

## Original Article

# The Economic Burden of Hepatitis A, B, and C in South Korea

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**SUMMARY:** The prevalence of hepatitis in South Korea is relatively high compared to that in other high-income countries. For this reason, viral hepatitis infection not only affects the population's health, but also impacts national healthcare costs. This study was performed in order to estimate the individual economic costs of the hepatitis A, B, and C viruses as well as to determine, using nationally representative data, the trends in South Korea with respect to these viruses during the 2008–2011 period. The study found that the prevalence of hepatitis A had decreased, but those of hepatitis B and C had increased overall. The mortality rate of hepatitis C was higher than that of the other two types. The mortality rate of hepatitis B had changed little, whereas that of hepatitis C had risen. The total cost of hepatitis A had decreased, from US \$62.2 million to US \$45.7 million, although a notable exception occurred in 2009, when the cost was US \$126.6 million. Conversely, the total cost of hepatitis B had increased rapidly during the same period, from US \$501.4 million to US \$607.8 million. Finally, the total cost of hepatitis C had also increased from US \$63.9 million to US \$90.7 million. The direct costs of hepatitis A, B, and C were estimated to account for approximately 35.5%, 46.6%, and 58.0% of the total, respectively. These findings demonstrate the economic burden associated with hepatitis A, B, and C, and demonstrate the need to establish an effective prevention and management policy for future planning in South Korea.

## INTRODUCTION

More than 1 million deaths per year are attributed to viral hepatitis infections worldwide, and the Global Burden of Disease study showed that 1.2% of global deaths in 2010 resulted from hepatitis. The total number of deaths resulting from hepatitis B was estimated to be 786,000, while hepatitis C caused 499,000 deaths. Thus, hepatitis B and C were the 15th and 25th greatest causes of death, respectively (1). Unlike hepatitis B and C, hepatitis A infection is rarely fatal, but it can cause debilitating symptoms or acute liver failure, the latter of which is associated with high mortality (2). Approximately 1.4 million cases of hepatitis occur globally every year. Furthermore, the hepatitis B and C viruses (HBV and HCV, respectively) are the leading causes of liver cancer worldwide, accounting for 78% of cases (1). In the context of South Korea, HBV infection especially is

known as one of the major causes of morbidity and mortality (3).

In South Korea, hepatitis is usually caused by 1 of 3 hepatitis viruses: the hepatitis A virus (HAV), HBV, or HCV. Indeed, these viruses are the major causes of acute and chronic hepatitis worldwide. These 3 aforementioned hepatitis viruses can also lead to acute disease, with symptoms of nausea, abdominal pain, fatigue, malaise, and jaundice. Furthermore, HBV and HCV can develop into chronic infections (4), which in turn, are likely to cause associated diseases such as cirrhosis and hepatocellular carcinoma (HCC) (5). Although HBV has been one of the major causes of acute hepatitis in the past, the incidence of HAV infection has increased rapidly in recent years in South Korea (6).

HBV infection is endemic in South Korea (7). According to the Korean National Health and Nutrition Examination Survey (KNHANES) conducted in 2010, the prevalence rate of the HBV surface antigen (HBsAg) among people aged 10 or older was about 3.0%. Following the implementation in the 1990s of a national HBV vaccination program for all neonates of HBsAg carrier mothers, the prevalence of HBV in those aged 10–18 dropped rapidly: from approximately 4–5% in the 1990s to 0.1% in 2010. However, the prevalence of HBV in people older than 30 years remains high (3.7% in 2010) (8).

Due to its high prevalence in South Korea, viral hepatitis not only affects the population's health status, but also impacts national healthcare costs. Despite this, there have been no studies examining the cost of hepatic

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tis, or estimating the individual costs of hepatitis A, B, and C. Therefore, this study was performed to estimate the costs of HAV, HBV, and HCV infection during the 2008–2011 period from a societal perspective, as well as to analyze recent trends in Korea.

## MATERIALS AND METHODS

**Prevalence and mortality rate:** Herein, the prevalence rate of hepatitis was defined as the total number of cases of hepatitis infection in the population, taken from the National Health Insurance Service (NHIS) claims data, divided by the total population, ascertained using population projections that were produced by the Korean Statistical Information Service (KOSIS) on the basis of sex and age (9). The NHIS was independently established as a single-payer in health insurance system in South Korea, and their claims data includes information on the entire population who use the healthcare service. The KOSIS is a national statistical database that is operated by Statistics Korea; it produces official statistics and sends the data to international organizations such as IMF (the International Money Fund), the World Bank, and OECD (the Organization for Economic Corporation and Development).

