ORIGINAL ARTICLES AND REVIEWS

A cost-consequence analysis of hepatitis B screening in an immigrant population

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Abstract

Objective. Screening for HBV among groups at risk, such as migrant populations, has proved to be a cost-effective strategy. With a view to advising local policy-makers, the cost-consequences of HBV screening was assessed using a modeling approach.

Methods. This cost-consequence analysis of an HBV screening strategy was conducted in a cohort of adult migrants in the province of Padua, northern Italy.

Results. The population targeted for screening consisted of 65 405 migrants, among whom the weighted rate for the prevalence of HBV was 0.04972, with 3251 people infected. Over a period of 5 years, the screening strategy prevented 565 cases/year of chronic hepatitis, 141 of compensated cirrhosis, 9 of decompensated cirrhosis, 14 hepatocellular carcinomas and 12 deaths. The above data revealed that the incremental cost of the screening strategy compared to no screening strategy was \in 7 974 959 over the five year period. The cost per life saved amounted to \in 676 709.

Conclusions. The present study provides useful information to policy-makers at local and regional levels.

Key words

- immigrants
- · screening program
- cost-consequence analysis
- · health care services
- modeling

INTRODUCTION

Hepatitis B virus (HBV) infection is a serious health problem over the world. Internationally, an estimated 240 million people are chronically infected with hepatitis B, and approximately 780 000 persons die each year from hepatitis B infection - 650 000 from cirrhosis and liver cancer due to chronic hepatitis B infection and another 130000 from acute hepatitis B [1]. Left untreated, persistent HBV infection leads to premature death due to cirrhosis or hepatocellular carcinoma in a large proportion of the individuals infected [2, 3]. Although HBV infection occurs everywhere in the world, nationality is strongly associated with the prevalence of HBV infection. In countries with the highest standards of living, like the United States, Canada and western Europe, its prevalence is low, while the highest rates of HBsAg carriers are found in developing countries in Africa, some parts of South America, and in other highpressure migrant countries, where hepatitis B is highly endemic such as eastern Europe, the eastern Mediterranean area, south-east Asia, China: in most of these areas, 5 to 15% of the population are chronically infected carriers of HBV, and in some areas may also carry HDV, which may lead to severe liver damage [4]. The prevalence of hepatitis B infection could consequently be high in immigrant communities, which often have limited access to generalist health services [5] or may be less well informed about the local health care system than the native population [6].

Other papers in the literature have analyzed the cost-effectiveness of screening for hepatitis B among groups at risk such as migrant populations. An economic assessment of interventions to identify cases of HBV and HCV infection among migrants to the UK reported an incremental cost-effectiveness ratio (ICER) of £ 21 000 per additional quality-adjusted life-year (QALY); this study was based on an estimated prevalence of 2% [7].

Other studies suggest that screening for chronic HBV in migrant populations could be cost-effective [8, 9]. Wong et al. reported that a selective hepatitis B screening program for immigrants in Canada prevents 59 HBV-related deaths per 10 000 population over the cohort's lifetime, and is likely to be moderately cost-effective, at \$ 69 209 per QALY gained [8]. The first study performed in Europe showed that screening and early treatment of chronic HBV in migrants was cost-effective. If case detection were improved by means of a screening program specifically targeting migrants, approximately 15% of the population with active, chronic hepatitis B would receive treatment (as opposed to

4% without screening), resulting in a 10% lower mortality. The ICER in this case was estimated at € 8966 per QALY gained, well below the € 20000 per QALY gained that was accepted as a threshold for considering the introduction of screening in the Netherlands [9]. These studies nevertheless demonstrate the value of HBV screening based on the calculation of the ICER. Cost-consequence analyses also play an essential part in the comprehensive economic assessment of a health care intervention. Decision-makers (e.g. reimbursement authorities) increasingly demand that such analyses be conducted in order to assess the affordability of implementing new public health strategies. Mauskopf, et al. claimed that economic impact assessments should include a classification of the policy-maker's information needs, a full and detailed breakdown of resource use and costs, and a list of expected health outcomes [10].

The aim of this study was to draw up a cost-consequence analysis of HBV screening in the immigrant population in the Italian province of Padua using a Markov modeling approach.

