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Heterogeneity in Hepatitis B Virus (HBV) Seroprevalence Estimates from US Adult Incarcerated Populations: A Systematic Review and Meta-Regression Analysis

Amy J. Harzke[1], Karen J. Goodman[2], Patricia Dolan Mullen[3], Jacques Baillargeon[1]

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ABSTRACT

Hepatitis B virus (HBV) seroprevalence estimates from US incarcerated populations are relatively high. However, the usefulness of these estimates for guiding HBV-related correctional healthcare policy is limited by wide variation in estimates across studies and little understanding of the sources of this variation. The authors systematically reviewed studies indexed from 1975-2005, meeting pre-specified criteria and reporting HBV seroprevalence estimates from US adult incarcerated populations. Using meta-regression techniques, the authors investigated report type, geographical region, serum collection year, facility type, serum source, sampling procedures, sample characteristics, and measurement procedures as potential study-level sources of heterogeneity in prevalence estimates for common HBV seromarkers. In bivariable meta-regression analyses, mean age ≥31 years was strongly associated with increased HBsAg prevalence (POR = 2.6), and serum collection year before 1991 was strongly associated with increased prevalence of any positive marker (POR = 2.0). Other moderate-to-strong associations were observed, but these were considered less certain because of small numbers of observations, influence of single studies, or potential confounding. Potential sources of heterogeneity should be considered when comparing HBV seroprevalence estimates in adult US incarcerated populations and when developing HBV screening and vaccination protocols in correctional settings.

INTRODUCTION

Although US incidence rates for hepatitis B virus (HBV) have declined substantially over the past two decades, HBV infection and its sequelae – chronic liver disease/cirrhosis and primary liver cancer – continue to present a significant public health problem. An estimated 800 000 to 1.4 million persons in the US are chronically infected with HBV (CDC, 2008), and these persons have a 15% to 25% lifetime risk of death from chronic liver disease or primary liver cancer (CDC, 1990). Conservative estimates suggest as many as 2000 to 4000 deaths annually are due to HBV-related liver disease and cancer (CDC, 2003; CDC, 2008). Incidence of HBV infection among those 25 years of age and older has remained steady since 1999 (CDC, 2005a; CDC, 2005b). As infected persons age and begin to experience HBV-related morbidity and mortality over the next 10 to 20 years, hospitalizations and deaths due to HBV-related conditions are anticipated to remain steady as well (CDC 2005a; CDC 2005b).

Chronic HBV infection and related conditions may have a particularly strong impact on correctional healthcare systems in the United States. Studies have consistently reported high prevalence of serologic markers of HBV infection in prison populations compared to the general US population (Koplan et al, 1978; Decker et al, 1984; Ruiz & Mikanda, 1996; Macalino et al, 2004). Typically tested seromarkers include HBV antigen (HBsAg) and HBV core antibody (anti-HBc); presence of HBV antigen indicates current infection, and presence of HBV core antibody indicates immune response and may reflect current or past infection. Studies suggest that the prevalence of current or past HBV infection in prison pop-

1. Division of Correctional Managed Care and the Department of Preventive Medicine and Community Health, University of Texas Medical Branch, Galveston, TX, USA
2. Division of Gastroenterology, Department of Medicine, University of Alberta, Edmonton, Canada
3. Division of Behavioral Sciences and Health Promotion, University of Texas School of Public Health, Houston, TX, USA

Address correspondence to: Amy Jo Harzke, University of Texas Medical Branch, 301 University Blvd, Mail Route 1008, Galveston, TX 77555. Phone: 409-747-2670; E-mail: ajharzke@utmb.edu.

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ulations is about four to five times greater than national estimates (Harzke et al, 2009). Moreover, the prison population is a growing and aging one. The US prison population has more than quadrupled since 1980, exceeding 1.5 million in 2002 (Harrison & Beck, 2003), and inmates over 45 years of age comprised 21.3% of all inmates in 2007, up from 13.6% in 1997 (Beck & Mumola, 1999; West & Sabol, 2008). Thus, the high prevalence of HBV seromarkers portends a high burden of chronic HBV infection and related conditions in incarcerated populations over the coming decades, assuming the prison population does not decline and HBV-infected inmates continue to age (Hammett et al, 2002; Mitka, 2004).

HBV seroprevalence estimates to date provide useful data for correctional healthcare planners and policy makers in the particular systems or facilities studied, but the usefulness of these estimates beyond the particular study contexts may be limited. HBV seroprevalence estimates vary widely across studies, and the sources of this variation have received little attention in the literature (Harzke et al, 2009). Reported prevalence estimates in US prisons have ranged from 0.9% to 8.0% for HBsAg (Decker et al, 1984; Koplan et al, 1978) and from 6.5% to 42.6% for anti-HBc (Decker et al, 1984; Barry et al, 1990). A majority of reported studies have examined *within* study variation in HBV seroprevalence estimates across demographic or risk factor strata; only a few reported studies, however, have discussed or otherwise addressed whether and how study-specific estimates differ from previous estimates or the degree to which the distribution of demographic characteristics and risk factors affect the comparability of seroprevalence estimates *across* studies (Ruiz & Mikanda, 1996; Ruiz et al, 2001). Furthermore, only a small number of reports have addressed the potential role of broader epidemiologic factors (e.g., geographic and temporal variation in background prevalence) and methodologic factors (e.g., sampling or measurement procedures) in producing variation in seroprevalence estimates across studies (Decker et al, 1984; Anda et al, 1985; Hammett et al, 2002). Several authors have claimed their seroprevalence estimates were comparable to previous estimates, implicitly assuming homogeneity of HBV seroprevalence and risk factors in different prison populations as well as assuming homogeneity of methods across seroprevalence studies (Harzke et al, 2009).

