

Patient preferences towards drug treatment of chronic hepatitis B: A Discrete Choice Experiment in Germany

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Introduction

Current antiviral therapies for chronic hepatitis B (CHB) rarely achieve functional cure, [defined as sustained hepatitis B surface antigen (HBsAg) loss]; thus, lifelong therapy is needed in most patients. A finite therapy achieving functional cure with long-term disease remission could change the treatment landscape substantially. However, it is unknown how patients would evaluate such a therapy, especially if it would be associated with additional treatment burden.

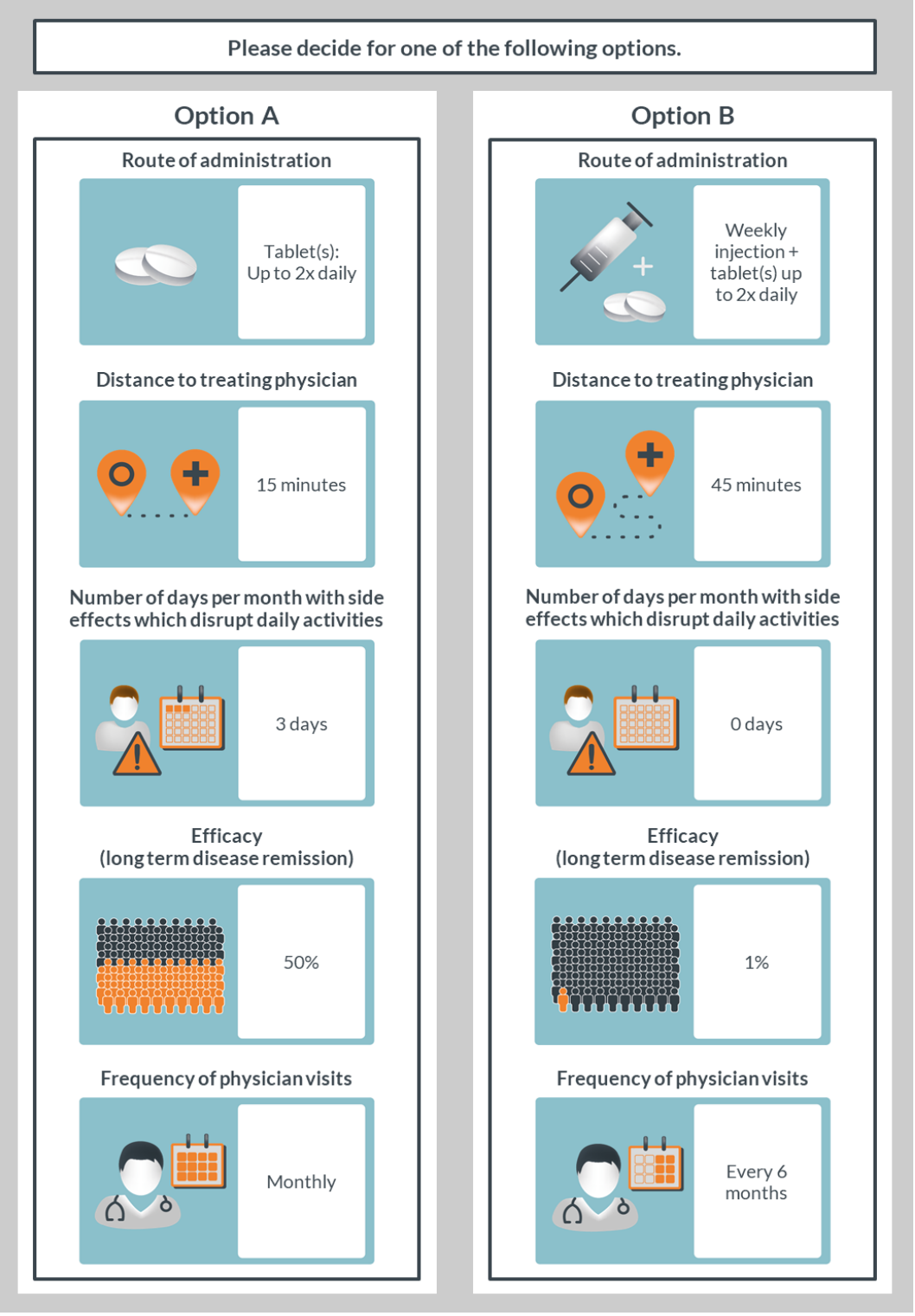
Study Objectives

This study aimed to describe CHB patients' preferences over treatment alternatives, and to estimate the relative importance of different treatment attributes in a discrete choice experiment (DCE) setup.