MATERIALS AND METHODS Target population

A cost-consequence analysis of HBV screening strategies was conducted on the cohort of adult migrants (> 20 years of age) in the province of Padua. The target population to undergo screening was drawn from the number of foreigners resident in the province, identifiable from the municipal population registry. The number of HBV carriers discovered in the target population was estimated from the prevalence of HBV for each nationality, weighted according to the sizes of the groups from different nations living in the province. Table 1 shows the prevalence of HBV infection among immigrants in the province by ethnicity. The prevalence estimates were obtained from data on the HBV screening of 450 regular healthy immigrants residing in Padua, and referred to our clinic by community leaders from March 2013 to October 2013 [11]. For the purposes of this analysis, the target population was considered as a fixed cohort within the five years of follow-up [12].

Model structure

Two approaches were used to investigate the cohort of immigrants in Padua, assessing their health outcomes and the related costs in two different scenarios:

Scenario 1) without any immigrant screening program, only 10% of the immigrants spontaneously came forward to be tested for HBV and those diagnosed as HBV-positive as a result of the test received treatment depending on their biochemical, serological and virological parameters; other infected immigrants not tested for HBV experienced the natural history of the disease while they remained asymptomatic and were only treated for symptomatic clinical conditions;

Scenario 2) if a screening program for immigrants was implemented, we assumed that 40% of the target population would be tested for HBV and those diagnosed as HBV-positive as a result of the screening program would receive treatment depending on their bio-

chemical, serological and virological parameters; other infected immigrants not tested for HBV experienced the natural history of the disease while they remained asymptomatic and were only treated for symptomatic clinical conditions:

A Markov chain model was developed using an Excel spreadsheet according to the assumptions outlined below. Eight states of health were defined and distinguished: 1) undetectable HBV DNA; 2) chronic hepatitis B; 3) compensated cirrhosis; 4) decompensated cirrhosis; 5) hepatocellular carcinoma; 6) liver transplantation; 7) HBsAg loss; and 8) death.

The intervention would consist of a one-off screening effort to identify cases of HBV in the migrant population living in the province of Padua, followed by the treatment of eligible patients. People in the target population would be invited by means of a letter written in their own language, containing information about the purpose of the screening program and a prescription that they could take to any nearby laboratory to have the test. Participants would be tested according to the following algorithm: antibody to hepatitis B core antigen (anti-HBc); if positive, HBsAg, HBeAg-anti-HBeAg and HBV DNA.

We assumed, as above specified, that: i) in the absence of screening, 10% of the population would spontaneously be tested for HBV (personal expert communication); and ii) in the event of a screening effort, 40% of the population would be supposed tested for HBV. The prevalence of hepatitis B in immigrants was reported in Table 1. The immigrants diagnosed as HBVpositive as a result of the test received would be referred to a specialist for antiviral therapy. Among the subjects found HBV-positive, we assumed that 65% were inactive carriers or had chronic hepatitis not warranting treatment (HBV-DNA < 20000 IU/ml, normal ALT or HBV-DNA > 20000 IU/ml, and normal ALT with no risk factors), 31.5% were cases of chronic hepatitis B warranting treatment, and 3.5% had cirrhosis (personal expert communication: Lobello & Martinez). In the first year of treatment, we assumed that interferon therapy could be administered to 50% of the patients and an alternative antiviral therapy (Tenofovir) to another 50%. After the first year, all patients (except for cases of HBsAg loss) would presumably be treated with Tenofovir. The probabilities of transition from one stage of disease to another with or without treatment, by HBeAg + and HBeAg- categories, were estimated, based on data in the international literature and expert opinions, as shown in Table 2.

Costs

The costs were estimated from the Italian public health service's perspective, taking the year 2010 for reference. Costs corresponding to the stages of progression of the disease were obtained from the Italian study by Colombo, et al. [32]. The unit costs used in the model are given in Table 3. The costs for antiviral therapy (Tenofovir) included periodic renal function monitoring, performed monthly during the first year and every 3 months thereafter. The costs of a sustained virological response were calculated assuming that patients

Table 1Target population [11] and prevalence of HBV by ethnicity (expert report: Lobello & Martinez)