The objectives of this study were to systematically identify and review studies reporting HBV seroprevalence estimates from US adult incarcerated populations and to investigate a range of study-level factors as potential sources of variation in these estimates. Investigating and identifying study-level sources of variation in HBV seroprevalence estimates may aid researchers and policymakers in interpreting and comparing existing studies and in designing and reporting future studies. Understanding study-level sources of variation may help guide correctional healthcare leaders in using existing data to assess the burden of HBV infection in correctional facilities not previously studied.

METHODS

Data Sources and Search

The following databases were searched for reports of HBV seroprevalence estimates in incarcerated adults indexed from January 1, 1975, through August 31, 2005, using the keywords "hepatitis" and "prison": Medline *via* Ovid; Web of Science-Science Citation Index and Social Sciences Citation Index; National Criminal Justice Reference Service Abstracts Database; and UMI Proquest Digital Dissertations. Bibliographies from initially eligible studies, review articles, and commonly cited reports (e.g., CDC, 2003) were also searched.

Study Selection

The following eligibility criteria were pre-specified and applied hierarchically in the order noted: (1) indexed or available from the author in the time period noted above (reliable serologic testing for HBV was not available until 1975); (2) conducted in the United States; (3) primary study; (4) reporting prevalence estimates of HBV infection; (5) study population sampled from prisons, jails, or other correctional facilities; (6) disease ascertainment methods included measurement of one or more standard serologic markers for HBV (HBsAg, Total anti-HBc, IgM anti-HBc, anti-HBs); (7) HBV seroprevalence estimates based on direct methods (i.e., not based on mathematical models or surveys of medical directors); (8) sample drawn exclusively from correctional system or facility housing primarily adults; (9) sample not drawn from a facility housing primarily non-US residents; and (10) sample not restricted to those with another illness. HBV seroprevalence in samples primarily comprised of juvenile detainees, non-US residents, or adult detainees with a specified co-morbidity may not be comparable to adult correctional populations (McQuillan et al, 1999; Ruiz & Mikanda, 1996; Ruiz et al, 1999). No restrictions were imposed with respect to publication type (e.g., full articles, abstracts, government reports, etc.). When unique citations reflected duplicate reports of the same data, HBV seroprevalence estimates and sample characteristics were drawn from the more complete report, and both reports were considered for ascertaining study methods.

Data Extraction

Study characteristics for extraction were pre-selected based on hypothesized potential sources of variation, using guidance from Loney et al (1998) and Stroup et al (2000). Study characteristics extracted included: publication type; geographic region; serum collection year; facility type; sampling procedures; sample size; sample demographics; sample distribution of behavioral risk factors; data source; timing of serum collection *vis-à-vis* incarceration; and generation of immunoassay. Geographic regions were those used by the US Centers for

Disease Control and Prevention (CDC) for hepatitis surveillance (CDC, 2005b). Region and serum collection year were considered proxies for background disease prevalence in the local non-incarcerated population. Although data were extracted on all reported behavioral risk factors, only history of injection drug use (IDU) and history of male sex with males (men who have sex with men [MSM]) were considered further in analyses because IDU and MSM histories were commonly reported and consistently operationalized. Generation of immunoassays was considered a potential source of variation because first generation tests demonstrated levels of sensitivity and specificity which were considerably lower than second generation tests. Immunoassays were not examined by manufacturer and version (e.g., Abbott Laboratories, Auszyme Monoclonal EIA) because specific tests exhibited similar levels of sensitivity and specificity within generation.

Data were extracted from eligible studies independently by two authors. The correlation coefficient and the percentage agreement were calculated for independent reviewers' responses to close-ended items on the data extraction form (total n = 1208, ~80 items per study) [r = 94.4; 89.4% (87.5%, 91.1%)]. Discrepancies were identified and resolved (A.J.H., K.J.G.).