Methods

A DCE (Figure 1) was conducted between 2018-2019 in Germany. Inclusion criteria of this multicenter study were: CHB diagnosis; age of at least 18 years; no hepatocellular carcinoma; no HIV or HCV/HDV co-infection. Patients were phone-interviewed and asked multiple times to decide between two hypothetical treatment options (Figure 1).

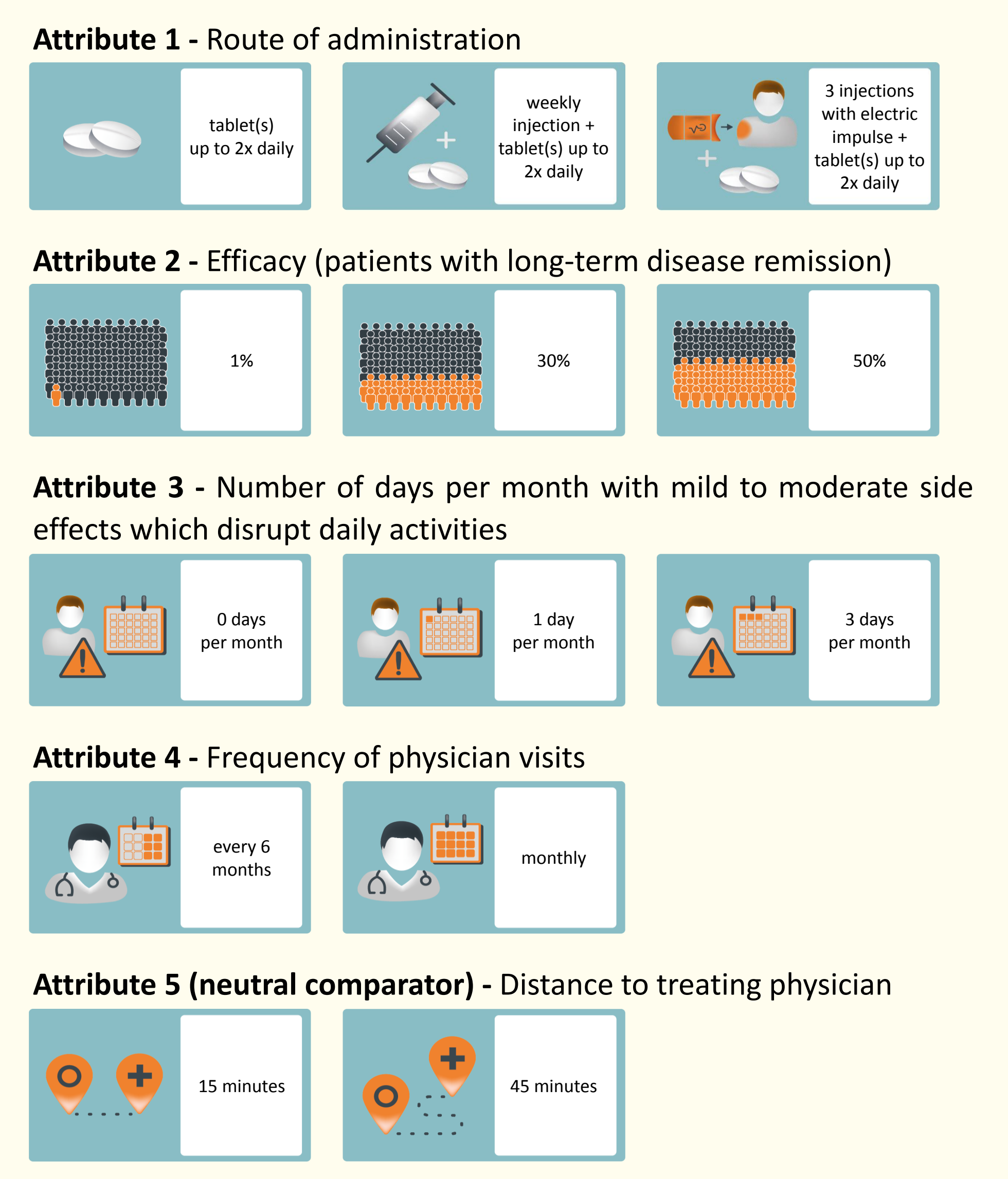
Figure 1. DCE Design



Attributes

The DCE included 5 attributes. Four of those were defined based on desk and literature research as well as on expert discussions regarding characteristics of current/future CHB treatments, one was added to include a measure of potential opportunity costs (distance to treating physician). Figure 2 illustrates the addressed attributes and their levels.