Cases of hepatitis infection were confirmed on the basis of a primary diagnosis in the claims data. To identify hepatitis cases, we used the International Classification of Disease (ICD)-10 code B15 for hepatitis A, from B16 to B19 (except B17.1 & B18.2) for hepatitis B, and B17.1 and B18.2 for hepatitis C. Hepatitis infection was confirmed when a policy-holder made at least 1 inpatient or outpatient claim, over the course of 1 year, with a primary diagnosis of hepatitis A, B, or C. The mortality rate of hepatitis was defined as the number of deaths caused by hepatitis infection, based on the cause of death data by sex and age provided by KOSIS, divided by the total population number, taken from the KOSIS data of population projections produced on the basis of sex and age (9). All statistics are shown as the rate per 100,000 people.

Costs related to hepatitis A, B, and C virus infections were estimated using a prevalence-based approach, wherein we analyzed the number of patients with each infection, as well as the number of deaths resulting from each hepatitis during the period from 2008 to 2011 period. Because there is mandatory health insurance for residents in Korea managed by the NHIS, the claims data used represented the entire population in the country (10). Therefore, access to this data allowed us to estimate the overall medical expenditure resulting from hepatitis infections in South Korea as a whole. The method used to estimate the economic burden of disease was as follows: *The Economic Burden = Direct costs + Indirect costs*

**Direct costs:** Direct costs comprised all direct medical care costs, including NHIS-covered care costs, non-NHIS-covered care costs and co-payments, and NHIS-covered drug and transportation costs for inpatient and outpatient care. The NHIS data included patient information according to primary diagnosis; using this data, we recorded the number of patients of each hepatitis type, the lengths of their stays in hospital, and the costs covered by the NHIS.

We estimated the non-NHIS-covered care costs, such as magnetic resonance imaging and ultrasound examinations, on the basis of “the Survey on the Benefit Coverage Rate of National Health Insurance 2011” (11), a survey conducted by the NHIS whose purpose was to collect cost data annually from sample hospitals. In this survey, the cost in 1,103 institutions (1.4% of total institutions in South Korea) were assessed in order to estimate non-NHIS-covered costs. Because there are several types of institutions in South Korea, such as tertiary hospitals, general hospitals, hospitals and clinics etc., all institutions were stratified into 10 subgroups before sampling to improve sampling accuracy. The sample institutions were then selected using the Neyman method, which allocates samples to strata on the basis of strata variances and similar sampling costs within the strata (12). The proportion of non-NHIS-covered care costs related to hepatitis A were 23.58% for inpatient care, and 22.17% for outpatient care; related to hepatitis B were 24.17% and 20.40%, respectively and related to hepatitis C were 14.15% and 26.07%, respectively.

We also considered transportation costs related to hepatitis A, B, and C. To estimate these costs, we used data from “the Korea Health Panel 2010” whose main purpose was to gather information regarding health service use and health expenditure. In this panel, about 8,000 households and their members were surveyed starting in 2004. The average transportation cost for patients with certain infectious and parasitic diseases, ascertained from the data was applied to our analysis. The survey sample was taken using a 2-stage cluster method, stratified sampling with probability proportionate to size. In other words, the size of the regional level was considered first, and sample households were then selected based on an order list at the second stage for sample allocation. In this way, the panel data also represented the entire South Korean population (13).

**Indirect costs:** Indirect costs consist of opportunity costs lost as a result of medical care, or premature death and caregiver costs. Opportunity costs were estimated using the human capital approach (14). Productivity loss because of inpatient care was estimated on the basis of average daily wage by sex and age available in the KOSIS (9). The lengths of inpatient hospital stays were obtained from NHIS claims data. However, productivity loss due to outpatient care was estimated on the basis of 1-third of the average daily wage. Patients aged  $\leq 19$  years and those aged  $\geq 65$  years were not included in the working age group, so we only calculated productivity loss for patients aged 20–64 years (15). The GDP deflator was used to estimate productivity loss during the 2008–2011 period.

For inpatient care, caregiver costs were estimated by multiplying the length of stay by the minimum daily wage (US \$58.82) for caregivers from the Korea Patient Helper Society (KPHS), the KPHS is a representative caregiver association in South Korea (16). For outpatient care, it was assumed that only patients aged  $\leq 19$  years and aged  $\geq 65$  years would require caregivers (15,17), and outpatient care was assumed to require approximately one-third of the patient’s daily working hours (18). In terms of productivity loss due to premature death, the number of deaths resulting from hepatitis A, B, and C were obtained from the KOSIS death

statistics (9). Productivity loss due to premature death was defined as potential income loss estimated on the basis on gender and age status. Subjects were divided into three groups according to age:  $\leq 19$  years, 20–64 years, and  $\geq 65$  years.

