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Do Patients and Physicians Have Similar Preferences for Chronic Hepatitis B Treatment Outcomes in Turkey?

Türkiye'de Hastaların ve Doktorların Kronik Hepatit Tedavi Sonlanımları İçin Tercihleri Benzer midir?

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SUMMARY

Introduction: *We aimed to quantify patients' and physicians' preferences for therapeutic trade-offs involving the efficacy, side-effect risks, and evidence uncertainty in chronic hepatitis B (CHB) treatments.*

Materials and Methods: *Physicians who treat CHB patients and adult patients with a self-reported physician diagnosis of CHB completed a web-enabled, discrete-choice experiment survey in Turkey. Both patients and physicians answered 12 treatment-choice questions. Each question required evaluating a pair of hypothetical CHB medication profiles defined by the years the medicine has been studied (weight of evidence), probability that the patient's viral load remains undetectable for five years with possible reversal of disease progression (efficacy), five-year treatment-related risks of a fracture and renal insufficiency, and monthly medication cost. Logit models were used to estimate preference weights for all attribute levels and the profile preference scores for three current CHB treatments. A choice format conjoint analysis was used.*

Results: *159 physicians and 117 patients completed the survey. Patients and physicians had discordant views on the relative importance of CHB treatment attributes. Patients ranked weight of evidence and efficacy as the most important attributes, while physicians ranked efficacy and risk of renal insufficiency as the most important attributes. Both groups preferred a CHB medication profile characterized by potent efficacy and low side-effect risk versus a medication profile characterized by a potent efficacy and moderate side-effect risk profile ($p > 0.05$). Both medication profiles were preferred over a CHB medication with poor efficacy and low side-effect risk profile ($p > 0.05$ for patients and $p < 0.05$ for physicians).*

Conclusion: *This is the first study to quantify patients' and physicians' preferences for CHB treatments in Turkey. Discordance between physicians' and patients' preferences can be explained by asymmetric knowledge and information regarding the importance of weight of evidence and efficacy versus side-effect risks. This fact highlights the need for reflection of physician and patient perspectives on regulatory and reimbursement decisions.*

Key words: *Hepatitis B, Outcome, Patient, Physician*

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ÖZET

Türkiye'de Hastaların ve Doktorların Kronik Hepatit Tedavi Sonlanımları İçin Tercihleri Benzer midir?

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Giriş: *Bu çalışmanın amacı kronik hepatit B (KHB) tedavisinde etkinlik, yan etki ve kanıt düzeyindeki belirsizlikler açısından hastaların ve doktorların sonlanım tercihlerini ölçmektir.*

Materyal ve Metod: *Türkiye'de KHB tedavisi yapan doktorlara ve en az bir doktor tarafından KHB tanısı konulduğunu bildiren hastalara, web tabanlı bir ayrık seçim deneysel anketi uygulandı. Hastalar ve doktorlar antiviral tedaviler hakkında, çoktan seçmeli 12 soruyu yanıtladı. İlacın ne kadar süredir araştırıldığı (kanıtın miktarı), beş yıl boyunca hastanın viral yükün belirlenemez olma ve ilerlemiş hastalığın geri dönme olasılığı (etkinlik), beş yıllık tedavide kırık ve böbrek yetersizliği riski ve aylık ilaç maliyetiyle tanımlanmış hipotetik KHB ilaçları hakkında soru çiftleri kullanılarak değerlendirme yapıldı. Mevcut üç KHB tedavisi için oluşturulan profillere yönelik tercih puanlarını ve tüm özellik düzeylerindeki tercih ağırlığını hesaplamak için logit modeller kullanıldı. Tercih yapısında konjoint analizi kullanıldı.*

Bulgular: *Anketi 159 doktor ve 117 hasta tamamladı. Hasta ve doktorların KHB tedavilerinin özelliklerinin görece önemleri değerlendirmesinde çelişkili görüşleri vardı. Hastalar kanıt düzeyini ve etkinliği en önemli özellik olarak sıralarken, doktorlar etkinlik ve böbrek yetmezliği riskini en önemli özellik olarak derecelendirdi. Her iki grup da, potent etkinlik ve düşük yan etki riskine sahip KHB ilacını, potent etkinlik ve orta yan etki risk profiline sahip ilaca göre tercih etti ($p> 0.05$). Her iki ilaç profili zayıf etkili ve düşük yan etkili risk profiline sahip KHB ilacına göre tercih edildi (hastalar için $p> 0.05$, doktorlar için $p< 0.005$).*

