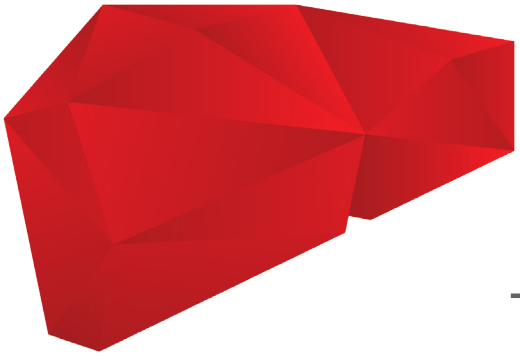

The unmet needs in chronic hepatitis B

Impact of aging and comorbidities

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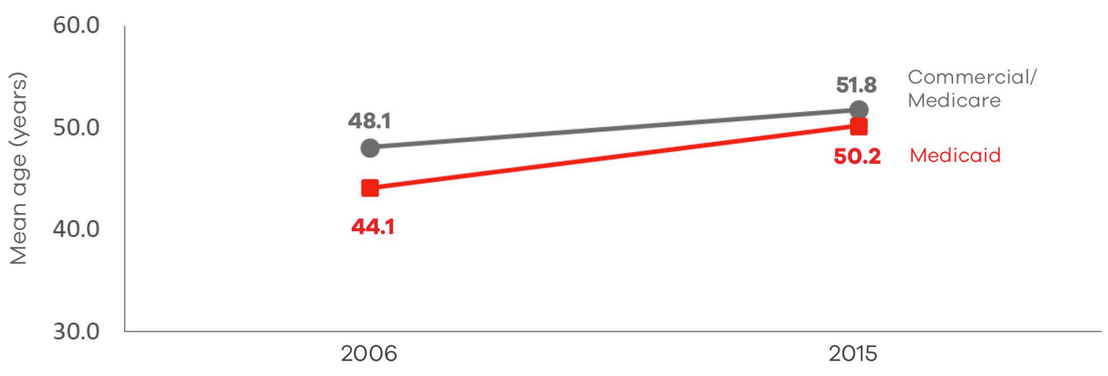
The CHB population in the U.S. is aging

CHB can be a lifelong infection[1]

In the U.S., the CHB patient population is aging, and the prevalence of CHB infection is higher in older age groups[2,3]

Mean age in 3 large U.S. patient cohorts with CHB infection[4,a]



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

[a]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]

Key Facts

Approximately 2 million persons are living with CHB in the U.S.[5,6,b]

Up to **95%** of foreign-born persons with CHB migrated from regions of intermediate and high endemicity[7]

1 in 12 Asian Americans have CHB[8]

1 in 10 African-born persons have CHB[6]

In the U.S., CHB is largely undiagnosed and untreated[9,c]

70% are undiagnosed[9]

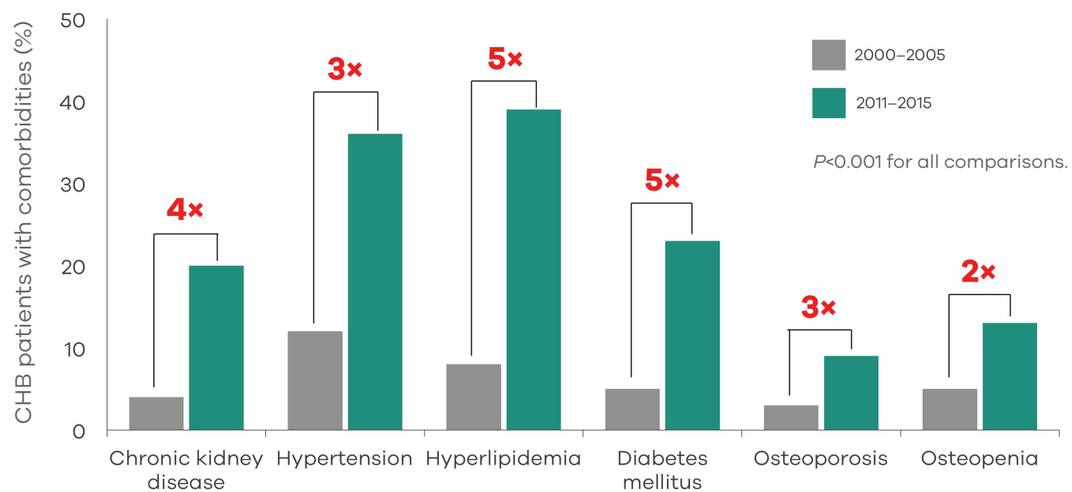
2.5% receive treatment[9]

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

[b]2012 estimate.
[c]2010 data.