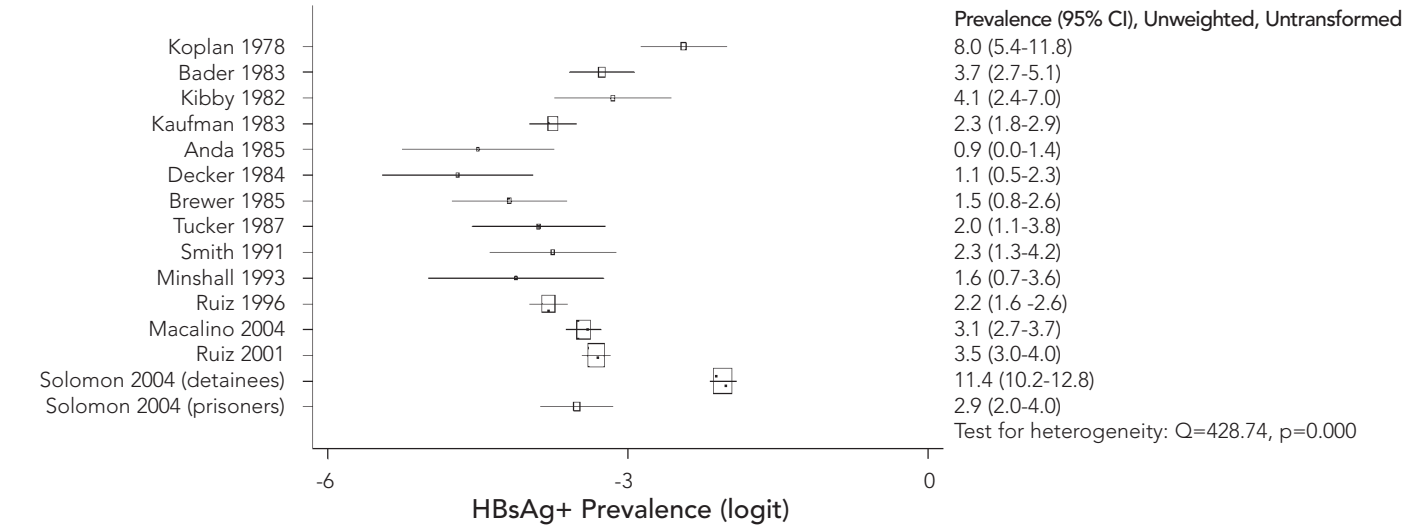
Analysis

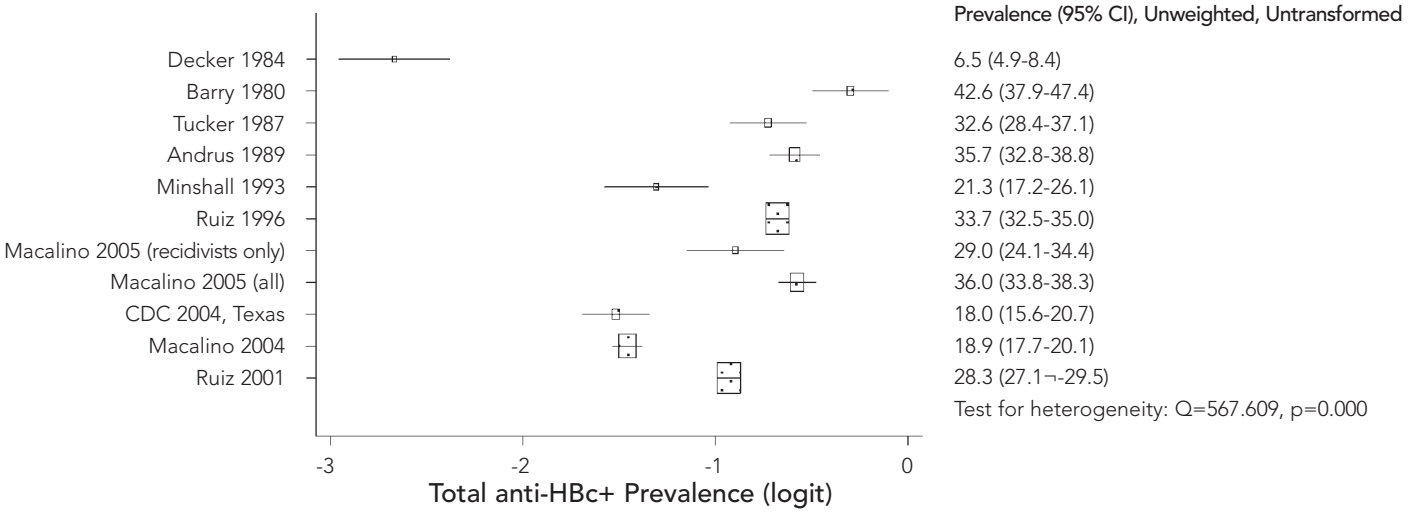
Data were analyzed using Stata 8.2 (College Station, TX: StataCorp LP). Outcomes of interest were prevalence estimates for the most commonly reported seromarkers: HBsAg, total anti-HBc, and any positive HBV marker (i.e., one or more seromarkers positive when more than one seromarker was tested). For each outcome, prevalence estimates with 95% Wilson confidence intervals (CIs) were calculated to display prevalence estimates using a common metric for precision. Wilson CIs were selected because of their overall statistical properties across sample sizes (Brown et al, 2001).

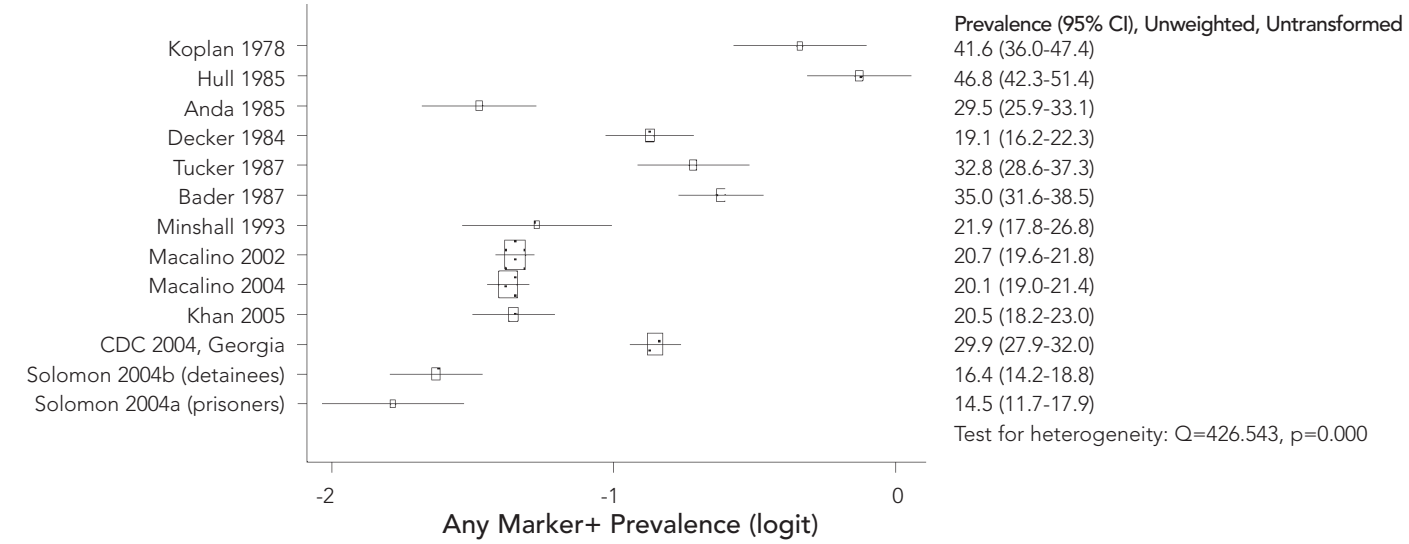
Meta-regression analysis was used to identify potential study-level sources of variation (Greenland, 1998; Thompson, 2001). Harzke et al (2009) previously demonstrated that adult incarcerated populations in the United States are heterogeneous with respect to prevalence estimates of the three commonly reported HBV seromarker outcomes; that is, the dispersion of these HBV seroprevalence estimates around their mean was far greater than would be expected from within-study sampling error alone. Heterogeneity persisted when analyses excluded identified statistical outliers, when analyses were limited to within study sub-groups (e.g., all males, all females, all IDUs), and when analyses were limited to within study-level strata, with one exception (all studies with samples that had ≤30% IDUs) (Harzke et al, 2009). Prior to performing meta-regression analyses, prevalence estimates and corresponding standard errors were transformed into *logits* (natural log of the division of the proportion by 1 minus the proportion) and weighted using the inverse variance method (*meta* command) (Lipsey & Wilson, 2001; Deeks et al, 2001). Logit transformation of proportions has been recommended for meta-analysis because untransformed proportions may overestimate hetereogeneity and because logits afford the advantages of a normal distribution and stable variance analysis (Lipsey & Wilson, 2001; Benjamin et al, 2003). Meta-regression analyses were conducted using a random effects model, which more accurately reflects uncertainty about sources of variation than a fixed model (Greenland, 1998). Because of small samples sizes overall and by strata, weighted logit prevalence estimates for each HBV seromarker prevalence outcome were regressed on each individual study characteristic (*metareg* command). Resulting coefficients were exponentiated to produce prevalence odds ratios (PORs) (Greenland, 1998; Benjamin et al, 2003). Sample demographic variables were dichotomized to capture non-linear relationships and/or to reflect important epidemiologic cut-points (e.g., mean age ≥31 years, because incidence of HBV infection increases sharply at ~30 years of age; CDC, 2005b) or heuristic cut-points [(e.g., >15% females would be considered high and operationally important in a correctional setting; >40% Caucasian or African American generally exceeds distributions for state prison populations (Harrison & Beck, 2003; West & Sabol, 2008)]. Study methods variables with three or more categories were initially modeled as multi-categorical variables, but were later dichotomized to improve precision.