Sonuç: *Türkiye'de KHB tedavileri için hasta ve doktor seçimlerini ölçen ilk çalışmadır. Doktor ve hasta tercihleri arasındaki uyumsuzluk, kanıtın ağırlığının önemi ve yan etki riskine karşın etkinlik hakkında taraflar arasındaki eşit olmayan bilgi düzeyi ile açıklanabilir. Bu bulgular, ruhsat ve geri ödeme kararlarına doktor ve hasta bakış açılarının da yansıtılması ihtiyacını göstermektedir.*

Anahtar Kelimeler: *Hepatit B, Sonlanım, Hasta, Hekim*

INTRODUCTION

Chronic hepatitis B (CHB) is an important public health problem and a leading cause of liver-related morbidity and mortality in Turkey[1]. About 3.5 million people are infected with the hepatitis B virus (HBV) in Turkey[2]. Approximately 15-40% of chronically infected patients die of hepatic complications secondary to the disease in Turkey. CHB will continue to be an important health problem in the future. Despite the availability of effective vaccines, its wide prevalence, association with serious morbidity and mortality, and the problems encountered in the treatment all contribute to making this disease an ongoing major health problem in Turkey[3]. In Turkey, hepatitis B is mainly treated and followed for complications by actively working 968 infectious disease specialists and 392 gastroenterohepatologists[4]. However, the specialists were unequally distributed between the highest and lowest density provinces. The majority of physicians (82.8%) were recruited by the public sector (Ministry of Health, 30%; Universities, 70%) and 53.7% of physicians were under 35 years of age[5].

The primary goal of treatment for CHB is to permanently suppress HBV replication, thereby reducing the pathogenicity of the virus, resulting in less hepatic necroinflammation. In clinical practice, the short-term objective of treatment is to achieve "initial response" in terms of HBeAg seroconversion and/or HBV-DNA suppression, alanine aminotransferase (ALT) normalization, and prevention of hepatic decompensation to ensure "maintained/sustained response" and to reduce hepatic necroinflammation and fibrosis during/after therapy[6]. National and international treatment guidelines also recommend treatment of CHB patients based on HBeAg status, HBV-DNA level, ALT level, and liver histopathology[6-8].

Currently, six drugs have been approved by the national health authorities in Turkey and are reimbursed for the management of CHB by the Social Security Institution: adefovir, entecavir, interferon alpha 2b, lamivudine, peginterferon alpha 2a, telbivudine, and tenofovir. At present, potent antivirals (entecavir, tenofovir) and peginterferon alpha 2a are the first-line drugs recommended by the medical treatment guidelines. Lamivudine has been removed recently from the list of preferred first-line drugs in Europe because of its known high rate of resistance and evidence showing the superiority of entecavir and telbivudine to lamivudine. However, current reimbursement guidelines in Turkey limit the use of first-line potent antivirals in patients with high HBV-DNA levels ($> 10^7$). Patients with HBV-DNA levels lower than this threshold must start treatment with lamivudine[9].

While health-technology assessment of HBV treatments has focused primarily on relative efficacy and cost, oral antiviral agents have also been associated with serious side effects with long latencies. The risk of developing renal side effects in particular is an increasing concern of the regulatory agencies. Detrimental side effects such as renal insufficiency evolve slowly and usually are not symptomatic. Problems in the follow-up of patients who do not present for appointments and in the sensitivity of laboratory methods used in routine practice are other causes for underdiagnosis of side effects of antivirals. Nevertheless, the long-term safety profile of CHB treatments is a critical consideration because CHB patients typically require chronic, long-term therapy.

Patients' knowledge and understanding of the efficacy and safety differences of the available treatments are limited and are usually based primarily on information provided by physicians. Because patients' preferences can help inform treatment decisions, evaluation of the treatment benefits and risks from a patient perspective is an important research topic. In addition to physicians' preferences, patients' preferences regarding the efficacy, renal and metabolic risks associated with oral antiviral treatment and clinical experience of these drugs in CHB can help inform optimal clinical decisions and improve long-term treatment adherence.

To our knowledge, this study is the first to elicit patients' preferences for outcomes associated with CHB treatments and to evaluate which CHB treatment attributes (or features) are most important to physicians in making treatment decisions for CHB patients. International best practice in health technology assessment requires evaluating the quantity and quality of available evidence in licensing new drugs. However, there are no existing data on the extent to which weight of evidence matters to physicians and patients when making treatment decisions. This study is also the first to measure the relative importance to physicians and patients of the amount of safety and efficacy data available for a specific treatment in Turkey or any other country.