As people with CHB age, the prevalence of comorbidities increases

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



[a]A retrospective, observational study of 2734 CHB patients across 3 time periods (2000–2005; 2006–2010; 2011–2015) at a university medical center and primary care clinics in the San Francisco Bay Area.[2]

Some of the comorbidities are more prevalent in CHB patients vs the uninfected population[4,10,11]

Chronic kidney disease

Cardiovascular disease (eg, hypertension)

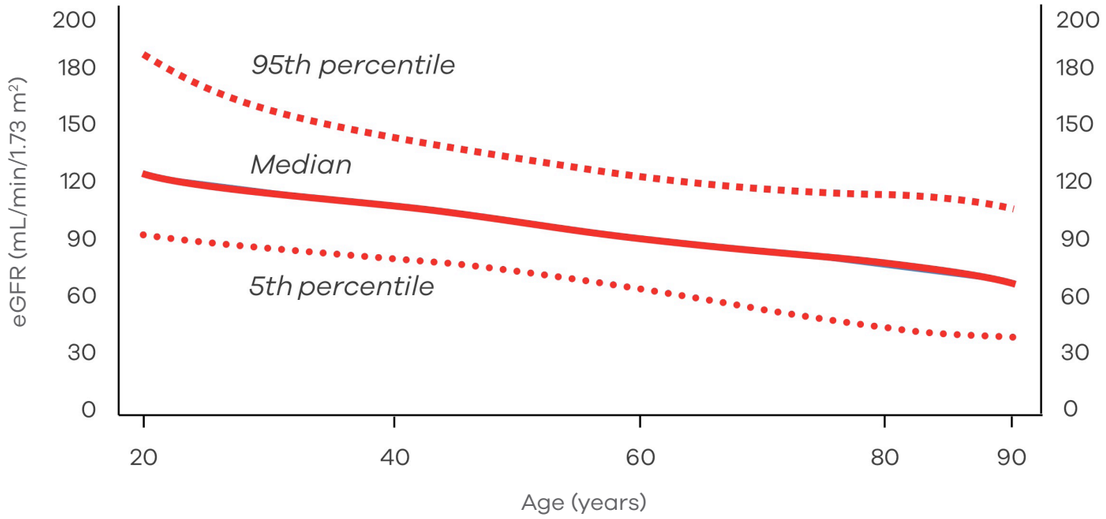
Metabolic disorders (eg, diabetes)

Bone disease (eg, osteoporosis)

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]

Percentiles of eGFR regressed on age (U.S. NHANES III, 1988-1994)[12]



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

Stages of CKD[14]	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
eGFR (mL/min/1.73 m²)	≥90	89–60	59–30	29–15	<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	Kidney **failure**[a] (or ESRD)

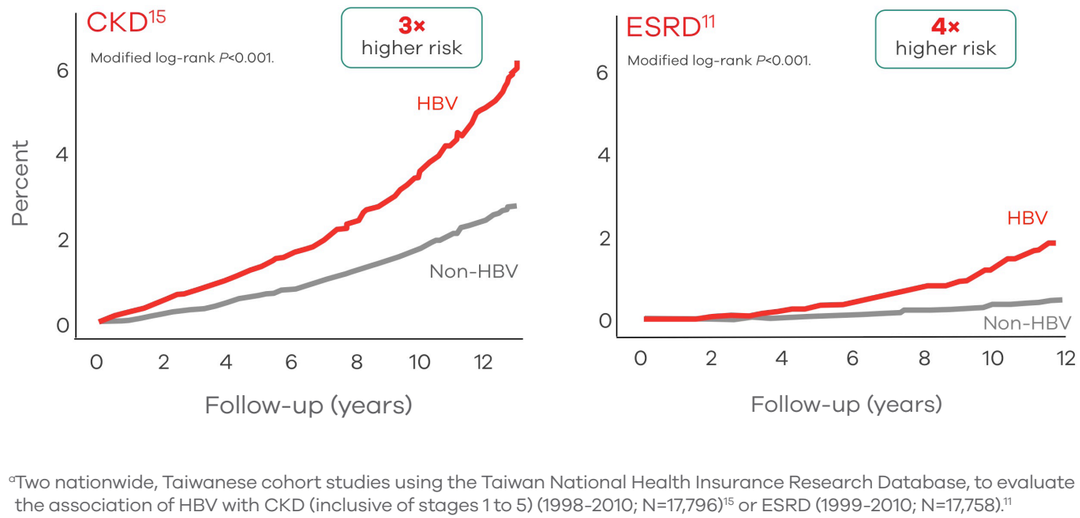
eGFR=estimated glomerular filtration rate; CKD=chronic kidney disease; ESRD=end-stage renal disease; HBsAg=hepatitis B surface antigen; NHANES=National Health and Nutrition Examination Survey.

[a]Requiring dialysis or transplant for survival.