Provenance		Subjects aged > 20	HBV-positive fraction	
		years	(estimated)	
Romania		20 903	0.05	
Republic of Moldova	Э	7 893	0.05	
Albania		5 913	0.04	
Ukraine		1 425	0.04	
Republic of Macedo	nia	1 149	0.04	
Bosnia and Herzegov	/ina	929	0.04	
Republic of Serbia		764	0.04	
Croatia		645	0.04	
Kosovo		328	0.04	
Other Central and Ea European countries	stern	1 191	0.04	
Morocco		8 005	0.04	
Nigeria		270	0.08	
Tunisia		893	0.07	
Senegal		712	0.07	
Ghana		546	0.07	
Cameroon		483	0.07	
Other African States		1 691	0.07	
Republic of China		4 376	0.10	
Philippines		1 573	0.08	
Bangladesh		967	0.02	
Sri Lanka (ex-Ceylon)	1	765	0.04	
India		626	0.04	
Other countries in As	sia	913	0.04	
Total immigrants		65 405		

needed three on their HBV DNA transaminase tests a year, and one clinical examination a year, including upper abdomen ultrasound and a blood count. In fact, costs and outcomes at different times are not directly comparable, so their comparison requires their adaptation to the same time period. The amount by which the value of something will drop each year into the future is known as the "discount rate". In this study, the costs were discounted at 3%.

For each case of HBV diagnosed we considered the cost of offering vaccination to relatives living with the HBV-infected case (2 people for every case identified).

Our results are presented year by year and by the eight states of health distinguished in the model.

Sensitivity analysis

One-way sensitivity analyses were performed on the target population. Given the paucity of reports on immigrant screening programs, it is hard to guess at the adherence of immigrants to such schemes, so two sepa-

rate analyses were run, assuming an adherence to the screening program of 20% (as the lowest estimate) and 60% (as the highest estimate).

RESULTS

The target population for the screening program consisted of 65 405 migrants, with a weighted rate of 0.04972 for the prevalence of HBV, resulting in 3251 people infected with the virus. In the event of a screening program, the rate of adherence to the HBV test was taken to amount to 40% (26 162 individuals) and 1300 (26 162 *0.04972) people were expected to be found HBV-positive. The proportion of the population presenting spontaneously for testing in the absence of any organized screening program was assumed to amount to 10% (6540 subjects) and the number of HBV cases discovered was calculated at 325 (6540 *0.04972).

Table 4 gives a summary of the intermediate and final outcomes with and without an HBV screening strategy over a period of five years, during which time the screening program would prevent 565 cases/year of chronic hepatitis, 141 cases/year of compensated cirrhosis, 9 cases/year of decompensated cirrhosis, 14 cases/year of hepatocellular carcinoma, and 12 deaths.

Table 5 shows that total five year cost of the scenario with screening was 11549781.29 and with total five year cost of the scenario without an active screening approach was 3574822.

The above data revealed that the incremental cost of the screening strategy was \in 7974959 over the five-year period. The cost per life saved amounted to \in 676709.47.

Sensitivity analysis

Assuming that 20% of the target population (the lower estimate) would adhere to the screening program, it was estimated that there would be prevented 4 deaths in five years. The associated incremental cost was estimated at 3557718.

If 60% of the individuals (the upper estimate) adhered to the screening program, it was estimated 20 prevented deaths in all in five years. The associated incremental cost was estimated at \in 12600740.7 (Table 6).

DISCUSSION

The present study concerns a cost-consequence analysis of screening immigrants residing in the province of Padua for HBV infection by comparison with a no screening strategy.

From the clinical standpoint, the study shows that screening prevents the evolution of the disease to later stages and increases the number of HBV-infected patients identified early stage in the course of the disease. These findings are consistent with our understanding of the natural history of chronic hepatitis B infection and our awareness that the public health impact of chronic HBV infection is related almost entirely to its long-term effects in terms of liver-related complications (e.g. hepatic decompensation, hepatocellular carcinoma) [37]. The opportunity to use new, more potent and effective antiviral treatments reduces the long-term morbidity and mortality due to this infection, increasing the



