>
<tr>
<td></td>
<td>Standalone</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Standalone</td>
<td>Hepatitis B Surface Antigen Prenatal, Serum</td>
<td>✓</td>
<td>HBAGP</td>
<td>87340</td>
<td><a href="http://www.mayomedicallaboratories.com/test-catalog/Overview/56185">http://www.mayomedicallaboratories.com/test-catalog/Overview/56185</a></td>
</tr>
<tr>
<td></td>
<td>Standalone</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
</tr>
</tbody>
</table>

*When an HBsAg test result is reactive, laboratories may automatically perform a confirmatory test without additional provider order.

**This CPT code corresponds only to the HBsAg screening component of this laboratory panel; additional CPT codes might be associated with other confirmatory tests in this laboratory panel.***

Notes: CDC recommends healthcare providers use prenatal HBsAg tests (vs. non-specific tests) for pregnant women, which allows for reporting of positive results along with pregnancy status to public health jurisdictions. Refer all HBsAg positive pregnant women to Prenatal Hepatitis B Prevention Program coordinators for case management of mother and infant: [http://www.cdc.gov/vaccines/vpd-vac/hb/prenatal-contacts.htm](http://www.cdc.gov/vaccines/vpd-vac/hb/prenatal-contacts.htm).

Laboratories reserve the right to add, modify, or stop performing tests at any time – providers should review any test notifications from laboratories for changes.

Screening and Referral Algorithm for Hepatitis B Virus (HBV) Infection among Pregnant Women

Assess if at high risk* for acquiring HBV infection

No

Yes

No further action needed

Consider vaccination during pregnancy or postpartum

Repeat HBsAg testing when admitted for delivery

HBsAg

HBsAg (hepatitis B surface antigen)

HBsAg

Order Additional Tests:
- HBeAg (hepatitis B e-antigen)
- HBV DNA Concentration
- ALT (alanine aminotransferase)

No

HBeAg

HBV DNA >20,000 IU/mL

ALT ≥19 IU/L

Refer for care postpartum

Refer to specialist immediately during pregnancy

*High risk for HBV infection includes: household or sexual contacts of HBsAg-positive persons; injection drug use; more than one sex partner during the past six months; evaluation or treatment for a sexually transmitted disease, HIV infection, chronic liver disease, or end-stage renal disease; and international travel to regions with HBsAg prevalence of ≥2%.


Available at http://www.cdc.gov/hepatitis/hbv/pdfs/prenatalhbsagtesting.pdf
Evaluation of Special Laboratory Reports (SLRs)

- Developed and pilot-tested a survey among PHBPP coordinators on the LRPS Workgroup

- 56 Perinatal Hepatitis B Prevention Program Coordinators (PHBPP) invited to participate in final survey
  - Web-based survey administered via SurveyMonkey
  - 75% (N=56) of invited PHBPP coordinators completed or partially completed the survey
Survey Results

- HBsAg+ Laboratory Reports by Gender in 2013 (n=83,755)

  Answered: 27  Skipped: 15

Males 52%
Females 48%
Survey Results, continued

- HBsAg+ Laboratory Reports by Type of Laboratory Performing Testing in 2013 (n=80,220)
  Answered: 25    Skipped: 17

**National**
- 34%
- 63%
- 2%
- 1%

**Texas**
- 25%
- 70%
- 5%

*Data collected through email communications with Ruthie Benson, 06/26/2014*
Survey Results, continued

- HBsAg+ Laboratory Reports by 4 Major Commercial Laboratories, 2013 (n=31,692)
  Answered: 23   Skipped: 19

National

- ARUP: 55%
- Mayo Medical Laboratories: 4%
- LabCorp: 39%
- Quest Diagnostics: 2%

Texas*

- ARUP: 58%
- Mayo Medical Laboratories: 1%
- LabCorp: 41%
- Quest Diagnostics: 0%

*Data collected through email communications with Ruthie Benson, 06/26/2014
Impact of SLRs, part I

- 65.6% (n=32) of participants reported that their health department receives SLR reporting of pregnancy status of HBsAg+ persons from one or more of the 4 major commercial labs.

- 34.8% (n=23) of participants reported identifying an increased number of HBsAg+ pregnant women since SLRs were implemented.
  - 65.2% (n=23) reported no change in the number identified.
  - Texas*: 24% increase in pregnant women identified between mid-year 2013 and mid-year 2014

*Data collected through email communications with Ruthie Benson, 06/26/2014
Impact of SLRs, part II

- From 2013-2014, 52.2% (n=23) of participants identified some HBsAg+ pregnant women initially or solely through SLR.
  - 90.0% (n=10) of these participants reported identifying these women initially through SLR.
  - 70.0% (n=10) of these participants reported identifying these women solely through SLR.

- Texas*: 48 HBsAg+ pregnant women were identified solely through SLR (over Jan-April 2014)

*Data collected through email communications with Ruthie Benson, 04/10/2014
23.8% (n=21) of participants reported spending a decreased amount of time and effort in identifying HBsAg+ pregnant women since SLRs were implemented.

