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## HAV & HBV vaccination among travellers participating in the National Health and Wellness Survey in five European countries

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KEYWORDS Hepatitis; HAV; HBV; Vaccines; Frequent travellers	<b>Summary</b> Background: A main cause of hepatitis A and B infections in European countries is travel to endemic countries. Most research on hepatitis vaccination among travellers from Europe has been conducted in airports or travel clinics, samples which potentially overrepresented frequent travellers. <i>Methods:</i> 2102 respondents across France, Germany, Italy, Spain, and UK completed an internet-based questionnaire. Vaccination status, travel to endemic countries, and other characteristics were compared across frequent, occasional, and non-travellers. Logistic regressions tested association between vaccination and travel adjusting for potential confounders. <i>Results:</i> Most respondents were occasional travellers (61%) and 24% were frequent travellers. Frequent travellers had 2.3–2.4 times the odds of being vaccinated relative to non-travellers, and odds of vaccination were 2.5–3.1 times higher among travellers to endemic areas relative to others (all p < .05). Frequent travellers were more aware of their vaccination status (HAV: 80% vs. 72%; HBV: 82% vs. 74%), though many who were vaccinated could not identify the number of injections to complete the series (47% vs. 29%) (all p < .05).

Abbreviations: HAV, Hepatitis A virus; HBV, Hepatitis B virus; NT, non-traveller; OT, occasional traveller; FT, frequent traveller; 5EU, France, Germany, Italy, Spain and UK; NHWS, National Health and Wellness Survey; ANOVA, analysis of variance; GPs, general practitioners; UMV, universal mass vaccination.

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*Conclusion:* Travel frequency and destination endemicity are associated with increased hepatitis A and B vaccination. The number of unvaccinated travellers and the lack of recall for the dosing schedule suggest the need to improve travellers' awareness and adherence to recommendations.

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### 1. Introduction

Europe is currently the world's largest source of international travellers [1,2]. Travel can increase risk of exposure to infections that can be vaccine-preventable, including hepatitis A (HAV) and hepatitis B (HBV), and many European travellers go to HAV or HBV endemic countries [3].

Approximately 1.5 million new clinical cases of HAV occur each year worldwide, with the incidence of infection as much as ten times higher than the number of reported clinical cases [4-6]. HAV is transmitted by ingestion of contaminated food or water and by personto-person exposure through the faecal-oral route. In countries of low endemicity such as European Union (EU) countries, the main causes of HAV infections and clinical cases are travel to endemic countries [7-9] and import of contaminated food [10-12], both of which may result in outbreaks.

HBV is transmitted via percutaneous (i.e. puncture through the skin) or mucosal contact with infectious blood or body fluids [13,14]; 4.5 million new HBV infections and 620,000 HBV-related deaths occur each year worldwide [15].

#### 1.1. Signs and symptoms of infection

HAV infections do not cause chronic liver disease and are often asymptomatic, especially in young children. However, the disease can be severe in adolescents and adults, and can cause debilitating symptoms [16,17]. HAV symptoms may persist for several weeks and, with greater severity in adults, and up to 15% of patients may experience relapsing illness up to six months [18]. Although rare, some patients may experience acute liver failure and in persons above 50 years old, the estimated case fatality rate can be up to 2.7% [7,19].

HBV can cause a potentially life-threatening liver infection, and the virus spreads through perinatal transmission, horizontal transmission, percutaneous or mucosal exposure to infected blood and body fluids, and sexual transmission [20,21]. HBV infection ranges from asymptomatic or mild disease and can lead to a wide spectrum of liver disease from fulminant hepatitis and acute liver failure to chronic hepatitis, cirrhosis, and hepatocellular carcinoma. HBV is more severe among adults aged >60 and is a common cause of liver disease and liver cancer. Most adults infected with the virus recover, but 5%-10% are unable to clear the virus and become chronically infected and therefore can infect others [22]. Approximately 50% of liver cancers are attributable to HBV [23].

#### 1.2. Vaccines for HAV and HBV

HAV vaccines available in Europe are manufactured from inactivated virus and administered via intramuscular injection. For travellers, the first injection is administered before departure and provides protection during the trip, and a booster administered 6 months later, provides immunity for decades [24]. There are several monovalent HAV vaccines produced by different companies. There is also a combination HAV/HBV vaccine, and a vaccine combining HAV and typhoid.

Vaccines for HBV include monovalent versions, the HAV/ HBV combination vaccine, and a heptavalent vaccine also including diphtheria, tetanus, pertussis, and *haemophilus influenzae* type b used in childhood vaccination. These vaccines are also given through intramuscular injection. The standard schedule includes three injections over six months.

#### 1.3. HAV & HBV vaccination programs in Europe

The World Health Organization recommends vaccination for HAV prior to travel to countries with moderate or higher endemicity [16,25,26]. A few regions in Europe include HAV vaccination in their standard childhood immunization schedules, notably the Catalonia region of Spain [27] and the region of Puglia in Italy [28], but vaccination against HAV is typically not included in standard vaccination schedules in Europe.

Universal mass vaccination programs (UMV) are common for HBV, and so today's adolescents and young adults in France, Germany, Italy, and Spain have developed immunity through the normal childhood vaccination schedule [29–32]. However, these programs were initiated too recently to have an impact on healthy adults in Europe born before 1984, as the first significant European UMV programs for HBV began in Italy and Catalonia for children aged  $\leq$ 12 years in 1991.

#### 1.4. Travel and vaccination

Previous research has found that travel is associated with increased risk of HAV and HBV transmission [33-38]. International travel is a major cause of HAV infection among Europeans, even for travellers who limit themselves to standard tourist facilities [37]. Moreover, travel duration, underlying health conditions, and the prevalence at the destination country have been positively associated with HBV transmission [33,39]. Numerous studies have found that travellers lack adequate knowledge of the risk of infection and 33–49% of them are exposed to high-risk

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