Finally, the economic burden of disease was estimated by summing the direct and indirect costs of hepatitis A, B, and C. All estimated costs were converted into US dollars using an exchange rate of US \$1 =

1160.81 South Korean won-the average exchange rate during the 2008–2011 period (19).

## RESULTS

The prevalence trend of hepatitis A was inconsistent during the study period. Specifically, the number of hepatitis A cases was higher in the second year of the study than in the first (24,524 cases in 2008; 54,832 cases

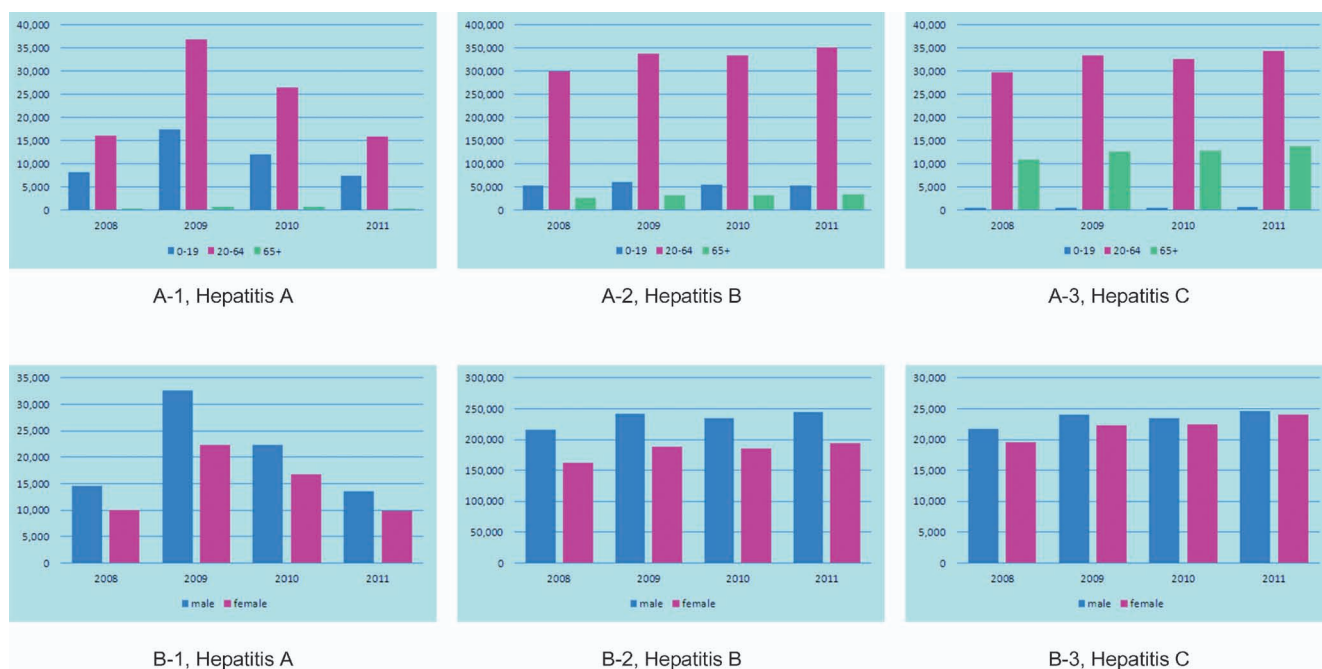


Fig. 1. (Color online) Four-year trends of number of patients in hepatitis A, B, and C according to age group (A1–A3) and classification of sex (B1–B3). A-1, hepatitis A; A-2, hepatitis B; A-3, hepatitis C; B-1, hepatitis A; B-2, hepatitis B; B-3, hepatitis C.

