Challenges in warranting access to prophylaxis and therapy for hepatitis B virus infection

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Chronic hepatitis B virus infection

- remains a major global health burden
- is one of the top 20 causes of mortality worldwide

HBV-related end stage liver disease and hepatocellular carcinoma (HCC)

- cause up to 1 million death per year
- are responsible for up to 10% of liver transplantations

Worldwide more than 240 million people suffer from chronic HBV infection
- only estimated 10% are diagnosed and estimated 1% actually treated

- Prevalence unchanged in the last decade despite vaccination and effective treatment options available
Challenges differ by resources and prevalence of infection

**Low- middle income countries**
- High prevalence
- Lack of availability of treatment
- Cost of treatment

**Middle – high income countries**
- Low prevalence
- Low screening rates
- Lack of awareness
- Social stigma
- Discrimination
HBV distribution in EU/EEA

About 5 million chronically infected patients, prevalence about 0.9%

European Centre for Disease Prevention and Control, 2016, ecdc.europa.eu
The most affected age group for both acute and chronic infections was the group of 25–34 year olds accounting for 33.8% of cases.
Prevention of HBV

Awareness and Prevention

HBV vaccine
• available since the 1980’s *
• universal infant vaccination reduces HBV¹

*in Germany since 1995

Percentage (%) of children vaccinated against HBV when entering school

- 1996: 0% completely vaccinated, 8% vaccination started
- 1997-1999: 0% completely vaccinated, 15% vaccination started, 26% completely vaccinated
- 2000: 0% completely vaccinated, 14% vaccination started, 45% completely vaccinated
- 2001: 11% vaccination started, 71% completely vaccinated
- 2002: 7% vaccination started, 71% completely vaccinated
- 2003: 5% vaccination started, 81% completely vaccinated
- 2004: 4% vaccination started, 84% completely vaccinated
- 2005: 4% vaccination started, 86% completely vaccinated
- 2006: 4% vaccination started, 87% completely vaccinated
Access to vaccination and treatment in intermediate-to low-prevalence regions (example Germany)

## Access to vaccination

### Recommendation for vaccination

<table>
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<th>Impfung</th>
<th>Alter in Wochen</th>
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<td>G2</td>
<td>G3</td>
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<td>G2&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
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<td>G1</td>
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<td>G3</td>
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<tr>
<td>Rotaviren</td>
<td>G1&lt;sup&gt;b&lt;/sup&gt;</td>
<td>G2</td>
<td>(G3)</td>
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<tr>
<td>Meningokokken C</td>
<td>G1 (ab 12 Monaten)</td>
<td>N</td>
<td></td>
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<tr>
<td>Masern</td>
<td>G1</td>
<td>G2</td>
<td>N</td>
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Access to vaccination and treatment in intermediate- to low-prevalence regions (example Germany)

Access to vaccination

- **Example Germany**
  - **Refugees have a higher HBsAg prevalence** than the German population 2.3% vs. 0.7%
  - Especially in young age **HBV immunization status is poor** → „every vaccination counts“
  - Social welfare covers treatment only if life is being threatened → **new transmission dynamics have to be expected**
  - To **reach certain sub-populations** with higher prevalence but limited access to treatment, e.g. refugees, people without health insurance, people who inject drugs or abuse alcohol, **HBV management programs need to be adopted**\(^1\),\(^2\)

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Access to vaccination and treatment in special populations: pregnant woman

Proposed scenario

- Screening of pregnant woman in the first trimester
- starting antiviral therapy at 28-32 weeks of gestation if HBV DNA is above 200,000 IU/mL
- Vaccination at birth

In high-income countries time-point of screening will need to be adapted, e.g. in Germany mothers are currently screened only in week 32 of gestation.
Awareness of clusters

Surveillance

- Example Germany

In Germany: 19% history of migration

**Top 3 countries of origin**
1. Turkey  
   HBsAg: 4.0%
2. Italy  
   HBsAg: 2.52%
3. Former Yugoslavia  
   HBsAg: 0.48%

increased HBsAg seroprevalence among immigrants
HBsAg prevalence in refuges

2.3% (18/793)