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]

Cumulative incidence of CKD and ESRD in untreated, Taiwanese CHB cohort[11,15]



[a]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)[15] or ESRD (1999-2010; N=17,758).[11]

IN THE U.S.

1.7×–2.5× **Higher prevalence of CKD in CHB patients vs uninfected population in 2015[4,b]**

[b]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]

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]

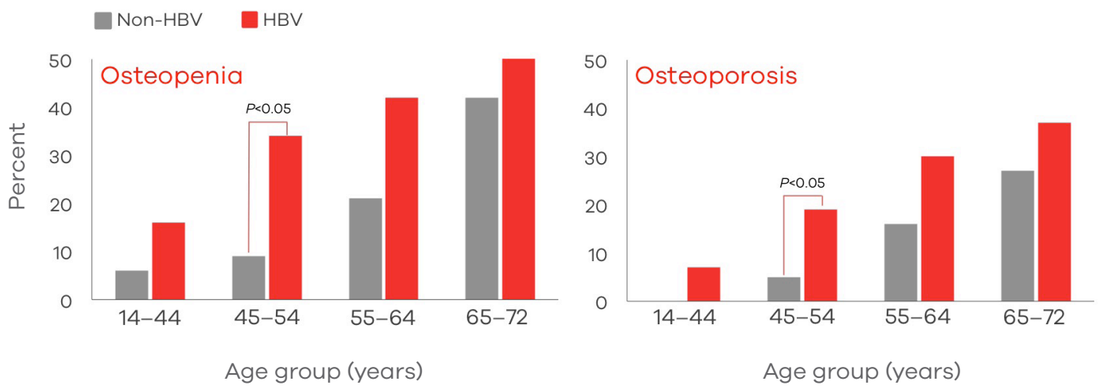
96% of people with kidney damage or mildly reduced function are not aware of their kidney damage or CKD[16]

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

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]

Prevalence of osteopenia and osteoporosis in a Chinese cohort[17,a]



[a]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 1.5× **Higher prevalence of osteoporosis and/or bone fracture in CHB patients vs uninfected population in 2015[4,b]**

[b]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]

Key Facts

Bone-related comorbidities are major health problems in the U.S.[18-20]

Prevalence[c]

48 million Osteopenia

9 million Osteoporosis

Combined lifetime risk of fractures[d]

13% (male)

40% (female)

[c]Based on 2010 data.[19]
[d]Combined risk for hip, forearm, and vertebral fracture at 50 years of age.[18]

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...[23]

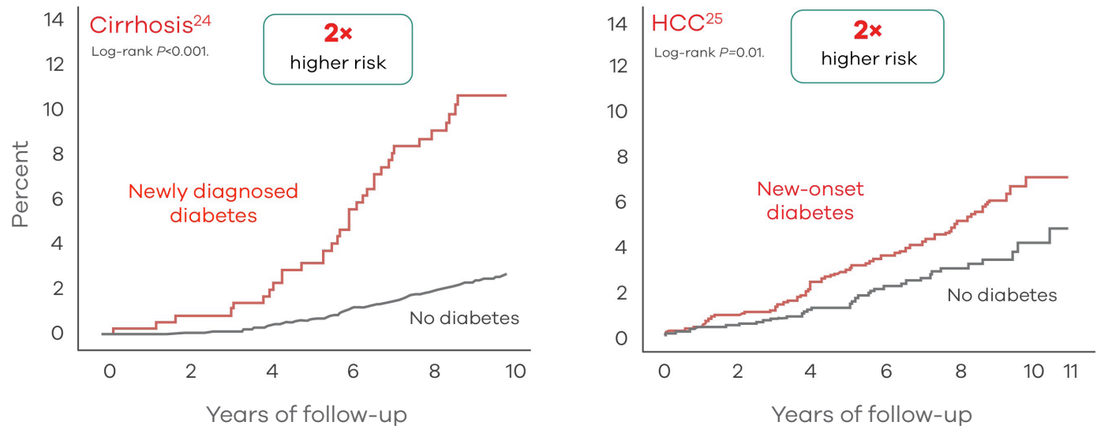
15% to 40%
develop cirrhosis, HCC, or liver failure

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]



Two nationwide cohort studies using the Taiwanese National Health Insurance Research Database (1997-2009). In the cirrhosis study,[24] 351 CHB patients had diabetes and 7886 patients had no diabetes; in the HCC study,[25] 2099 CHB patients had diabetes and 2080 patients had no diabetes.

- Metabolic syndrome (eg, obesity and diabetes) is associated with cirrhosis and HCC in CHB patients[26]

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)	**Hypertension**	**Hyperlipidemia**	**Diabetes**	**Osteopenia and Osteoporosis**
2×–4×	**2×–3×**	**3×–5×**	**1.5×–5×**	**2×–3×**

- 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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