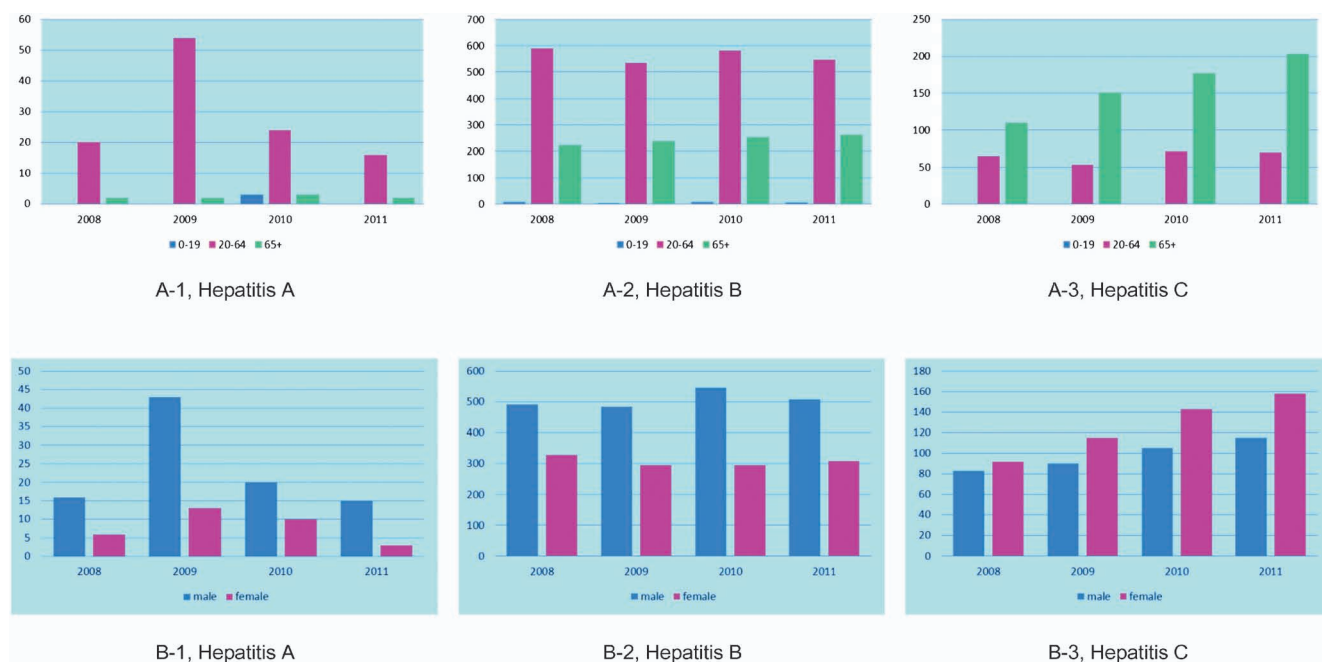


Fig. 2. (Color online) Four-year trends of number of deaths in hepatitis A, B, and C according to age group (A1–A3) and classification of sex (B1–B3). A-1, hepatitis A; A-2, hepatitis B; A-3, hepatitis C; B-1, hepatitis A; B-2, hepatitis B; B-3, hepatitis C.

Table 1. Four-year trends in hepatitis A, B, and C in Korea: numbers of patients and deaths, prevalence, and mortality rates