18 HBsAg positive patients
- 0/18 elevated AST
- 2/18 elevated ALT (58 U/l, 107 U/l)

⇒ PPV 0 for AST and 0.016 for ALT

Hampel, Solbach, Cornberg et al., Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2016 May;59(5):578-83.
Relative contribution of migrants to the total number of CHB cases per EU/EEA country
Access to vaccination and treatment in intermediate-to low-prevalence regions (example Europe)

Surveillance

- Surveillance data will help **adjusting national programs** to respond **to new dynamics of HBV infections** (e.g. HBV genotype, HBeAg status, mode of transmission)
- **Pointed analysis of HBV endemicity** needed as general picture of low endemicity may **mask local clusters of high endemicity and infection**

Antiviral treatment of treatment-eligible patients

Meta analysis of 13 studies (6 US, 7 non-US) including 31342 patients
Lack of awareness in clinical practice (Example: Germany)

Clinicans, GPs:

Elevated ALT = alcohol abuse

Normal ALT = no need to screen for viral hepatitis
Lack of awareness in clinical practice (Example: Chinese population in England)

Clinicians, GPs:

“I am not sure that any GP is going to have a sufficient population of Chinese to know that this is a major risk factor …”

“I’m hoping that there will be more ethnic training”

“put down some hepatitis B results in front of any of us … I suspect we would probably have to go and have a little read on the internet or in the books.”

“Because most of us trained more than ten years ago, there’s a perception that well there’s no point in treating hepatitis.”
Lack of awareness in clinical practice (Example: Chinese population in England)

Patients:

“[We] really know nothing about this (disease).”

“What’s the point of taking all the blood tests, and (getting) no treatment?”

“…HBV is easily transmitted through social contacts, so HBV carriers are … a public nuisance… are expected to …. keep their distance”

What if other people see me going into a sexual health clinic (for a hepatitis B test)? What will they think about me?
Lack of awareness in clinical practice (Example: Chinese population in England)

Community:

“The community takes on … new entrants and support them in a way that means they are not as visible”

“So if there’s a different language (involved) you know you definitely have to make sure that what you’ve said is being understood.”

“Maybe they have no understanding of the NHS system. Maybe they are new to this country.”

“Well I do believe we need the help from the (Chinese) population to push their own cause ….. Then it is more difficult to argue against I think.”
Treatment

- **awareness campaigns** will help to **reduce barriers to access** in many western countries
  - due to **lack of awareness, social stigma and discrimination**
  - due to **suboptimal transition from diagnosis to care** by lack of evidence-based knowledge of HBV preventing appropriate patient management¹

- ➔ **invests will be needed to increase proportion of HBV-infected individuals that receive treatment**²

² Papatheodoridis et al. *J Viral Hepat.* 2016;23(Suppl 1):1-12-
Low rates of hepatitis B virus screening at the onset of chemotherapy.

8942 not screened:
134 unidentified HBsAg positive (1.5%)?
662 unidentified anti-HBc positive (7.4%)?
Access to vaccination and treatment in special populations: patients with immunosuppressive therapy

HBsAg pos and HBsAg neg, anti HBc positive patients undergoing immunosuppressive therapy are at high risk

• of HBV reactivation

• and subsequent liver failure and death \(^1\)

Prophylactic antiviral therapy is highly effective and current guidelines recommend screening everyone undergoing immunosuppressive treatment \(^2\), **BUT**

• screening rate is low, even among specialists \(^3\)-\(^5\)

**→ NEEDED:** efforts to improve screening and treatment as mortality to HBV reactivation can be prevented.

Conclusion – an invisible disease in an invisible population

Policymakers
- Understand the medical need and the consequences of untreated infection
- Clarify roles and responsibilities for special populations (migrants, IV drug users, prisoners,……)
- Recognise community diversity and tailor responses to local needs and context
- Ensure adequate resources for prevention, screening, surveillance and treatment measures
- Look to make services sustainable and accessible
- Explore collaboration with other agencies and the voluntary sector

Community-level
- Improve knowledge and awareness of the disease in at-risk groups (consequences of untreated infection)
- Raise awareness of the asymptomatic nature of disease
- Tackle misperceptions
- Provide health system navigators and clarify entitlements to health services
- Integrate family to influence testing and longer term compliance

Healthcare practitioners and services
- Improve healthcare practitioners’ knowledge of the disease, and raise their awareness of risk groups
- Provide language support
- Make greater use of informational aids and tools such as patient alerts in electronic health records