MATERIALS and METHODS

Survey Instrument

Choice-format conjoint-analysis studies or discrete-choice experiments have been used increasingly to quantify preferences for the attributes of health, health care, and health care policy[10,11]. Choice-format conjoint analysis is a systematic method of eliciting trade-offs to quantify the relative importance respondents assign to various treatment attributes or outcomes. It is based on the premise that medical interventions are composed of a set of attributes or outcomes and that the attractiveness of a particular intervention to an individual is a function of these attributes[12-18].

The attributes were chosen to meet two criteria: attributes were clinically relevant, and attributes incorporated physicians' assessment of patient concerns. Likewise, the range of levels of each attribute met three criteria: the range of levels for each attribute spanned the clinically relevant range of outcomes seen in clinical trials or clinical practice, differences in levels encompassed the range of improvements in efficacy outcomes or the range of increases in side-effect or risk outcomes that were seen in clinical trials or clinical practice, and the range of levels for each attribute encompassed the range over which respondents were willing to accept trade-offs among attributes. Based on input from clinical experts, review of product inserts, and face-to-face interviews with 10 physicians who treat CHB patients in Spain, 10 CHB patients in Spain, and five CHB patients in France, we identified five treatment attributes to describe the CHB treatment alternatives in this study (Table 1): how long the medication has been studied

Table 1. Attributes and levels for the treatment-choice questions

Patient attribute	Physician attribute	Abbreviated attribute label	Levels
How long the medicine has been studied (weight of evidence)	How long the medicine has been studied (weight of evidence)	How long the medication has been studied	6 years 3 years 1 year
What doctors think the chance is that the medicine will work well for 5 years (long-term efficacy)	Probability that the patient's viral load remains undetectable for 5 years, with possible histological improvement or reversal of disease progression	Probability viral load is undetectable	95 out of 100 (95%) 80 out of 100 (80%) 70 out of 100 (70%)
What doctors think the chance is that you will have a broken bone if you take the medicine for 5 years (5-year fracture risk)	5-year treatment-related risk of a fracture	5-year treatment-related risk of a fracture	None 1 out of 100 (1%) 5 out of 100 (5%) 10 out of 100 (10%)
What doctors think the chance is that you will have kidney damage if you take the medicine for 5 years (5-year risk of kidney disease)	5-year treatment-related risk of renal insufficiency, where a fracture has not been detected yet	5-year treatment-related risk of renal insufficiency	None 1 out of 100 (1%) 5 out of 100 (5%) 10 out of 100 (10%)
Personal cost to you each month	Personal cost to the patient each month	Cost	0 Euro 10 Euro 25 Euro 75 or 150 Euro

(weight of evidence), probability that the patient's viral load remains undetectable for five years with possible histological improvement or reversal of disease progression (long-term efficacy), five-year treatment-related risk of a fracture, five-year treatment-related risk of renal insufficiency where a fracture has not been detected yet, and personal medication cost to the patient each month. As indicated in Table 1, the same attributes and levels were included in both the patient and physician survey versions, but the labels were slightly different to adapt the survey language to each sample. The survey instrument was translated from English to Turkish, and the translation was verified using forward and backward translation methods.

Patients answered 12 treatment-choice questions from among constructed medication profiles (Figure 1). Physicians answered 12 treatment-choice questions from among constructed medication profiles for three hypothetical patients (4 treatment-choice questions for each patient profile) (Figure 2). Each medication profile was defined by varying levels of the five treatment attributes. Respondents were asked to state the hypothetical medication they would choose if these were the only medications available. The three hypothetical patients were developed to encompass the range of possible CHB patients physicians may treat.

To create treatment profiles for the treatment-choice questions, we employed a commonly used algorithm to construct a statistically efficient experimental design resulting in 36 choice pairs[19-21]. The final experimental design consisted of three survey versions, each containing 12 treatment-choice questions. Each respondent was randomly assigned to one of the three versions. In addition, the patient survey elicited standard demographic information (e.g., age, gender, race, marital status, and education) as