Annual estimated	progression in the natural h	istory of active hepatitis B and trea	tment-related annual transition	estimates	
a) Annual estima	ted progression in natural h	nistory of active hepatitis B			
Initial state	Evolution	Progression	Progression/year (%)		
		HBeAg+	HBeAg-		
Hepatitis B	Undetectable HBV DNA	6.9	1.6	[13, 14]	
	Cirrhosis	2.7	6.2	[15]	
	Hepatocellular carcinoma	0.4	0.4	[15]	
Cirrhosis	Cirrhosis decompensated	3.9	2.7	[16-18]	
	Hepatocellular carcinoma	1.8	2.9	[16-18]	
	Death	4	4	[19]	
Decompensated	Liver transplant	6.6	6.6	[20]	
cirrhosis	Hepatocellular carcinoma	1.8	2.9	[15]	
	Death	26	26	[15]	
Hepatocellular	Liver transplant	4	4	[20]	
carcinoma	Death	35	35	[13, 14]	
Liver transplant	Death	5.1	5.1	[20]	
b) Treatment-rela	ted annual transition estim	ates			
Initial state	Evolution	Progression	References		
		HBeAg+	HBeAg-		
Chronic hepatitis	HBsAg loss	11	8.7	[21, 22]	
B (PEG-IFN therapy)		(cumulative 3-year probability)	(cumulative 3-year probability)		
ттегару)	Undetectable HBV DNA	37 (cumulative 3-year probability)	28 (cumulative 3-year probability)	[21, 22]	
	Cirrhosis	0.2	0.6	[13, 23, 24]	
	Hepatocellular carcinoma	0.2	0.2	[25]	
Chronic hepatitis	HBsAg loss	3.2 (1year)	0	[26, 27]	
B (Tenofovir therapy)	Undetectable HBV DNA	76 (1year) 73 (cumulative 3-year probability)	93 (1year) 87 (cumulative 3-year probability)	[26, 27]	
	Cirrhosis	0.2	0.6	[13, 14, 23, 24]	
	Hepatocellular carcinoma	0.2	0.2	[25]	
	Resistance	1 Entecavir 0 Tenofovir	1 Entecavir 0 Tenofovir	[23, 24, 28]	
Chronic hepatitis	Cirrhosis	2.7	6.2	[13- 15]	
B (non-responder)	Hepatocellular carcinoma	0.4	0.4	[13-15]	
Cirrhosis	Undetectable HBV DNA	70.5	70.5	[29]	
(Tenofovir therapy)	Resistance	1 Entecavir 0 Tenofovir	1 Entecavir 0 Tenofovir	[13-15]	
	Decompensated cirrhosis	1.9	1.9	[13-15]	
	Hepatocellular carcinoma	1.6	1.6	[13-15]	
	Death	2.4	2.4	[13-15]	
Cirrhosis (non-responder)	Decompensated cirrhosis	3.9	3.9	[15]	
	Hepatocellular carcinoma	1.8	2.9	[13-15]	
	Death	3.1	3.1	[13-15]	
Decompensated	Liver transplant	3.3	3.3	[30]	
cirrhosis	Death	26	26	[13-15]	
Hepatocellular	Liver transplant	1.2	1.2	[30]	
carcinoma	Death	35	35	[13-15]	
Liver transplant	Death	5.1	5.1	[31]	

Table 3Cost data: average cost of different stages of the disease and annual drug costs [32]

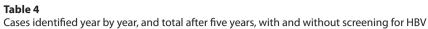
	Annual costs (€, 2010) References			
ending letters of invitation	1.80	Cost of stamp and letter		
aboratory tests				
AntiHBcAg	12.10	[33]		
HBsAg	12.10	[33]		
HBV DNA	12.10	[33]		
Blood count	4.75	[33]		
Transaminases (AST, ALT)	5.3	[33]		
pecialist visit	18.95	[33]		
Jltrasound	73.75	[33]		
ntiviral therapy				
Peg interferon	8356.55	[34]		
Entecavir	4595.35	[34]		
Tenofovir	3062.35	[34]		
nactive carriers	223.90	Calculated as below*		
Disease state				
Chronic hepatitis B	1977.02	[35]		
Compensated cirrhosis	3384.56	[35]		
Decompensated cirrhosis	3384.56	[35]		
Hepatocellular carcinoma	6808.71	[35]		
Liver transplantation	82 867.40	[35]		
Follow-up post-transplantation	6358.04	[36]		

^{*}Taking into account the cost of three tests a year on HBV DNA and transaminases; one check-up visit a year, one upper abdominal ultrasound and one blood

chances of an adequate disease management by means of its early-stage treatment [38, 39]. New treatments that reduce the viral load in the blood more effectively have now become available, and could avert serious outcomes [40]. The literature nonetheless demonstrates that the number of hospitalizations and outpatient visits, and the expenditure associated with HBV have continued to increase over the past 20 years, with long-term effects [37]. Other studies have shown that the early detection and treatment of HBV by means of mass screening programs in high-risk populations, such as immigrants (especially from countries with an intermediate or high prevalence of HBsAg carriers), can impact both health outcomes and costs in the short and long run [8, 9]. Screening programs also foster the immigrant population's usage of the health services, giving subjects with HBV the opportunity to be treated earlier, and preventing many cases from going undetected until they develop symptoms and complications [38]. Another study concluded that early care for hepatitis B by means of screening in a US cohort improved health, reduced premature deaths, and prevented expensive complications, making it highly cost-effective in the long term [39].