Statistical outliers among weighted logit prevalence estimates were identified using the method proposed by Hamilton (2003) (*iqr* command). To examine the influence of particular study-specific prevalence estimates on meta-regression analyses, analyses were repeated excluding identified outliers. Given sparse data for several potential confounders, the following steps were taken to identify potential confounding: we identified study characteristics that showed at least moderate crude associations with HBV seroprevalence outcomes (POR ≥1.5 for categorical contrasts); we determined which of these study characteristic variables had sufficient numbers of observations to produce PORs by strata (i.e., no zero cells in cross-tabulations of study characteristic variables, and three or more observations in each stratum of a variable, a requirement for meta-regression in Stata 8.2); for study characteristic variables with sufficient observations to do so, we produced and examined PORs for each study characteristic across strata of each of the other study characteristics; finally, when there appeared to be evidence of moderate or strong confounding (i.e., substantial differences between crude and stratified PORs), the variable of interest and the potential confounder variable were entered together into a meta-regression model to examine the influence of the adjustment on the POR for each variable.

FIGURE 1 | HBV seromarker prevalence estimates with 95% CIs and heterogeneity statistics







RESULTS

Search and Study Selection

A total of 579 unique citations were screened. From these, 23 unique studies meeting eligibility criteria were identified. Two eligible studies estimated HBV seroprevalence for two distinct populations, so we treated them as separate estimates. In Solomon et al (2004), one sample was comprised entirely of sentenced state inmates, and the other was comprised of county inmates and detainees along with state detainees awaiting sentencing or transport [hereafter referred to as Solomon et al, 2004a and 2004b, respectively]. In Macalino et al (2005), one sample included only recidivist women (i.e., those with more than one incarceration during the study period), and the other included all women incarcerated during the study period [hereafter referred to as Macalino et al, 2005a and 2005b, respectively]. Thus, our analyses included reported HBV seroprevalence estimates from 25 distinct US incarcerated samples, with 15 estimates of HBsAg prevalence, 11 of anti-HBc, and 13 of any positive HBV marker.

Seroprevalence Estimates and Study Characteristics

Point estimates ranged from 0.9% to 11.4% for HBsAg prevalence, 6.5% to 42.6% for anti-HBc prevalence, and 16.4% to 46.8% for any positive HBV marker prevalence (Figure 1; Table 1). A majority (n = 15) of study populations were composed entirely or predominately (>85%) of male inmates. Nearly all studies (n = 20) were conducted in state prison systems or units, and more than one-third of the studies were conducted in the Southern region of the United States (n = 9). Serum for HBV screening was collected at a single time point during incarceration in five studies and sequentially upon inmate admission in all other studies.

Less than half (n = 10) of the studies reported prevalence estimates for markers providing indications of both current infection (HBsAg) and past infection (anti-HBc or any marker positive). Two recent studies reported their findings in terms of disease states that either were not explicitly defined in terms of seromarkers (CDC, 2004b) or were defined by combinations of seromarkers inconsistent with previous studies (Khan et al, 2005). Findings from these studies were excluded from analyses of the HBsAg and anti-HBc outcomes but were included in analyses for the any positive HBV marker outcome.

Hispanic ethnicity was reported for less than half (n = 12) of the study populations, and when reported, was defined inconsistently across studies. Slightly more than half of the eligible studies reported any behavioral risk factor data, with only 14 studies reporting on history of IDU and only nine studies reporting on MSM history. A majority of HBV seroprevalence estimates (n = 13) were reported in short reports or abstracts rather than in full study reports.