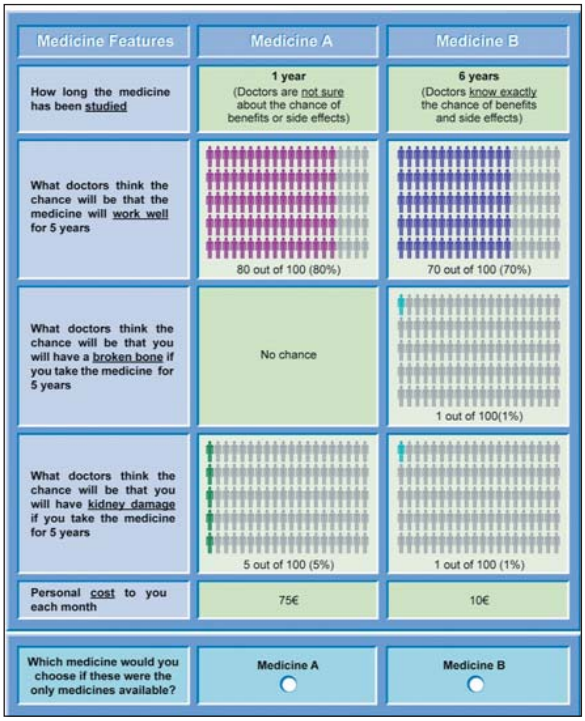

Figure 1. Example treatment-choice question (patient version).

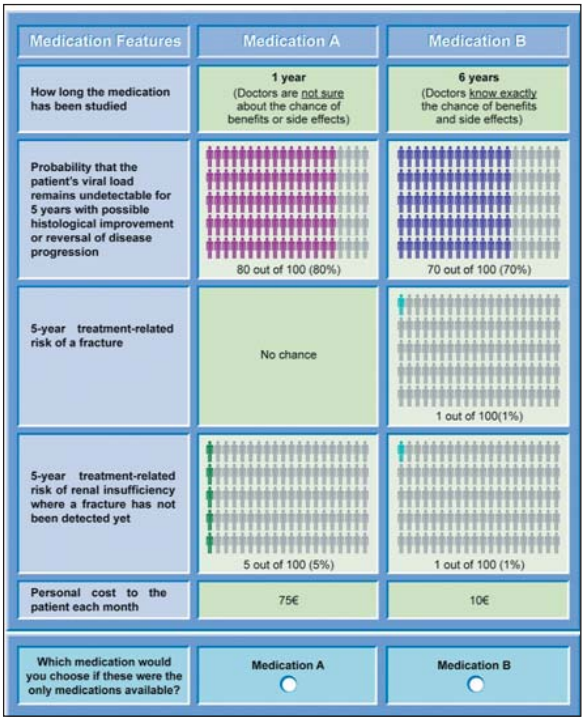

Figure 2. Example treatment-choice question (physician version).
Patient 1: A 55-year-old female has chronic hepatitis B. She is HBeAg (-), with HBV-DNA at 2.500 IU/mL and ALT at 2 x ULN. A liver biopsy showed severe active necroinflammation. The patient's health is otherwise good (no significant comorbidities).

well as a number of items about the patients' experiences with CHB. The physician survey instrument also collected information on gender, years in practice, average number of CHB patients treated each month, average number of CHB patients each month that are prescribed CHB antiviral treatments, practice type, and practice setting. The survey was approved by RTI International's Office of Research Protection and Ethics (Research Triangle Park, NC, United States).

Survey Sample

All patients were required to be 18 years of age or older and have a self-reported physician diagnosis of CHB. All physicians were required to be board-certified (or eligible) physicians currently treating CHB patients. Harris Interactive (HI) (Rochester, NY, United States), an international market-research company that specializes in survey research using both telephone and online surveys, recruited respondents in Turkey. First, physicians were selected using hospital directories and physician association lists. Second, physicians were contacted by direct telephone at their workplace. For the study, physicians were recruited via an e-mail invitation asking them to participate in the online survey. Subsequent reminder e-mails were sent within a week of the invitation. If a physician did not complete the survey, HI followed up with a telephone reminder. Patients were selected through clinics and physician referrals and contacted by telephone and invited to take the online survey. Patients for the study were recruited via an e-mail invitation asking them to participate in the online survey. Subsequent reminder e-mails were sent within a week of the invitation. HI administered the Web-enabled survey to all respondents in May 2010.

Statistical Analysis

We used multivariate, random-parameters logit for the physician sample and nested-logit for the patient sample to estimate the choice models. Random-

parameters logit avoids potential estimation bias from unobserved decision-weight heterogeneity in discrete-choice models by estimating a distribution of preference weights across respondents for each choice parameter[22,23]. In addition, because each respondent provided responses to more than one treatment-choice question, the model controlled for within-respondent correlation.