From the economic point of view, the present study shows a higher cost of the screening strategy compared with no screening, which could be attributed to the resources used to treat patients diagnosed at an early stage. This outlay at a time when the disease could still be reversible and curable would mean a cost reduction for patients in its more advanced and irreversible stages, and extending the time horizon of the study would probably reduce the difference in the incremental costs between the two strategies. As shown in Table 5, the cost of HBV without a screening strategy increased from € 544073 in the first year to € 801756 in the fifth year (+ 30%), whereas the cost with a screening program rose from € 1 960 872 in the first year to € 2080952 in the fifth year (+ 6%). The cost of the lives saved by the screening program amounted to € 675 843, and the mean annual cost was € 135 169 an amount comparable with those reported for other screening programs. For example, White found in 1995 that the mean annual cost of mammographic screening per life "saved" was around \$ 1.2 million (£ 558000) [41].

Our findings concern an immigrant population with a 5% prevalence of HBV. The prevalence of a given infection or disease is an important issue to consider in any economic assessment of the cost and health consequences of case-finding interventions [7]. In another cost-effectiveness analysis, for instance, Miners found that the ICER for HBV case finding was approximately £ 21000 per additional QALY if the prevalence of the condition was 2%, but this ICER dropped to approximately £ 12000 per additional QALY if the prevalence



Outcomes		Outcomes without screening	Outcomes with screening	Δ outcomes
HbsAg loss	1 year	2.33	9.32	6.99
	2 years	1.07	4.28	3.21
	3 years	1.12	4.48	3.36
	4 years	1.66	4.66	3
	5 years	1.21	4.84	3.63
Total cases of HbsAg loss		7.39	27.58	20.19
Undetectable	1 year	2 184.62	2 349.34	164.72
HBV DNA	2 years	2 192.67	2 342.79	150.12
	3 years	2 198.15	2 334.99	136.84
	4 years	2 201.34	2 325.82	124.48
	5 years	2 202.51	2 315.43	112.92
Total inactive carriers		10 979.29	11 668.37	689.08
Chronic hepatitis B	1 year	906.08	748.47	-157.61
	2 years	854.69	721.26	-133.43
	3 years	808.27	697.04	-111.23
	4 years	766.33	675.46	-90.87
	5 years	728.36	656.24	-72.12
otal chronic hepatitis B cases		4 063.73	3 498.47	-565.26
Cirrhosis	1 year	144.65	133.33	-11.32
	2 years	169.80	148.42	-21.38
	3 years	190.26	160.51	-29.75
	4 years	206.70	170.04	-36.66
	5 years	219.68	177.39	-42.29
otal cirrhosis cases		931.09	789.69	-141.4
Decompensated cirrhosis	1 year	3.60	3.12	-0.48
	2 years	6.89	5.83	-1.06
	3 years	9.78	8.07	-1.71
	4 years	12.27	9.90	-2.37
	5 years	14.37	11.37	-3
otal decompensated cirrhosis cases		46.91	38.29	-8.62
Hepatocellular carcinoma	1 year	6.48	5.61	-0.87
	2 years	11.25	9.27	-1.98
	3 years	14.87	11.96	-2.91
	4 years	17.65	13.97	-3.68
	5 years	19.79	15.48	-4.31
Total HCC cases		70.04	56.29	-13.75
iver transplant	1 year	0	0	0
	2 years	0.25	0.27	0.02
	3 years	0.48	0.47	-0.01
	4 years	1.24	0.63	-0.61
	5 years	1.52	1.21	-0.31
otal liver transplants		3.49	2.58	-0.91
Death	1 year	4.18	3.05	-1.13
	2 years	8.82	7.43	-1.39
	3 years	12.37	10.05	-2.32
	4 years	15.23	12.11	-3.12
	5 years	17.55	13.72	-3.83
otal deaths		58.15	46.36	-11.79