Meta-Regression

In bivariable meta-regression analyses (Table 2), the following study characteristics showed strong positive crude associations (POR ≥2.0) with increased HBsAg prevalence: mean age ≥31, <85% male, <40% Caucasian, <4% MSM, and non-probability sampling (vs. census or probability). Study characteristics showing moderate associations (POR ≥1.5 and <2.0) with increased HBsAg prevalence included use of discarded/stored serum (vs. study-specific screening), serum collection year prior to 1991, and non-state prison facility type. Study characteristics showing strong crude associations with increased anti-HBc prevalence included <40% African American, <4% MSM, and second generation test (vs. first generation). Study characteristics showing moderate crude associations with increased anti-HBc prevalence were <85% male, <40% Caucasian, ≥30% IDU, short report/abstract (vs. full report), and serum collection during incarceration (vs. at admission). Study characteristics showing strong crude associations with increased prevalence of any positive marker included: ≥20% Hispanic/Latino, ≥30% IDU, <4% MSM, serum collection year before 1991, and serum collection during incarceration (vs. at admission). Study characteristics showing moderate associations with increased prevalence of any positive marker included <85% male and West/Midwest region (vs. South/Northeast region).

In general, CIs for crude associations with HBsAg and anti-HBc prevalence estimates were fairly wide, indicating poor precision. Confidence intervals for crude associations with prevalence estimates based on any positive HBV marker were fairly narrow, indicating reasonably good precision. However, for all three markers, nearly all POR estimates ≥2.0 had CIs that excluded values <1.0, and all POR estimates >1.5 had CIs with values overwhelmingly in the positive direction.

Some crude associations were based on a small number of observations overall (e.g., <10 observations) and/or the small number of observations in one of the categories being contrasted (e.g., <3 observations). These associations included: associations of <85% male and <4% MSM with increased HBsAg prevalence; all associations with increased anti-HBc prevalence; and associations of <85% male, ≥20% Hispanic/Latino, ≥30% IDU, and <4% MSM with increased prevalence of any positive HBV marker.

Some crude associations appeared to be strongly influenced by particular studies. The associations of <40% Caucasian and non-state facility type with increased HBsAg prevalence were influenced largely by a single study (Solomon et al, 2004b). These associations were reduced from POR = 2.3 to POR = 1.5 and from POR = 1.9 to POR = 1.3, respectively, when excluding the influential study. Excluding Solomon et al, 2004b, the strength of the association of serum collection year before 1991 with decreased HBsAg prevalence was also reduced to near null

TABLE 1 | Study characteristics and reported prevalence estimates of HBV serologic markers in US incarcerated populations, ordered by year of serum collection

Citation Author, Pub Yr (Serum collection yr) Report type	**Setting** State Region[a] Type	**Serum source/ Sampling**[b]	**Sample characteristics**[c]								**Prevalence estimate(s), 95% Wilson confidence interval(s)**		
			N	Mean Age[d]	Male %	White %	Black %	Hispanic %	IDU %	MSM %	HBsAg+ %	Anti-HBc+ %	Any + marker %
Koplan,1978[e] (1974) Short report/brief	Kansas Midwest State unit	1c	286								8.0 (5.4,11.8)		41.6 (36.0, 47.4)
Bader, 1983 (1980) Letter	Wisconsin Midwest Federal (5 sites)		1045								3.7 (2.7, 5.1)		
Kibby, 1982 (1981) Letter	North Carolina South Federal	1a	293		100						4.1 (2.4, 7.0)		
Hull, 1985e (1982) Short report/brief	New Mexico West State system	1a	455	30.3	100	25.1	7.9	59.1[f]	41.3	3.6			46.8 (42.3, 51.4)
Kaufman, 1983 (1982) Letter	Michigan Midwest State system	4a	3092		100						2.3 (1.8, 2.9)		
Decker, 1984[e] (1983) Full	Tennessee South State system	1b	759	30.5	100	42	57		47	22	0.9 (0.0, 1.4)	6.5 (4.9, 8.4)	29.5 (25.9, 33.1)
Anda,1985 (1983) Short report/brief	Wisconsin Midwest State system	1c	619	25.1	100	58	32	4	28.6	4	1.1 (0.5, 2.3)		19.1 (16.2, 22.3)
Brewer, 1985 (1985) Short report/brief	Maryland South State system	1a	797						28[g]		1.5 (0.8, 2.6)		
Barry, 1990[e] (1985) Short report/brief	Massachusetts Northeast County facility	1a	406	27.8					33.5	3.0		42.6 (37.9, 47.4)	
Tucker,1987 (1985) Full	Virginia South State system	1a	445	33.4	100	42			30	8	2.0 (1.1, 3.8)	32.6 (28.4, 37.1)	32.8 (28.6, 37.3)
Andrus, 1989 (1987) Short report/brief	Oregon West State system	2b	977	30.0	91.4	73.9	16.5	6.2	53.1	3.07		35.7 (32.8, 38.8)	
Bader, 1987 (1987) Abstract	Multiple states Federal (6 sites)		741		77.5								35.0 (31.6, 38.5)
Smith, 1991 (1988) Full	New York Northeast State system	4a	430	29.4	0	17.7	44.8	37.5	28.6	N/A	2.3 (1.3, 4.2)		
Minshall,1993 (1991) Full	Indiana Midwest County facility	1a	319	30.8	86.2	44.5	44.8	10.0	19.4		1.6 (0.7, 3.6)	21.3 (17.2, 26.1)	21.9 (17.8, 26.8)
Ruiz,1996[f] (1994) Govt. agency report	California West State system	1b	5144	33.1	87.8	28.4	29.4	30.6	97.1	0.3%	2.2 (1.6, 2.6)	33.7 (32.5, 35.0)	

TABLE 1 *(cont.)* | **Study characteristics and reported prevalence estimates of HBV serologic markers in US incarcerated populations, ordered by year of serum collection**