The random-parameters and nested-logit choice models estimate the effect of each attribute on the probability of choosing a medication alternative. We used effects coding (where the parameter for the omitted category is the negative sum of the included categories) instead of dummy coding for the probability that the viral load is undetectable, five-year treatment-related risk of renal insufficiency, and five-year treatment-related risk of a fracture[24]. In addition, for the physician sample, the "none" and "1%" levels for five-year treatment-related risk of a fracture were combined as "0.5%" because physicians indicated no difference in preferences between these two adjacent levels. How long the medication has been studied and costs were modeled as linear variables based on the results of specification tests. The appendix contains Table 2 and 3 with the model coefficients for each sample. These log-odds coefficients can be interpreted as mean preference weights, indicating the relative strength of preference for each attribute level. In addition, we also calculated profile preference scores using the estimated weights for the attributes of three different hypothetical medication profiles used to treat CHB: Medication A (poor efficacy & low side-effect risk), Medication B (potent efficacy & moderate side-effect risk) and Medication C (potent efficacy & low side-effect risk) (Table 4).

The data obtained from physicians in this study has been published in a multi-center study[25].

RESULTS

Study Sample

In Turkey, 117 patients and 159 physicians were eligible and agreed to participate in the survey. The majority of all patients were female (54%), single (65%), and had a secondary school qualification or less (64%). The mean age of the patients was 29 years (standard deviation = 9 years). The majority of patients had been diagnosed with hepatitis B in the past two years (61%), and had seen a health care professional for their infection three times or less in the past year (69%). Most patients did not report having hypertension (96%), diabetes (95%), or osteoporosis (99%). Twenty-eight percent of patients were taking oral prescription pills to treat hepatitis B (with 74% of those on prescription pills taken once daily).

The majority of all physicians were male (76%) and had practiced medicine for over 10 years (76%). Twenty-three percent of physicians treat more than 10 CHB patients per month in their practice, and 13% also administer antiviral medications to more than 10 patients per month in their practice. The most common practice types were public (43%) and university hospitals (25%). Twenty-six percent were gastroenterohepatologists, 16% were infectious disease specialists, 35% were internists, 9% were nephrologists, and 14% were classified as "other". All respondents provided an online informed consent to participate in the survey.

Drug Profile Scores

Figure 3 presents the patient-preference-weighted profile scores and 95% confidence intervals for the three drugs. For Medication A, probability the viral load is undetectable had a negligible effect on patient preferences due to the low rate of 42% compared to the other two drugs. How long the medication

Table 4. Drug profiles

Attribute label	A	B	C
How long the medication has been studied	5 years	4 years	5 years
Probability viral load is undetectable in 5 years	Low	High	High
5-year treatment-related risk of a fracture	Low	Moderate	Low
5-year treatment-related risk of renal insufficiency	Low	Moderate	Low

Table 2. Coefficient estimates for patients[a]

Attribute label	Levels	Coefficient	Standard error	Test-statistic	p value	Deviation
How long the medication has been studied	N/A	0.215	0.032	6.686	0.000	0.144
Probability viral load is undetectable	95%	1.025	0.105	9.738	0.000	0.206
	80%	-0.199	0.067	-2.982	0.003	0.131
	70%	-0.827	0.104	-7.980	0.000	0.203
5-year treatment-related risk of a fracture	0.5%	0.550	0.083	6.648	0.000	0.162
	5%	-0.072	0.076	-0.949	0.343	0.150
	10%	-0.478	0.100	-4.765	0.000	0.197
5-year treatment-related risk of renal insufficiency	No chance	1.172	0.119	9.880	0.000	0.233
	1%	0.674	0.103	6.561	0.000	0.201
	5%	-0.347	0.089	-3.881	0.000	0.175
	10%	-1.499	0.149	-10.030	0.000	0.293
Cost (linear)	N/A	-0.011	0.002	-6.601	0.000	0.003

[a] Each parameter was normally distributed. This table presents the log-odds or coefficients from the choice model.
N/A = Not applicable.

