The unmet needs in chronic hepatitis B

*Impact of aging and comorbidities*
CHB can be a lifelong infection¹
In the U.S., the CHB patient population is aging, and the prevalence of CHB infection is higher in older age groups²³.

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

b2012 estimate.

c2010 data.

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 2015.⁴

“CHB patients with comorbidities (%)

Mean age in 3 large U.S. patient cohorts with CHB infection⁴ᵃ

<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>51.8</td>
</tr>
<tr>
<td>2015</td>
<td>50.2</td>
<td>50.2</td>
</tr>
</tbody>
</table>

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

As people with CHB age, the prevalence of comorbidities increases

Comorbidities in CHB patients during a 15-year period (San Francisco Bay Area cohort)²ᵃ

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic kidney disease</td>
<td>4x</td>
<td>5x</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3x</td>
<td>5x</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>5x</td>
<td>5x</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3x</td>
<td>3x</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td></td>
<td>2x</td>
</tr>
<tr>
<td>Osteopenia</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P<0.001 for all comparisons.

Some of the comorbidities are more prevalent in CHB patients vs the uninfected population⁴¹⁰¹¹

Key Facts
Approximately 2 million persons are living with CHB in the U.S.⁵⁶ᵃ

- Up to 95% of foreign-born persons with CHB migrated from regions of intermediate and high endemicity²
- 1 in 12 Asian Americans have CHB⁴
- 1 in 10 African-born persons have CHB⁶
- In the U.S., CHB is largely undiagnosed and untreated⁴⁵
- 70% are undiagnosed⁴⁵
- 2.5% receive treatment³

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

²2012 estimate.
³2010 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.12

People with CHB infection have a significantly higher prevalence (and also higher risk) of CKD and ESRD than those without CHB.11,15,a

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.13

Key Facts
- According to the CDC, CKD is common among adults in the U.S.16
- 30 million adults in the U.S. have CKD.16
- 96% of people with kidney damage or mildly reduced function are not aware of their kidney damage or CKD.16

Key Facts
- Stages of CKD:14 Stage 1: eGFR ≥90 (mL/min/1.73 m²); Stage 2: 89–60; Stage 3: 59–30; Stage 4: 29–15; Stage 5: <15
- 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 (or ESRD), Kidney failure (or ESRD)

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.11,15,a

Key Facts
- IN THE U.S.
- 1.7×–2.5× Higher prevalence of CKD in CHB patients vs uninfected population in 2015.4,b

Key Facts
- CDC=Centers for Disease Control and Prevention; HBV=hepatitis B virus.
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.**\(^ {18-20}\)
  - **Prevalence**
    - 48 million Osteopenia
    - 9 million Osteoporosis
  - Combined lifetime risk of fractures
    - 13% (male)
    - 40% (female)

IN THE U.S.

Up to **1.5x** Higher prevalence of osteoporosis and/or bone fracture in CHB patients vs uninfected population in 2015.\(^ {4,6}\)

Prevalence of osteopenia and osteoporosis in a Chinese cohort\(^ {17, a}\)

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Osteopenia</th>
<th>Osteoporosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>14-44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>45-54</td>
<td></td>
<td></td>
</tr>
<tr>
<td>55-64</td>
<td></td>
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</tr>
<tr>
<td>65-72</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* 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.\(^ {17}\)

Burden of bone-related comorbidities in CHB infection

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

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**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\(^4\)).

### Renal Impairments (eg, CKD, ESRD)

- Renal function typically decreases with age\(^12\)
- Renal impairment (eg, CKD, ESRD) is observed more frequently in CHB patients than in uninfected people\(^4\)

### Hypertension

- 2×–3×

### Hyperlipidemia

- 3×–5×

### Diabetes

- 1.5×–5×

### Osteopenia and Osteoporosis

- 2×–3×

- 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\(^2\).

References:

18. Johnell O, Kanis J. Osteoporos Int. 2005;16(suppl 2):S3-S7;