Citation Author, Pub Yr (Serum collection yr) Report type	**Setting** State Region[a] Type	**Serum source/ Sampling**[b]	**Sample characteristics**[c]								**Prevalence estimate(s), 95% Wilson confidence interval(s)**		
			N	Mean Age[d]	Male %	White %	Black %	Hispanic %	IDU %	MSM %	HBsAg+ %	Anti-HBc+ %	Any + marker %
Macalino, 2005-a[g] (1996) Full	Rhode Island Northeast State system	2c	297	30.9	0	65.0	25.6	9.4	40.4			29.0 (24.1, 34.4)	
Macalino, 2005-b[h] (1996) Sub-study	Rhode Island Northeast State system	2a	1805	32	0	71	21	6				36.0 (33.8, 38.3)	
CDC, 2004[i] (1999) Govt. agency report	Texas South State system	3b	889									18.0 (15.6, 20.7)	
Macalino, 2002 (1999) Abstract	Rhode Island Northeast State system	2a	5053		87.5	59.0	24.9	16.2					20.7 (19.6, 21.8)
Macalino, 2004 (1999) Full	Rhode Island Northeast State system	2a	4269	31.8	100	57.4	25.6	16.2	10.6		3.1 (2.7, 3.7)	18.9 (17.7, 20.1)	20.1 (19.0, 21.4)
Ruiz, 2001[j] (1999) Govt. agency report	California West State system	1b	5595	34.8	87.1	24.1	28.4	33.1	36.3	1.2	3.5 (3.0, 4.0)	28.3 (27.1, 29.5)	
Khan, 2005 (2000) Full	Georgia South State unit	1a	1124	32.5	100	24.3	66.3	6.7	11.6	5.6			20.5 (18.2, 23.0)
Solomon, 2004-a[k] (2002) Full	Maryland South State system	2c	1081	33.1	90.3	31.8	68.0				2.9 (2.0, 4.0)		16.4 (14.2, 18.8)
Solomon, 2004-b[l] (2002) Full	Maryland South County facility	2c	2236	33.9	83.6	13.9	85.2				11.4 (10.2, 12.8)		29.9 (27.9, 32.0)
CDC, 2004[m] (2003) Govt. agency report	Georgia South State unit	1d	489										14.5 (11.7, 17.9)

a Regions used by the US Centers for Disease Control and Prevention (CDC) for hepatitis surveillance in the United States (CDC, 2005).
b Serum Source/Sampling: 1=Screening specifically for prevalence study, a=census, b=probability, c=non-probability, d=not reported; 2=Discarded or stored serum from correctional health routine/mandatory serum collection (e.g., as for syphilis or HIV testing), a-d as previously noted; 3=Discarded/stored serum from previous study, a-d as previously noted; 4=Correctional health HBV screening, a=mandatory/routine, b=targeted.
c Percentages were re-calculated by reviewing authors and reported to first decimal place unless raw data were not provided.
d When age categories were reported without a value for mean age, mean age was calculated by assuming that the mid-point of each age category was the mean of the category.
e Unless reported otherwise, first generation assays were assumed to be used in studies testing serum before 1985.
f Six (of 10) reception/intake centers (four male, two female). Behavioral risk factor data were based on 899 inmates. Only anti-HBc positives were tested for HBsAg.
g Single intake facility serves as both jail & prison. Sampling frame restricted to women recidivists (i.e., more than one incarceration at the site during the study period).
h Baseline estimate from Macalino et al (2005-a) for all female admits (both non-recidivists & recidivists). Sample size value estimated from data provided. Baseline estimate treated as a short report/brief in analyses
i Texas system includes state jails (for those with less than two-year sentence).
j Six (of 10) reception/intake centers (four male, two female). Behavioral risk factor data drawn from Table 13 in Ruiz et al (2001), with 4318 reporting for IDU question and 1148 reporting for MSM question.
k Intake facility for the Maryland Department of Corrections for sentenced inmates. Sample included inmates not tested at Baltimore Municipal Detention Center while awaiting sentencing. Hierarchical sampling scheme using excess serum (screening for HIV, followed by HCV, HBsAg, and core and surface HBV antibodies). Denominator for HBsAg prevalence=1050. For core and surface antibodies (aggregate) prevalence, denominator=1018
l Intake facility and detention center for the county of Baltimore. Denominator for HBsAg=2236 and for core and surface antibodies=1892.
m Includes four (of five) intake facilities.

(POR = 0.91, from POR = 0.69). The strength of the associations of discarded serum (vs. study-specific screening) and non-probability sampling procedures with increased HBsAg prevalence were also diminished when the Solomon et al 2004b study was excluded, from POR = 1.8 to POR = 1.3 and from and POR = 2.0 to POR = 1.5, respectively. The association of <40% African American with increased anti-HBc prevalence were largely influenced by Decker et al, (1984) (from POR = 3.1 to POR = 1.6 excluding this study).

Although assessment of potential confounding was limited by the small number of studies and reported strata, evidence suggestive of confounding was apparent for some associations with HBsAg and any positive HBV marker prevalence estimates. After adjusting for mean age and excluding Solomon et al (2004b) (due to results of influence analysis), the association of <40% Caucasian with increased HBsAg prevalence reversed its direction to a modest degree (adjusted POR = 0.83). Similarly, the association of non-probability sampling procedures with increased HBsAg prevalence approached null when excluding Solomon (2004-b) and adjusting for percent Caucasian, percent African American, or serum source. Serum collection year appeared to confound several associations with any positive HBV marker. Notably, adjusted for serum collection year, PORs were 0.61 for serum collection during incarceration and (crude POR = 2.2) and 1.1 for West/Midwest region (crude POR = 1.6). So, after adjustment for each of the other potential sources of variation, mean age ≥31 remained strongly associated with increased HBsAg prevalence, and serum collection year <1991 remained strongly associated with increased prevalence of any positive HBV marker. It may also be noted, although based on a fairly small number of observations (n = 7), the association of ≥30% IDU with increased prevalence of any positive HBV marker also remained strong after adjustment for each of the other potential sources of variation.