Table 5Costs discounting results

Costs with screening (€, 2010)						
Costs with screening (e, 2010)	1st year	2 nd year	3 rd year	4 th year	5 th year	Total
HbsAq loss	93 516	41 690	42 336	42 812	43 132	263 486
Inactive carriers	232 843	223 122	213 807	204 881	196 328	1 070, 982
Chronic hepatitis B	1 293 171	1 316 961	1 335 340	1 348 761	1 357 673	6 651 907
Cirrhosis	277 147	256 814	238 371	221 645	206 466	1 200 444
Decompensated cirrhosis	19 519	35 455	47 606	56 679	63, 256	222 515
Hepatocellular carcinoma	35 119	56 299	70 569	80 039	86 101	328 127
Liver transplant	0.00	21 686	36 953	48 159	89 843	96 642
Death	9 557	22 576	29 660	34 669	38 154	134 616
Total	1 960 872	1 974 604	2 014 644	2 037 647	2 080 952	10 068 719
Cost of screening	797 681					
Cost of HBV testing+ antiHBV vaccination for cohabitants	683 381					
Total cost						11 549 781.29
Costs without screening (€)						
	1st year	2 nd year	3 rd year	4 th year	5 th year	Total
HbsAg loss	23 379	10 422	10 584	10 703	10 772	65 861
Inactive carriers	58 211	55 781	53 452	51 220	49 082	267 745
Chronic hepatitis B	323 293	329 240	333 835	337 190	339 114	1 662 673
Cirrhosis	69 287	64 203	59 593	55 411	51 624	300 118
Decompensated cirrhosis	22 511	41 845	57 693	70 271	79 917	272 237
Hepatocellular carcinoma	28 067	68 342	87 749	101 125	110 076	395 360
Liver transplant	0.00	20 481	37 408	94 700	112 368	264 957
Death	19 326	26 798	36 488	43 611	48 802	175,025
Total	544 073	617 113	676 802	764 233	801 756	3 403 977
Cost of HBV testing + antiHBV vaccination	170 845					
for cohabitants						

Table 6Results of sensitivity analysis

	No screening	20% adherence	40% adherence	60% adherence
Undetectable HBV DNA	6.9	14.3	27.6	43.0
Death	58.1	54.2	46.4	38.5
Lives saved		4.0	11.8	19.6
Costs	€ 3 577 791.42	€ 7 135 509.79	€ 11 549 781.27	€ 16 178 532.08
Delta cost		€ 3 557 718.36	€ 7 971 989.85	€ 12 600 740.66
Cost per life saved		€ 898 287.72	€ 676 709.47	€ 641 659.52

was assumed to be 20%, a figure believed to be representative of the infection's prevalence in some UK Chinese communities [7].

The decision to perform this cost-consequence analysis, albeit with a limited time horizon, arose from the need to focus on the costs that could be sustained and the negative outcomes that could be avoided by means of efforts to ensure the early diagnosis and manage-

ment of this chronic disease in the province of Padua's immigrant population. Several previous studies on this issue involved cost-effectiveness analyses [8, 9]. It is more common for cost-effectiveness ratios (CERs) to be used to assess the value of a health program, but researchers have recently shown that policy-makers rarely use CER estimates in making formulary decisions. By making the impact of a new treatment or screening pro-

gram as comprehensive and transparent as possible, the cost-consequence approach can help decision-makers to select the most relevant components from their perspective and will also give them confidence in the credibility of the data and use them as the grounds for their resource allocation decisions.

Our study has some limitations. First of all, it only simulated a stable cohort, not a dynamic one. The study also fails to take into account the impact (in terms of outcome) of vaccination strategies for relatives of infected cases. Chronically-infected immigrants can become a reservoir of infection, giving rise to new infections in Italy; identifying these cases can complement vaccination strategies with a view to limiting the spread of HBV [42]. Another weakness of our study lies in the short follow-up, which could also have prevented us from measuring the health outcome gains appearing

in the longer term. According to Post et al. [39], treating chronic hepatitis B infection (before any late-stage complications become manifest) would be cost-effective over as short a period as ten years. As this study was conducted from the national public health service perspective, indirect costs such as loss of productivity were not taken into account.

In conclusion, the results of the present study could support policy-makers in this area, and provide an overview to help them decide whether it is worth investing in HBV screening programs.

Conflict of interest statement

No competing financial interests exist.