Table 3. Coefficient estimates for physicians[a]

Attribute label	Levels	Coefficient	Standard error	Test-statistic	p value	Deviation
How long the medication has been studied	N/A	0.107	0.020	5.320	0.000	0.039
Probability viral load is undetectable	95%	0.174	0.024	7.368	0.000	0.046
	80%	-0.049	0.018	-2.767	0.006	0.035
	70%	-0.125	0.020	-6.114	0.000	0.040
5-year treatment-related risk of a fracture	No chance	0.076	0.024	3.187	0.001	0.047
	1%	0.057	0.023	2.498	0.013	0.045
	5%	-0.026	0.023	-1.119	0.263	0.045
	10%	-0.107	0.024	-4.365	0.000	0.048
5-year treatment-related risk of renal insufficiency	No chance	0.172	0.027	6.435	0.000	0.052
	1%	0.054	0.022	2.400	0.016	0.044
	5%	-0.032	0.023	-1.399	0.162	0.045
	10%	-0.193	0.024	-8.148	0.000	0.047
Cost (linear)	N/A	-0.571	0.103	-5.555	0.000	0.202

[a] Each parameter was normally distributed. This table presents the log-odds or coefficients from the choice model.
N/A = Not applicable.

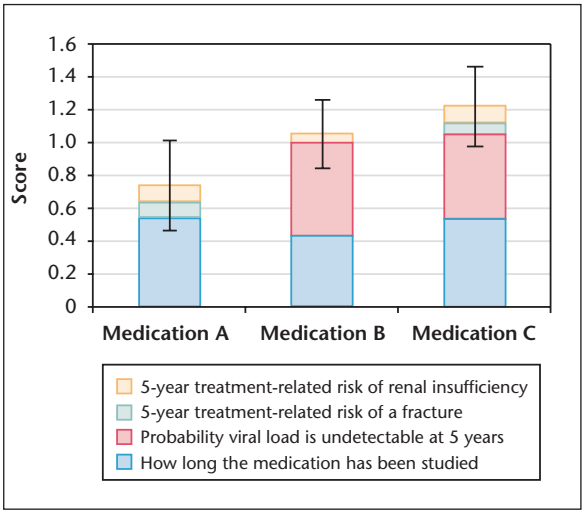

Figure 3. Patient-preference-weighted drug profile scores.

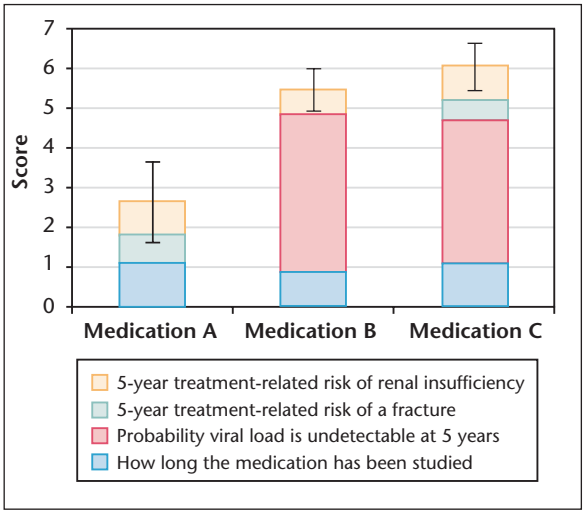

Figure 4. Physician-preference-weighted drug profile scores.

has been studied (indicated in blue) had the largest positive impact, followed by five-year treatment-related risk of renal insufficiency (indicated in yellow) and five-year treatment-related risk of a fracture (indicated in green). For Medication B, five-year treatment-related risk of a fracture had a negligible effect on patient preferences, whereas probability the viral load is undetectable (indicated in red) had the largest impact, followed by how long the medication has been studied and five-year treatment-related risk of renal insufficiency. For Medication C, how long the medication has been studied had the largest effect, followed by probability the viral load is undetectable, five-year treatment-related risk of renal insufficiency, and five-year treatment-related risk of a fracture. In general, for patients, how long the medication has been studied and probability the viral load is undetectable had larger impacts on CHB treatment preferences than five-year treatment-related risk of renal insufficiency and five-year treatment-related risk of a fracture.

Figure 4 presents the physician-preference-weighted profile scores and 95% confidence intervals for the three drugs. For Medication A, probability the viral load is undetectable had a negligible effect on physician preferences. How long the medication has been studied had the largest impact, followed by five-year treatment-related risk of renal insufficiency and five-year treatment-related risk of a fracture. For Medication B, five-year treatment-related risk of a fracture had a negligible effect on physician preferences, whereas probability the viral load is undetectable had the largest impact, followed by how long the medication has been studied and five-year treatment-related risk of renal insufficiency. For Medication C, probability the viral load is undetectable had the largest effect, followed by how long the medication has been studied, five-year treatment-related risk of renal insufficiency, and five-year treatment-related risk of a fracture. In general, for physicians, probability the viral load is undetectable and five-year treatment-related risk of renal insufficiency had larger impacts on CHB treatment preferences than how long the medication has been studied and five-year treatment-related risk of a fracture.