Figure 2. Attributes used in the DCE



Data analyses

In a conditional logit regression model, the influence of different attribute levels on the probability of a patient's decision to choose the specific choice alternative was estimated. Also, the relative importance of each attribute was quantified by estimating marginal utilities for each attribute level. Subgroup analyses were performed to evaluate possible influencing factors and to confirm the main outcomes.

Results

Baseline characteristics

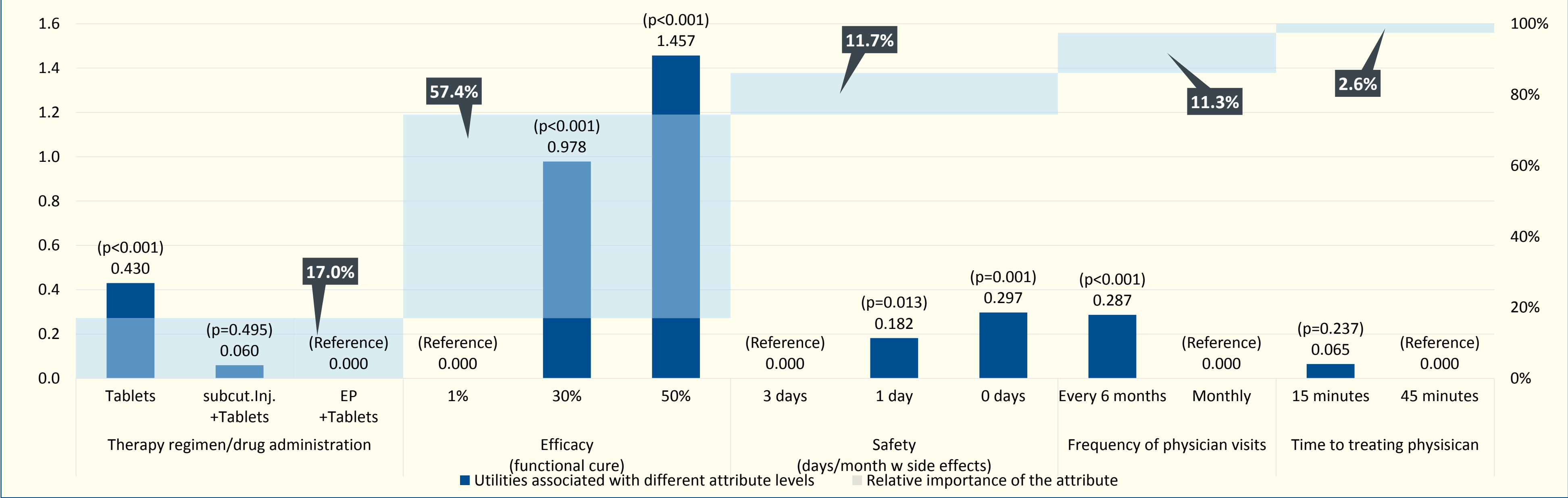
Of 141 enrolled patients 130 completed the DCE and 108 (mean age 49.1, female 37.5%) showed consistent responses based on a test card. There were no statistically significant differences in sociodemographic and clinical characteristics between patients initially enrolled and patients who successfully completed the DCE survey. Baseline characteristics of patients with consistent DCE responses are shown in Table 1.

Within the final analysis sample of 108 patients, more than half of the patients had HBsAg chronic HBV infection (52.8%) and were currently taking Tenofovir (56.5%). Regarding treatment, most of the patients did not use interferon before (84.3%) and reported no previous side-effect experience (80.6%).

Preference outcomes

The conditional logit regression model is shown in Figure 3. Efficacy was found to be the main driver of decisions for/against treatment options (impacted 57% of patients' decisions), followed by therapy regimen (17%), safety profile (11.7%) and number of physician visits (11.3%).