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REFERENCES

- World Health Organization. Hepatitis B, Fact sheet n. 204. Geneva: WHO; 2015. Available from: www.who.int/mediacentre/factsheets/fs204/en.
- Hollinger FB, Liang TJ. Hepatitis B virus. In: Knipe DM, et al. (Eds). Fields Virology. 4thed. Philadelphia: Lippincott Williams & Wilkins; 2001. p. 2971-3036.
- 3. Robinson WS. Hepatitis B virus and hepatitis D virus. In: Mandell GL, Bennett JE, Dolin R. (Eds). *Principles and practice of infectious diseases*. 4th ed. New York: Churchill Livingstone; 1995. p. 1406-39.
- World Health Organization. Global Alert and Response. Hepatitis B-incidence/ epidemiology. Available from: www. who.int/csr/disease/hepatitis/whocdscsrlyo20022/en/in-dex4 html
- Wallace J, McNally S, Richmond J. National hepatitis B needs assessment. Australian Research Centre in Sex, Health and Society 2007.
- Hogan L. Promising practices to improve immigrants' health and well-being. Program Director. Access to Health Services. The California Endowment.
- 7. Miners A, Ghosh A, Martin N, Vickerman P. An economic evaluation of finding cases of hepatitis B and C infection in UK migrant populations. London: London School of Hygiene & Tropical Medecine; 2012.
- 8. Wong WWL, Woo G, Heathcote EJ, Krahn M. Cost effectiveness of screening immigrants for hepatitis B. *Liver Intern* 2011;1179-1190. DOI:10.1111/j.1478-3231.2011.02559.x
- 9. Veldhuijzen IK, Toy M, Hahné SJ, De Wit GA, Schalm SW, De Man RA, et al. Screening and early treatment of migrants for chronic hepatitis B virus infection is costeffective. Gastroenterology 2010;138(2):522-30.
- Mauskopf JA, Paul JE, Grant DM. The role of cost-consequence analysis in healthcare decision-making. *Phar*macoeconomics 1998;13(3):277-88.
- Peraro L, et al. 47th Annual Meeting of the Italian Association for the Study of the Liver. Rome, February 20:-21t, 2014.
- Mauskopf JA, Sullivan SD, Annemans L, Caro J, Mullins CD, Nuijten M, et al. Principles of Good Practice for Budget Impact Analysis. Report of the ISPOR Task Force on Good Research Practices Budget Impact Analysis. Val Health 2007;10(5):336-47.
- 13. Kanwal F, Gralnek IM, Martin P, Dulai GS, Farid M,

- Spiegel BMR. Treatment alternatives for chronic hepatitis B virus infection: a cost-effectiveness analysis. *Ann Intern Med* 2005;142:821-31.
- Kanwal F, Farid M, Martin P, Chen G, Gralnek IM, Dulai GS, et al. Treatment alternatives for hepatitis B cirrhosis: a cost-effectiveness analysis. Am J Gastroenterol 2006:101:2076-89.
- Fattovich G, Bortolotti F, Donato F. Natural history of chronic hepatitis B: special emphasis on disease progression and prognostic factors. *J Hepatol* 2008;48:335-52.
- Fattovich G, Pantalena M, Zagni I, Realdi G, Schalm SW, Christensen E. Effect of hepatitis B and C virus infections on the natural history of compensated cirrhosis: a cohort study of 297 patients. *Am J Gastroenterol* 2002;97:2886-95.
- Fattovich G, Giustina G, Schalm SW, Hadziyannis S, Sanchez-Tapias J, Almasio P, et al. Occurrence of hepatocellular carcinoma and decompensation in Western European patients with cirrhosis type B. The EUROHEP Study Group on Hepatitis B Virus and Cirrhosis. Hepatology 1995;21:77-82.
- Realdi G, Fattovich G, Hadziyannis S, Schalm SW, Almasio P, Sanchez-Tapias J, et al. Survival and prognostic factors in 366 patients with compensated cirrhosis type B: a multicenter study. The investigators of the European Concerted Action on Viral Hepatitis (EUROHEP). J Hepatol 1994;21:656-6.
- D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. *J Hepatol* 2006;44(1):217-31.
- 20. Data on the local liver transplant. Azienda Ospedaliera Padua.
- Buster EH, Flink HJ, Cakaloglu Y, Simon K, Trojan J, Tabak F, et al. Sustained HBeAg and HBsAg loss after long-term follow-up of HBeAg-positive patients treated with peginterferon-2b. Gastroenterology 2008;135:459-67.
- Marcellin P, Bonino F, Lau GK, Farci P, Yurdaydin C, Piratvisuth T, et al. Sustained response of hepatitis B e antigen-negative patients 3 years after treatment with peginterferon alpha-2a. Gastroenterology 2009;136(7):2169-279.e1-4. DOI: 10.1053/j.gastro.2009.03.006.
- 23. Chang TT, Gish RG, De Man R, Gadano A, Sollano J, Chao YC, et al. A comparison of entecavir and lamivu-