The results indicate that even though the relative attribute contributions were similar between physicians and patients, how long the medication has been studied had a larger effect on patient preferences than physician preferences. Furthermore, five-year treatment-related risk of renal insufficiency was more important to physicians than patients when selecting CHB treatments. With respect to the three drugs, both physicians and patients preferred Medication C to Medication B ($p > 0.05$), Medication B to Medication A ($p > 0.05$ for patients, $p < 0.05$ for physicians) and Medication C to Medication A ($p > 0.05$ for patients, $p < 0.05$ for physicians). Although the effect differences may be clinically meaningful, the estima-

tes were not always statistically significant in these sample sizes ($p > 0.05$).

DISCUSSION

This study is the first to measure the relative importance to physicians and patients of the amount of safety and efficacy data available for a specific treatment in Turkey or any other country. This study of physicians' and patients' preferences for CHB treatments yielded several important results. First, the pattern of choices observed in the treatment-choice questions indicated that patients and physicians attributed different relative importance to CHB treatment attributes. Patients ranked how long the medication has been studied and probability that the viral load is undetectable as the most important attributes, while physicians ranked probability that the viral load is undetectable and five-year treatment-related risk of renal insufficiency as the most important attributes. Both groups ranked five-year treatment-related risk of a fracture (where decrease in phosphorus levels is used as a proxy of fracture risk) as the least important attribute. To our knowledge, these results provide the first systematic, quantitative evaluation of physicians' and patients' preferences for CHB treatments in Turkey.

All of these results are best interpreted with an awareness of several issues and qualifications. First, while choice-format conjoint-analysis methods are increasingly used to support regulatory decisions, to identify optimal treatment guidelines, and to promote patient-centered medicine, they have limitations. The most important limitation is that respondents evaluate hypothetical treatments. These trade-offs are intended to simulate possible clinical decisions, but obviously do not have the clinical consequences of actual decisions. Thus, differences can arise between stated and actual choices. In this study, an attempt was made to minimize such potential differences by offering alternatives that mimic real-world trade-offs as closely as possible. Nevertheless, there are many factors that can influence actual treatment decisions that are not accounted for in our study. This study was also based on relatively small physician and patient samples. If these samples are insufficiently representative, our comparisons could be affected. Subgroup analysis according to physicians' specialties and settings could not be performed because of the relatively small sample size. As there is no study showing relative risk of fracture due to antiviral use in hepatitis B, decrease in phosphorus levels were used as a proxy. However, risk of fracture term was used in the questionnaire for ease of understanding of patients. Another potential limitation is the sources of the attribute levels for the three drug profiles reported in Table 4. If any of the profiles are different to those reported in Table 4 based on additional clinical data, the results will be slightly different and would have to be updated. The results included in this paper are really more of an illustration to demonstrate how choice-format conjoint studies can be applied to help regulators or other decision-makers understand physicians' and patients' preferences for CHB treatments and also to understand how those preferences may differ.

Discordance between the priorities for improvements elected by patients and by their respective physicians is an important concern in other diseases areas[26,27]. Discordance between physicians and patients regarding treatment attributes can be explained by asymmetric knowledge and differences in expectancies and priorities for health status. This fact highlights the need for reflection of physician and patient perspectives on regulatory and reimbursement decisions.

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REFERENCES

1. *World Health Organization. Hepatitis B Fact Sheet. August 2008. Available from: http://www.who.int/mediacentre/factsheets/fs204/en/ Accessed April 21, 2011.*