Figure 3. Conditional logit model

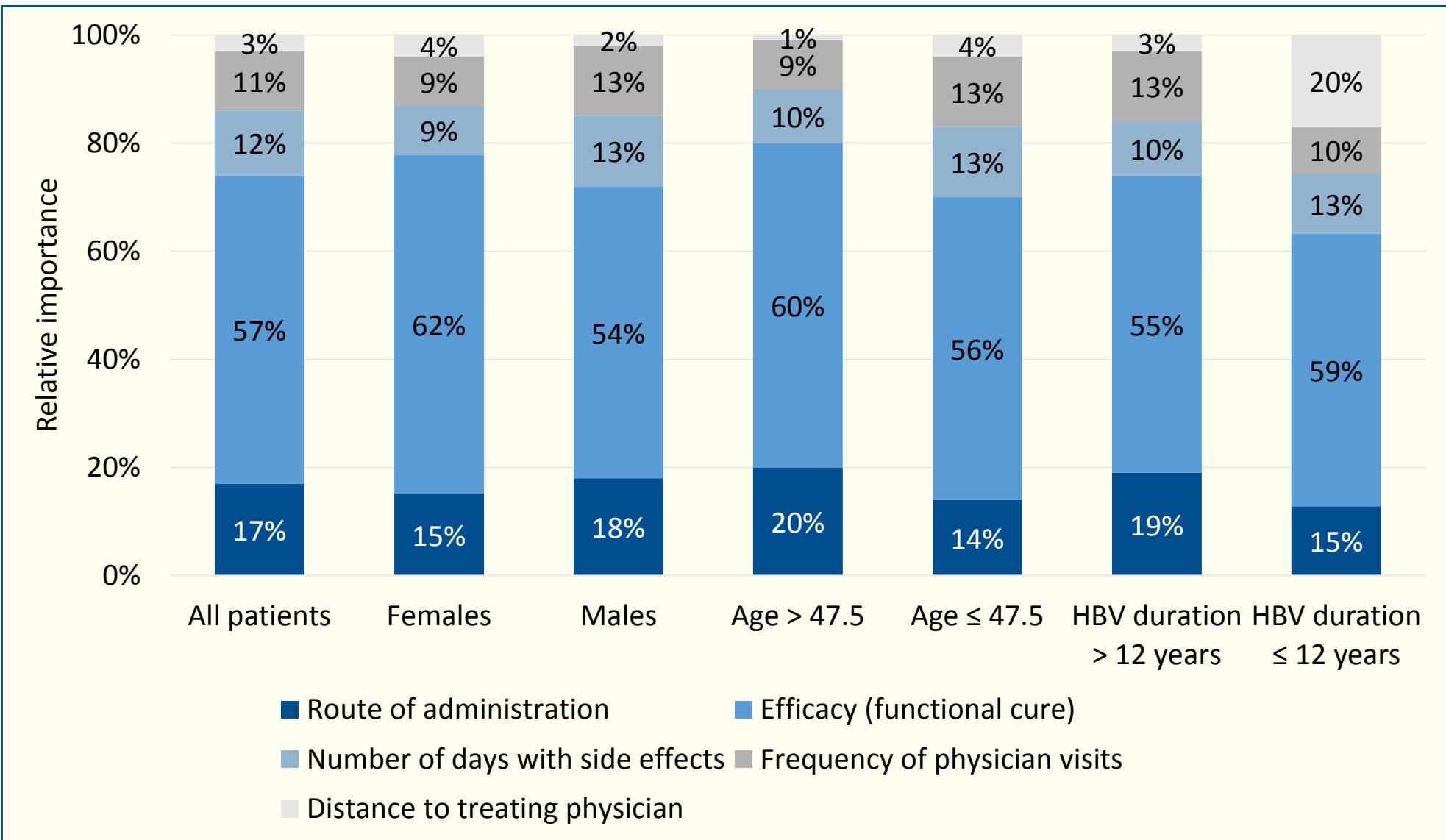


Relative utility values were: (1) therapy regimen (reference EP+tablets): tablets 0.430 (p<0.001), subcutaneous monthly injection+tablets 0.060 (p=0.495); (2) efficacy (reference 1%): 30% 0.978 (p<0.001), 50% 1.457 (p<0.001); (3) Side effects (reference 3 days): 1 day 0.182 (p=0.013), 0 days 0.297 (p=0.001); (4) frequency of physician visits (reference monthly): half yearly 0.287 (p<0.001); (5) travel time (reference 45 min): 15 min 0.065 (p=0.237).