- dine for HBeAg-positive chronic hepatitis B. N Engl J Med 2006;354:1001-10.
- Lai CL, Shouval D, Lok AS, Chang TT, Cheinquer H, Goodman Z, et al. Entecavir versus lamivudine for patients with HBeAg-negative chronic hepatitis B. N Engl J Med 2006:354:1011-20.
- Liaw YF, Sung JJ, Chow WC, Farrell G, Lee CZ, Yuen H, et al. Lamivudine for patients with chronic hepatitis B and advanced liver disease. N Engl J Med 2004;351:1521-31.
- 26. Heathcote EJ, Marcellin P, Buti M, Gane Ed, De Man RA, Krastev Z, et al. Three-year efficacy and safety of tenofovir disoproxil fumarate treatment for chronic hepatitis B. *Gastroenterology* 2011;140(1):132-43.
- Marcellin P, Heathcote EJ, Buti M, Gane Ed, De Man RA, Krastev Z, et al. Tenofovir disoproxil fumarate versus adefovir dipivoxil for chronic hepatitis B. N Engl J Med 2008;359(23):2442-55. DOI:10.1056/NEJMoa0802878.
- 28. Colonno RJ, Rose RE, Pokornowski K, Baldick CJ, Eggers B, Xu D, et al. Four-year assessment of entecavir resistance in nucleoside-naive and lamivudine-refractory patients. J Hepatol 2007;46(Suppl. 1):S294.
- Moucari R, Korevaar A, Lada O, Martinot-Peignoux M, Boyer N, Mackiewicz V, et al. High rates of HBsAg seroconversion in HBeAg-positive chronic hepatitis B patients responding to interferon: a long-term follow-up study. J Hepatol 2009;50:1084-92.
- 30. Nederlandse Transplantatie Stichting. Available from: www.transplant.org.
- 31. Centro Nazionale Trapianti Sito ufficiale. Available from: www.trapianti.salute.gov.it/cnt/cntStatistiche.jsp?s otmenu=normativa&area=cntgenerale&label=datdoc&m enu=menuPrincipale&titolo=2008&etichetta=+-+Anno+2008&anno=2008.
- Colombo GL, Gaeta GB, Viganò M, Di Matteo S. A cost-effectiveness analysis of different therapies in patients with chronic hepatitis B in Italy. Clinicoecon Outcomes Res 2011:37-46. DOI: 10.2147/CEOR.S16655

- 33. Veneto Region. Tariff nomenclature Performance Specialist Outpatient.
- 34. Italy. Health Ministry. Nomenclatore delle Prestazioni di assistenza specialistica ambulatoriale. [National Tariff Nomenclature]. Roma: Ministero della Salute; 2010.
- 35. Conferenza delle Regioni e delle Province autonome 1O/014/CR10a/C7. DRG 206, Tariffa Unica Convenzionale (TUC) per le prestazioni di assistenza ospedaliera, regole e tariffe valide per l'anno 2009 secondo CMS-DRG Versione 24. DRG 206; DRG 202; DRG 199; DRG 480; Roma 2010.
- 36. Tumiatti C, Bezzon C, Guasti F, Franchin M. *Il costo del trapianto d'organo: risultati di uno studio condotto presso l'Azienda Ospedaliera di Padova*. Azienda Ospedaliera di Padova. 1999:39. valori attualizzati al 2009.
- 37. Lo Re V. Economic analysis of hepatitis B screening and treatment. *Clin Infect Dis* 2011;52(11):1307-9.
- 38. Beca J. Should hepatitis B screening be added to the United States Immigration medical exam? A cost-utility model. Masters of Science Health Policy, Management and Evaluation University of Toronto: 2010.
- Post SE, Sodhi NK, Peng Ch, Wan K, Pollack HJ. A simulation shows that early treatment of chronic hepatitis B infection can cut deaths and be cost-effective. *Health Aff* 2011;30:340-8. DOI: 10.1377/hlthaff.2008.0905.
- 40. Lin SM, Sheen IS, Chien RN, Chu CM, Liaw YF. Long-term beneficial effect of interferon therapy in patients with chronic hepatitis B virus infection. *Hepatology* 1999:29(3):971-75.
- 41. Wright CJ, Mueller CB. Screening mammography and public health policy: the need for perspective. *Lancet* 1995;346:29-32.
- 42. Weinbaum CM, Williams I, Mast EE, Wang SA, Finelli L, Wasley A, et al. Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. MMWR Recomm Reports 2008;57(No. RR-8):1-20.