2. *Ozdemir D, Kurt H. Epidemiology of hepatitis B virus infection. In: Tabak F, Balik I, Tekeli E (eds). Viral Hepatit 2007. Ankara: Fight Against Viral Hepatitis Publications, 2007:108-17.*
3. *Yim HJ, Lok AS. Natural history of chronic hepatitis B virus infection: what we knew in 1981 and what we know in 2005. Hepatology 2006;43(2 Suppl 1):S173-81.*
4. *Turkish Ministry of Health, Turkey Health Force Report, Page 39; Table 10. March 2008, Ankara.*
5. *Vujicic M, Sparkes S, Mollahaliloglu S. Health Workforce Policy in Turkey Recent Reforms and Issues for the Future, www.worldbank.org July 2009.*
6. *Liaw YF, Leung N, Kao JH, Piratvisuth T, Gane E, Han KH; Chronic Hepatitis B Guideline Working Party of the Asian-Pacific Association for the Study of the Liver, et al. Asian-Pacific consensus statement on the management of chronic hepatitis B: a 2008 update. Hepatol Int 2008;2:263-83.*
7. *European Association for the Study of the Liver EASL clinical practice guidelines: management of chronic hepatitis B. J Hepatol 2009;50:227-42.*
8. *Lok ASF, McMahon BJ. AASLD Practice Guideline Update. Chronic Hepatitis B: Update 2009. Available at: www.aasld.org Accessed April 18, 2011.*
9. *Turkish Republic Official Gazette. Health Implementation Guideline 25th March 2010. Number: 27532.*
10. *Bridges JF, Hauber AB, Marshall D, Lloyd A, Prosser LA, Regier DA, et al. Conjoint analysis applications in health - how are studies being designed and reported? An update on current practice in the published literature between 2005 and 2008. Patient 2010;3:249-56.*
11. *Bridges JFP , Kinter ET, Kidane L, Heinzen RR, McCormick C. Things are looking up since we started listening to patients: trends in the application of conjoint analysis in health 1982-2007. Patient 2008;1:273-82.*
12. *Johnson FR, Ozdemir S, Mansfield C, Hass S, Miller DW, Siegel CA, et al. Crohn's disease patients' risk-benefit preferences: serious adverse event risks versus treatment efficacy. Gastroenterology 2007;133:769-77.*
13. *Johnson FR, Hauber AB, Özdemir S, Siegel CA, Hass S, Sands BE. Are gastroenterologists less tolerant of treatment risks than patients? Benefit-risk preferences in Crohn's disease management. Journal of Managed Care Pharmacy 2010;16:616-28.*
14. *Hauber AB, Mohamed AF, Watson ME, Johnson FR, Hernandez JE. Benefits, risks, and uncertainty: preferences of antiretroviral-naïve African Americans for HIV treatments. AIDS Patient Care STDS 2009;23:29-34.*
15. *Ettinger DS, Grunberg SM, Hauber AB, Mohamed AF. Evaluation of the relative importance of chemotherapeutic and antiemetic efficacy in various oncologic settings. Support Care Cancer 2009;17:405-11.*
16. *Hauber AB, Mohamed AF, Johnson FR, Falvey H. Treatment preferences and medication adherence of people with type 2 diabetes using oral glucose-lowering agents. Diabet Med 2009;26:416-24.*
17. *Hauber AB, Johnson FR, Fillit H, Mohamed AF, Leibman C, Arrighi HM, et al. Older Americans' risk-benefit preferences for modifying the course of Alzheimer's disease. Alzheimer Dis Assoc Disord 2009;23:23-32.*
18. *Hauber AB, Johnson FR, Grotzinger KM, Ozdemir S. Patients' benefit-risk preferences for chronic idiopathic thrombocytopenic purpura (ITP) therapies. Ann Pharmacother 2010;44:479-88.*
19. *Huber J, Zwerina K. The importance of utility balance in efficient choice designs. J Marketing Res 1996;33:307-17.*
20. *Kanninen B. Optimal design for multinomial choice experiments. J Marketing Res 2002;39:214-27.*
21. *Dey A. Orthogonal Fractional Factorial Designs. New York: Halstead Press, 1985.*
22. *Train K, Sonnier G. Mixed logit with bounded distributions of correlated partworths. In: Scarpa R, Alberini A (eds). Applications of Simulation Methods in Environmental and Resource Economics. Dordrecht: Springer Publisher, 2005:117-34.*
23. *Hensher DA, Rose JM, Greene WH. Applied Choice Analysis. Cambridge: Cambridge University Press, 2005.*
24. *Train K. Discrete Choice Methods with Simulation. Cambridge: Cambridge University Press, 2003:138-54.*
25. *Mohamed AF, Johnson FR, Hauber AB, Lescrauwaet B, Masterson A. Physicians' stated trade-off preferences for chronic hepatitis B treatment outcomes in Germany, France, Spain, Italy, and Turkey. Eur J Gastroenterol Hepatol 2012;24:419-26.*
26. *da Silva JA, Ramiro S, Pedro S, Rodrigues A, Vasconcelos JC, Benito-Garcia E. Patients- and physicians- priorities for improvement. The case of rheumatic diseases. Acta Reumatol Port 2010;35:192-9.*
27. *Allegretti A, Borkan J, Reis S, Griffiths F. Paired interviews of shared experiences around chronic low back pain: classic mismatch between patients and their doctors. Fam Pract 2010;27:676-83.*

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