Subgroup analyses

Figure 4 shows the relative importance of each attribute on patients' choices in analyzed subgroups. Generally, the relative importance of attributes in the subgroups was largely similar to that in the overall patient sample and confirmed the dominant effect of functional cure in the decision-making process of CHB patients. Small differences could be observed with regard to gender, as female patients seemed to have a stronger preference for choosing a treatment based on superior efficacy (relative importance 62% in females compared to 54% in males). Further, older patients tended to evaluate a treatment to a higher percentage based on its route of administration than younger patients (20% vs. 14%).

Figure 4. Relative importance in patient subgroups



Conclusion

- Patients attached a statistically significant additional utility to higher efficacy (lasting remission after 12 months), efficacy was also the main driver of decisions for or against a specific treatment
- Patients preferred oral administration (tablets) compared to the two considered injection types

Table 1. Baseline characteristics of analyzed patients

Patients successfully completed DCE w/o inconsistent DCE responses (N = 108)	
Sociodemographic characteristics	
Mean/Median age in years (SD)	49.1/47.5 (13.1)
Mean/Median age at first HBV diagnosis (SD)	35.1/30.9 (14.1)
Mean/Median years since first HBV diagnosis (SD)	14.0/12.0 (9.6)
Female gender (%)	40 (37.0)
eAg status	
HBeAg-positive chronic HBV infection (%)	5 (4.6)
HBeAg-positive chronic hepatitis (%)	7 (6.5)
HBeAg-negative chronic HBV infection (%)	38 (35.2)
HBsAg chronic HBV infection (%)	57 (52.8)
HBsAg-negative occult HBV infection (%)	1 (0.9)
Treatment characteristics	
Currently receiving medication – yes (%)	80 (74.1)
Current medication – Tenofovir (%)	61 (56.5)
Current medication – Lamivudine (%)	7 (6.5)
Current medication – Entecavir (%)	12 (11.1)
Previously received other CHB medication – yes (%)	28 (25.9)
Interferon used before – yes (%)	14 (13.0)
Experiences with adverse events/side effects	
Side-effect experience – yes (%)	20 (18.5)
Side-effect experience – no (%)	87 (80.6%)

- Intramuscular electroporation (electric impulse) was not associated with a negative utility, compared to traditional injection
- A treatment associated with higher efficacy is preferred by patients, even if it is associated with additional treatment burden.

Limitations

- Due to the nature of a DCE, attribute levels mirror real-life treatment alternatives only in simplified terms.
- Furthermore, the number of attributes and attribute levels that can be presented to patients in a DCE is limited.
- The difference in upper and lower levels of the presented attributes might have influenced patients' decisions for or against a specific treatment alternative. However, the attribute levels presented to patients were not randomly chosen but presented current as well as potential future therapy options, as described on respective SmPCs or clinical trial publications.

Abbreviations

CHB, Chronic hepatitis B; DCE, Discrete choice experiment; eAg, e Antigen; HBeAg, Hepatitis B e antigen; HBsAg, Hepatitis B surface antigen; HBV, Hepatitis B Virus; HCV, Hepatitis C Virus; HDV, Hepatitis D Virus; HIV, Human immuno-deficiency virus

Keywords

Hepatitis B; Antiviral therapies; Sustained virologic response; Functional cure; Discrete choice experiment; Patient preferences

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Conflict of Interest

US is an employee of Janssen Pharmaceutica NV Belgium. SVS is an employee of Janssen Pharmaceuticals US. Both hold stocks at Johnson & Johnson. Zeki Kocaata and Fränze Hardtstock participated in this study as a staff members of Ingress-Health; the work of Ingress-Health in this study was sponsored by Janssen Pharmaceutica NV. Thomas Wilke has received honoraria from several pharmaceutical/consultancy companies e.g. Novo Nordisk, AbbVie, Merck, GSK, BMS, LEO Pharma, Astra Zeneca, Bayer, Boehringer Ingelheim, Pharmarit.