DISCUSSION

Because HBV seroprevalence estimates from US incarcerated population vary widely, the purpose of this study was to investigate a range of study-level factors as potential sources of variation in prevalence estimates of HBV serologic markers from adult incarcerated populations in the United States. Results of bivariable meta-regression analyses indicated that higher mean age of the study sample (≥31 years) was strongly associated with increased HBsAg prevalence (POR = 2.5), and earlier serum collection year (before 1991) was strongly associated with increased prevalence of any positive marker (POR = 2.0). These associations were fairly precise and were not influenced by particular studies or apparent confounding. Other study-level characteristics, including the distribution of race/ethnicity and behavioral risk factors (IDU and MSM) and specific sampling and measurement procedures, showed moderate-to-strong associations with HBV seroprevalence estimates, but were considered less certain because of small numbers of observations, influence of single studies, or potential confounding. However, these epidemiologic and methodologic factors cannot be ruled out by the available data as potential sources of heterogeneity in HBV seroprevalence estimates.

The association of older mean age with increased HBsAg prevalence suggests that the age distribution of an incarcerated population may be an important consideration for determining HBV-related policy in correctional settings. The associations of behavioral risk factors (e.g., IDU history) with HBV seroprevalence have often been assessed in previous studies with the explicit aim of informing decisions about targeted HBV vaccination programming in incarcerated populations. In contrast, although age has been consistently and often strongly associated with HBV seroprevalence (for all markers) within study samples, the age distribution of a study sample or prison population has seldom been discussed as an important consideration in policy-making. The association of older mean age with prevalence of HBsAg, which indicates active HBV infections, suggests that incarcerated populations with older mean ages may have a greater burden of active, infectious cases of HBV. This knowledge may inform HBV screening and vaccination protocols in incarcerated populations, particularly given evidence of continued HBV transmission in these populations (CDC, 2004b; Macalino et al, 2004; Khan et al, 2005). Additionally, the distributions of race/ethnicity and behavioral risk factors – particularly Hispanic/Latino ethnicity and IDU – cannot be ruled out as sources of heterogeneity in HBV seroprevalence in incarcerated populations, because small numbers of studies reporting complete risk factor data prevented us from obtaining valid and precise estimates of these associations.

The association of earlier serum collection year (before 1991) with increased prevalence of any positive marker suggests that temporal variation in background prevalence may be partially responsible for heterogeneity of these estimates in incarcerated populations. In previous studies, HBV seroprevalence estimates have been assumed to be homogeneous over time and space and have been compared only with national average HBV seroprevalence estimates (e.g., Anda et al, 1985; Tucker et al, 1987; Macalino et al, 2004; Solomon et al, 2004). With a few previously noted exceptions, HBV seroprevalence estimates in incarcerated populations have not been contrasted with other incarcerated populations or with background prevalence across time and space. Consideration of existing background prevalence data may be useful in interpreting comparisons of overall burden of HBV seroprevalence estimates across incarcerated populations. Considering existing background prevalence data may

TABLE 2 | Results of bivariable meta-regression analyses relating sample characteristics and study methods to HBV seromarker prevalence estimates[a]

		HBsAg				Anti-HBc				Any positive HBV marker			
Characteristic	**Category**	n	POR	95% CI		n	POR	95% CI		n	POR	95% CI	
Mean Age	<31 yrs (ref)	4				5				4			
	≥31 yrs	6	2.6	1.1	6.0	5	1.3	0.55	3.1	5	0.78	0.41	1.5
% Male	≥85% (ref)	10				7				9			
	<85%	2	2.7	1.1	6.3	2	1.6	0.55	4.5	2	1.5	0.75	2.9
% White	≥40% (ref)	5				7				6			
	<40%	5	2.3	0.87	5.3	2	1.5	0.50	4.2	4	1.2	0.67	2.2
% Black	≥40% (ref)	5				2				5			
	<40%	4	0.84	0.28	2.5	6	3.1	1.4	6.7	4	1.1	0.59	2.1
% Hispanic	<20% (ref)	4				4				6			
	≥20%	3	0.84	0.24	3.0	2	1.2	0.59	2.4	1	3.2	1.9	5.2
% IDU	<30% (ref)	4				2				4			
	≥30%	4	1.0	0.51	2.1	7	1.5	0.50	4.6	3	2.2	1.5	3.3
% MSM	≥4% (ref)	3				2				4			
	<4%	2	2.2	1.1	4.4	4	2.9	0.85	10.0	1	2.6	1.2	3.2
Report type	Full study (ref)	7				5				7			
	Short report/abstract/other	8	1.1	0.52	2.3	6	1.9	0.94	3.9	6	1.2	0.70	2.2
Serum collection year	1991 or later (ref)	6				7				7			
	Before 1991	9	0.69	0.34	1.4	4	0.99	0.43	2.3	6	2.0	1.3	3.0
Region	South/Northeast (ref)	8				7				8			
	West/Mid-west	7	0.98	0.47	2.0	4	1.3	0.58	3.0	4	1.6	0.86	2.8
Facility type	State prison (ref)	11				9				10			
	Other	4	1.9	0.92	4.1	2	1.4	0.49	3.8	3	1.2	0.62	2.4
Serum source	Study-specific screen (ref)	7				4				8			
	Discarded serum	5	1.8	0.76	4.3	7	1.3	0.59	3.1	4	0.73	0.40	1.4
Sampling protocol	Census/Probability (ref)	10				10				7			
	Non-probability	5	2.0	1.0	3.9	1	1.2	0.29	4.9	6	0.90	0.51	1.6
Serum collection timing	At admission (ref)	13				9				10			
	During incarceration	2	1.1	0.40	3.3	2	0.60	0.22	1.6	3	2.2	1.3	3.6
Test generation	First (ref)	6				2							
	Second	9	0.99	0.47	2.1	9	2.4	0.99	5.8	--	--	--	--

a Meta-regression analyses assumed a random effects model and used logit transformations of HBV seroprevalence estimates as the dependent variable.

also be useful for estimating HBV seroprevalence or projecting future disease burden in incarcerated populations, particularly when site- or system-specific correctional data are limited.

Our analysis was limited to studies indexed prior to August 31, 2005; however, only one subsequently published study has reported HBV seroprevalence estimates from an adult incarcerated population (jail detainees, specifically) (Hennessey et al, 2009). Estimates reported from this study would likely have been excluded from our analysis because these estimates reflected complex weighting methods which would not have been comparable to the estimates included in our analysis. The any positive HBV marker outcome may be viewed as inherently heterogeneous because it reflects the use of different seromarkers across studies. However, this heterogeneity may actually be limited, because in all identified studies, the any positive marker prevalence outcome reflected the combination of a marker indicating current infection (e.g., HBsAg or IgM anti-HBc) with a marker indicating past infection (e.g., IgG anti-HBc, total anti-HBc, or anti-HBs in the pre-vaccination era). Our analysis included prevalence estimates from several different types of correctional samples, including federal, state, and county inmates as well as county and state detainees. It may be suggested, on the basis of the relatively high HBsAg prevalence estimate from the sample comprised primarily of county and state detainees (Solomon et al, 2004b) and the strong influence of this estimate on meta-regression analyses, that estimates

from detainee samples could have been initially excluded from analysis. However, only a few studies have reported HBV seroprevalence estimates from detainee populations (Solomon et al, 2004b; Hennessey et al, 2009), and it is unclear from these studies how prevalence estimates of HBsAg or other HBV seromarkers from jail populations compare to estimates from prison populations.

The small number of studies reporting data relevant for meta-regression analyses affected the precision of our estimated associations and limited multivariable analyses, which impaired our assessment of interaction and confounding. Thus, our systematic review and meta-regression analyses highlight the limitations of the literature and point toward recommendations for designing and reporting future HBV seroprevalence studies. First, at a minimum, HBV seroprevalence studies should measure and report both HBsAg and anti-HBc for all members of the study sample. This would optimize comparability with other studies and support further investigations of across-study variation. Ideally, future studies would also test for anti-HBs, the seromarker which indicates immunity due to vaccination. Measuring all three of these HBV seromarkers would make it possible to report HBV seroprevalence in a manner that distinguishes infection and immune states: susceptible (HBsAg–, anti-HBc–, anti-HBs–); acute infection (HBsAg+, anti-HBc–, anti-HBs–); chronic infection (HBsAg+, anti-HBc+, anti-HBs+);* past infection with immunity (HBsAg–, anti-HBc+, anti-HBs+); and immune due to vaccination (anti-HBsAg–, anti-HBc–, anti-HBs+). Describing the distribution of infection and immune states would provide guidance to correctional healthcare planners and administrators in projecting the burden of HBV disease in prison populations and in targeting prevention efforts.

Second, it is important that study samples are described in detail and HBV seroprevalence estimates are reported across strata of race/ethnicity and behavioral risk factors. To reiterate, Hispanic/Latino ethnicity was reported for less than half (n = 12) of the study populations, and when reported, was defined inconsistently across studies. It is particularly critical that Hispanic/Latino ethnicity be considered in future studies. Hispanic/Latino persons represent a growing portion of the US population and the US prison population. In the non-incarcerated US population, estimates of HBV seroprevalence historically have been considerably higher among African Americans compared to other race/ethnic groups; however, studies have shown that HBV seroprevalence among Hispanic/Latino prisoners approaches or surpasses that among African-American prisoners (Ruiz & Mikanda, 1996; Ruiz et al, 2001; Macalino et al, 2004; Hennessey et al, 2009).

With respect to behavioral risk factors, a history of IDU and a history of multiple sex partners (particularly among MSM) are the most common risk factors for incident HBV infection (CDC, 2009), but only 14 studies included in our review reported on history of IDU and only nine reported on history of MSM. Indeed, in our analysis, estimated associations of the history of IDU with the prevalence of any given HBV seromarker outcome were based on <10 studies, and associations of the history of MSM with the prevalence of any given HBV seromarker outcome were based on less than six studies. So, although the associations of histories of IDU or MSM with prevalence of HBV seromarkers were moderate-to-strong, these associations were considered less certain because they were based on small numbers of observations. However, given the evidence from the general population and the evidence available from incarcerated populations to date, it is reasonable to think that the distributions of these risk factors are sources of variation in HBV seroprevalence across studies of incarcerated samples. Where possible, the distributions of these behavioral risk factors and stratum-specific prevalence estimates should be included in studies reporting HBV seroprevalence estimates from incarcerated populations. Behavioral risk factor information is often readily available to investigators, because information regarding IDU and sexual history are routinely included in the medical intake process in prison healthcare settings to assess risk of HIV and viral hepatitis infections and to recommend further screening.

Despite its limitations, our study contributes to the prison healthcare literature in several ways. It provides detailed descriptive information about all reports of HBV seroprevalence estimates (meeting pre-specified criteria) from US adult incarcerated populations. On that basis, our study supports specific recommendations for the design and reporting of future studies – namely, to measure and report a standard set of HBV seromarkers and to improve reporting of race/ethnicity categories and behavioral risk factors. Furthermore, our study suggests several potential sources of across-study heterogeneity in HBV seroprevalence estimates from US incarcerated populations. Specifically, in meta-regression analyses, it appeared that mean age was a source of heterogeneity in HBsAg prevalence and serum collection year was a source of heterogeneity in the prevalence of any positive HBV marker. However, other potential sources of variation could not be ruled out by the available data. Heterogeneity in HBV seroprevalence estimates may potentially be influenced by a range of factors including the distribution of other demographic characteristics (e.g., race/ethnicity) and behavioral risk factors (IDU and MSM) in study samples as well as geographic and temporal variation in background prevalence and study methods (sampling procedures, serum source, and serum collection timing). These factors

* A small proportion of persons who test HBsAg+ and anti-HBc+ may be in the process of developing immunity and resolving their infection.

should be considered when comparing HBV seroprevalence estimates from incarcerated populations across studies and when developing HBV screening and vaccination protocols in correctional settings.

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