- 19.1% (n=21) reported spending an increased amount of time and effort.
- 57.1% (n=21) reported spending the same amount of time and effort.

*Data collected through email communications with Ruthie Benson, 04/10/2014*
<table>
<thead>
<tr>
<th>Time Spent in Identifying HBsAg+ Pregnant Women</th>
<th>Rationale</th>
</tr>
</thead>
</table>
| **Increased**                              | • We receive an alert to our program if any HBsAg-positive possibly pregnant women are identified through this process.  
• Capture recapture helps as well.  
• Because I am getting duplicates, I am validating same information twice.  
• Must go through lab data list and contact MD offices to determine pregnancy status and confirm lab results with MD |

Texas*: increased time and effort spent

Reason: “We started calling the rest of providers to ascertain pregnancy status on the women of childbearing age (something we couldn’t do before because due to volume

*Data collected through email communications with Ruthie Benson, 04/10/2014
Advantages of SLR

- Saves time in determining pregnancy status (x6)
- Helps identify women who are not identified otherwise (x4)
- Early prenatal identification of pregnant HBsAg+ women (x3)
- Identify pregnancy status (x2)
Disadvantages of SLR

- None (x5)
- Lack of available confirmatory testing (x2)
- Increased time spent in identifying/confirming cases (x2)
- Difficulty locating correct provider/contacts (x2)
- Not receiving SLR from all labs (x2)
- Inconsistent/Delayed reporting (x1)
What do PHBPPs think should be the next effort for improving identification of HBsAg+ pregnant women?

- Recruit more laboratories to report pregnancy status (x11)
- Improve SLR (e.g. standardize reporting) (x6)
- Require pregnancy status reporting on lab forms (x2)
- Expand pregnancy reporting to HBeAg and HBV DNA test results (x2)
- Educate providers on appropriate testing (x2)
Expanding Pregnancy Reporting by Laboratories

- Memo to all US labs requesting reporting of pregnancy status on HBsAg+ results
- Long-term solutions for pregnancy reporting
- Expanding laboratory-based pregnancy reporting to other diseases (including hepatitis C, HIV, and syphilis)
  - Collaborate with additional groups at CDC including perinatal groups at NCHHSTP and NEDSS group at DHIS/CSELS

*NOTE: LabCorp reports pregnancy status of a woman testing positive for any reportable disease when the disease assay is ordered through a LabCorp prenatal or obstetric panel (diseases include, but are not limited to, hepatitis C, HIV, and syphilis).
Final Messages

1) Annual estimates of infants born to HBV-infected women
   - Programmatic goals for PHBPPs to optimize identification of HBV-infected women and their infants
   - Maternal characteristics of race/ethnicity and/or birth origin provide possible groups that could be targeted for outreach

2) Laboratory reporting of pregnant women testing positive for HBV infection
   - Helps PHBPPs identify more women for case-management
   - Can reduce burden on PHBPPs for determining which positive HBV tests are for pregnant women
Acknowledgements

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- Noele Nelson
- Sarah Schillie
- Henry Roberts
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Immunization Services Division, NCIRD, CDC

- Nancy Fenlon
Questions?

For more information, please contact:
Alaya Koneru, MPH
Email: xjq8@cdc.gov

Division of Viral Hepatitis
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Centers for Disease Control and Prevention

*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.
### Proposed Method – Maternal Country of Birth Categories

#### United States-born Women by Race/Ethnicity, total
- White, non-Hispanic
- Black, non-Hispanic
- Hispanic
- Asian/Pacific Islander
- Other/Unknown

#### United States Territory-born Women by Territory, total
- American Samoa
- Guam
- Northern Mariana Islands
- Puerto Rico
- Virgin Islands

### Foreign-born Women by Region, total

#### Africa
- East Asia
- South Asia
- Southeast Asia
- West/Central Asia
- Australia/Oceania

#### Asia

#### Europe
- Eastern Europe
- Southern Europe
- Western and Northern Europe
- Haiti
- Mexico and Central America
- Middle East
- North America
- Pacific Islands
- South America
Enhanced Perinatal Hepatitis B Prevention Program

- HBsAg-positive pregnant women identified; program staff collected and reported maternal and infant data to CDC

- 5 sites
  - Florida
  - Michigan
  - Minnesota
  - New York City
  - Texas (excluding Houston and San Antonio)

- 2007-2013
Enhanced Perinatal Hepatitis B Prevention Program

- 17,951 mother-infant pairs identified

- Median maternal age: 30.0 years (range: 14.5-51.6 years)

- Most infants born to mothers who were
  - Asian/Pacific Islander (61.2%)
  - Foreign-born (88.7%)

- Data for certain characteristics or outcomes not available for all mother-infant pairs
Resources

- Prenatal HBsAg Test Guide and Screening/Referral Algorithm:
  - CDC: