The unmet needs in chronic hepatitis B

Impact of aging and comorbidities
The CHB population in the U.S. is aging

CHB can be a lifelong infection

In the U.S., the CHB patient population is aging, and the prevalence of CHB infection is higher in older age groups.

Mean age in 3 large U.S. patient cohorts with CHB infection

<table>
<thead>
<tr>
<th>Year</th>
<th>Commercial/Medicare</th>
<th>Medicaid</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>48.1</td>
<td>44.1</td>
</tr>
<tr>
<td>2015</td>
<td>51.8</td>
<td>50.2</td>
</tr>
</tbody>
</table>

All comparisons of 2006 vs 2015 are significant at P<0.001

CHB=chronic hepatitis B; HDV=hepatitis D virus.

As people with CHB age, the prevalence of comorbidities increases

Comorbidities in CHB patients during a 15-year period (San Francisco Bay Area cohort)

- Chronic kidney disease: 4x increase
- Hypertension: 3x increase
- Hyperlipidemia: 5x increase
- Diabetes mellitus: 5x increase
- Osteoporosis: 3x increase
- Osteopenia: 2x increase

Some of the comorbidities are more prevalent in CHB patients vs the uninfected population

Key Facts

Approximately 2 million persons are living with CHB in the U.S.

- Up to 95% of foreign-born persons with CHB migrated from regions of intermediate and high endemicity.
- 1 in 12 Asian Americans have CHB.
- 1 in 10 African-born persons have CHB.
- In the U.S., CHB is largely undiagnosed and untreated.
- 70% are undiagnosed.
- 2.5% receive treatment.

CHB=chronic hepatitis B; HDV=hepatitis D virus.

* A retrospective, observational study with case matching of CHB patients without HDV coinfection, based on U.S. administrative healthcare claims from Commercial/Medicare (n=32,623) and Medicaid (n=11,603) databases from 2006 to 2015.


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*2012 estimate.

*2010 data.
As people age, their renal function declines

In the general population, the mean eGFR decline is approximately 1 mL/min/1.73 m² annually in men and women after age 20–30 years; this decline increases in older adults.

People with CHB infection have a significantly higher prevalence (and also higher risk) of CKD and ESRD than those without CHB.

Renal function may be impaired in patients with CHB before they start treatment:
- In one ex-U.S. cohort (N=260), 2 in 3 treatment-naïve HBsAg-positive individuals had some degree of kidney disease.

Key Facts

<table>
<thead>
<tr>
<th>Stages of CKD</th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
<th>Stage 4</th>
<th>Stage 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR (mL/min/1.73 m²)</td>
<td>≥90</td>
<td>89–60</td>
<td>59–30</td>
<td>29–15</td>
<td>&lt;15</td>
</tr>
</tbody>
</table>

- Kidney damage with normal kidney function
- Kidney damage with mild loss of kidney function
- Mild to severe loss of kidney function
- Severe loss of kidney function
- Kidney failure
  - (or ESRD)

eGFR=estimated glomerular filtration rate; CKD=chronic kidney disease; ESRD=end-stage renal disease; HBsAg=hepatitis B surface antigen; NHANES=National Health and Nutrition Examination Survey.

Key Facts

According to the CDC, CKD is common among adults in the U.S.:
- 30 million adults in the U.S. have CKD
- 96% of people with kidney damage or mildly reduced function are not aware of their kidney damage or CKD

CDC=Centers for Disease Control and Prevention; HBV=hepatitis B virus.

Burden of renal impairment in CHB infection

People with CHB infection have a significantly higher prevalence (and also higher risk) of CKD and ESRD than those without CHB.

IN THE U.S.

1.7×–2.5× Higher prevalence of CKD in CHB patients vs uninfected population in 2015.

*Two nationwide, Taiwanese cohort studies using the Taiwan National Health Insurance Research Database, to evaluate the association of HBV with CKD (inclusive of stages 1 to 5) (1998–2010; N=17,796) or ESRD (1999–2010; N=17,758).

*A retrospective, observational study with case matching of CHB patients without HDV coinfection, based on U.S. administrative healthcare claims from Commercial/Medicare (n=32,523) and Medicaid (n=11,503) databases from 2006 to 2015.
Complications of CHB infection

CHB patients may be asymptomatic for 20-30 years, but the infection can progressively damage the liver over time.\(^{21,22}\)

If left untreated, of persons with CHB infection...

- 15% to 40% develop cirrhosis, HCC, or liver failure
- 25% die prematurely of these complications

Impact of metabolic diseases on liver complications in CHB patients

- CHB patients with new-onset diabetes have a significantly higher incidence (and higher risk) of cirrhosis and HCC vs those without diabetes.\(^{24,25}\)

Cumulative incidence of cirrhosis and HCC in Taiwanese CHB cohorts\(^{24,25}\)

Key Facts

Bone-related comorbidities are major health problems in the U.S.\(^{18-20}\)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence</th>
<th>Combined lifetime risk of fractures(^{2})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteopenia</td>
<td>48 million</td>
<td>13% (male) 13% (female)</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>9 million</td>
<td>20% (male) 40% (female)</td>
</tr>
</tbody>
</table>

Burden of bone-related comorbidities in CHB infection

Patients with CHB infection demonstrated a higher prevalence of osteoporosis and osteopenia than uninfected persons.\(^{17,18}\)

A study conducted in China (2014-2015) of 148 CHB patients vs age- and gender-matched healthy controls, to investigate the prevalence of osteoporosis in CHB patients.\(^{17}\)

IN THE U.S.

Up to 1.5x Higher prevalence of osteoporosis and/or bone fracture in CHB patients vs uninfected population in 2015\(^{4,5}\)

A retrospective, observational study with case matching of CHB patients without HDV coinfection, based on U.S. administrative healthcare claims from Commercial/Medicare (n=32,523) and Medicaid (n=11,603) databases from 2006 to 2015.\(^{5}\)

HCC=hepatocellular carcinoma.
Aging and comorbidities – Summary

In the U.S., the CHB patient population is growing older and has more comorbidities, such as kidney- and bone-related conditions, as they age\(^2,^4\)

In two studies, the prevalence of comorbidities in CHB patients significantly increased in the U.S. over time (2000–2005 vs 2011–2015\(^2\) and 2006 vs 2015\(^4\))

<table>
<thead>
<tr>
<th>Renal Impairments (eg, CKD, ESRD)</th>
<th>Hypertension</th>
<th>Hyperlipidemia</th>
<th>Diabetes</th>
<th>Osteopenia and Osteoporosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>(2\times-4\times)</td>
<td>(2\times-3\times)</td>
<td>(3\times-5\times)</td>
<td>(1.5\times-5\times)</td>
<td>(2\times-3\times)</td>
</tr>
</tbody>
</table>

- Renal function typically decreases with age\(^12\)
- Renal impairment (eg, CKD, ESRD) is observed more frequently in CHB patients than in uninfected people\(^4\)
- Bone density may decrease with age\(^27\)
- Osteoporosis and bone fracture are observed more frequently in CHB patients than in uninfected people\(^4\)

Due to the associations between CHB infection and comorbidities, careful evaluation and consideration are needed when managing CHB patients\(^28\)

Early diagnosis and disease management are needed to prevent and mitigate liver as well as non-liver comorbidities\(^2\)


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