Year	Sex	Age group	Hepatitis A				Hepatitis B				Hepatitis C			
			No. of patients	No. of deaths	Prevalence	Mortality rate	No. of patients	No. of deaths	Prevalence	Mortality rate	No. of patients	No. of deaths	Prevalence	Mortality rate
2008	Men	≤ 19	1410	0	22.73	0.00	12939	4	208.59	0.00	322	0	5.19	0.00
		20–64	12976	16	79.47	0.10	191236	411	1171.22	0.04	16414	47	100.53	0.29
		≥ 65	148	0	7.24	0.00	11722	77	573.16	0.10	4940	36	241.55	1.76
		Men sum	14534	16	59.14	0.07	21589	492	878.48	2.00	21676	83	88.20	0.34
	Women	≤ 19	6695	0	119.29	0.00	40242	3	717.01	0.00	164	0	2.92	0.00
		20–64	3119	4	24.40	0.03	108197	180	846.59	0.02	13398	18	85.05	0.11
		≥ 65	176	2	5.85	0.07	14666	146	487.73	0.13	5985	74	199.03	2.46
		Women sum	9990	6	46.68	0.03	163105	329	762.18	1.54	19547	92	80.20	0.38
	Subtotal		24524	22	53.34	0.05	379002	821	824.35	0.03	41223	175	84.22	0.36
2009	Men	≤ 19	2775	0	45.44	0.00	14281	2	233.84	0.00	339	0	5.55	0.00
		20–64	29520	42	179.78	0.26	213477	384	1300.08	0.03	18202	38	110.85	0.23
		≥ 65	286	1	13.38	0.05	13576	98	635.28	0.19	5558	52	260.08	2.43
		Men sum	32581	43	132.10	0.17	241334	484	978.47	1.96	24099	90	97.71	0.36
	Women	≤ 19	14627	0	264.09	0.00	46993	2	848.47	0.00	181	0	3.27	0.00
		20–64	7290	12	55.89	0.09	124057	153	951.14	0.03	15196	16	116.51	0.12
		≥ 65	334	1	10.71	0.03	17293	141	554.47	0.10	6972	99	223.55	3.17
		Women sum	22251	13	102.54	0.06	188343	296	867.93	1.36	22349	115	102.99	0.53
	Subtotal		54832	56	118.26	0.12	429677	780	926.73	0.03	46448	205	100.18	0.44
2010	Men	≤ 19	2239	3	37.36	0.05	12783	4	213.32	0.00	329	0	5.49	0.00
		20–64	19897	17	120.31	0.10	208398	439	1260.10	0.05	17622	52	106.55	0.31
		≥ 65	266	0	11.94	0.00	14154	103	635.52	0.13	5542	53	248.84	2.38
		Men sum	22402	20	90.48	0.08	235335	546	950.55	2.21	23493	105	94.89	0.42
	Women	≤ 19	9878	0	181.24	0.00	42207	3	774.42	0.00	165	0	3.03	0.00
		20–64	6514	7	49.04	0.05	125255	143	942.93	0.02	15115	19	113.79	0.14
		≥ 65	344	3	10.67	0.09	17806	150	552.07	0.12	7230	124	224.16	3.84
		Women sum	16736	10	76.21	0.05	185268	296	843.70	1.35	22510	143	102.51	0.65
	Subtotal		39138	30	83.78	0.06	420603	842	900.32	0.04	46003	248	98.47	0.53
2011	Men	≤ 19	1403	0	23.87	0.00	11813	5	201.01	0.00	384	0	6.53	0.00
		20–64	12071	14	72.09	0.08	218132	406	1302.68	0.05	18313	48	109.36	0.29
		≥ 65	139	1	5.99	0.04	15086	96	650.06	0.09	5916	67	254.92	2.89
		Men sum	13613	15	54.58	0.06	245031	507	982.39	2.03	24613	115	98.68	0.46
	Women	≤ 19	5915	0	110.30	0.00	41149	0	767.33	0.00	216	0	4.03	0.00
		20–64	3763	2	27.82	0.01	133556	141	987.37	0.02	16114	22	119.13	0.16
		≥ 65	195	1	5.85	0.03	19137	167	573.78	0.06	7761	136	232.69	4.08
		Women sum	9873	3	44.42	0.01	193842	308	872.20	1.39	24091	158	108.40	0.71
	Subtotal		23486	18	49.79	0.04	438873	815	930.47	0.03	48704	273	103.26	0.58

in 2009), however, the number decreased thereafter (Table 1). The prevalence of hepatitis A also decreased rapidly from 2009 to 2011 (118.26 per 100,000 in 2009; 49.79 in 2011). The mortality rate of hepatitis C was slightly higher than the individual mortality rates of hepatitis A and B. Although the mortality rate of hepatitis A tended to decrease overall, was still more than 3 times of the individual mortality rates of hepatitis B in 2009 (Table 1, Fig. 3).

With regard to sex and age status, both the prevalence and mortality rate of hepatitis A was higher for men aged 20–64 years than for men in other age groups during the study period. However, the prevalence was higher for women aged  $\leq 19$  years than for women in other age groups, and the mortality rate was higher for women aged  $\geq 65$  years than for women in other age groups during the same period.

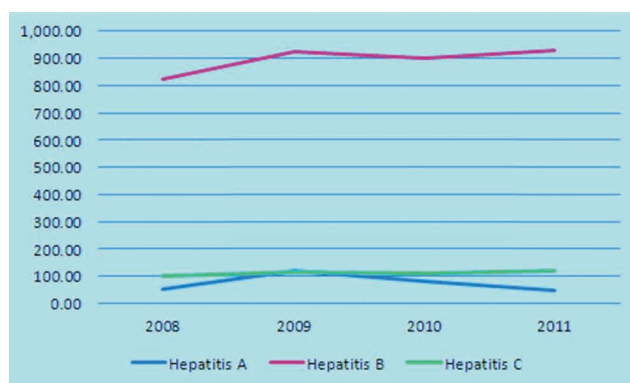
The total number of treated cases of hepatitis B slightly increased from 2008 to 2011, with 379,002; 429,677; 420,603; and 438,873 cases in each year from 2008 to 2011, respectively. The overall hepatitis B prevalence showed similar trend over the same period. However, the mortality rate due to hepatitis B changed little, remaining approximately 0.03 per 100,000. In terms of sex and age, the hepatitis B prevalence per 100,000 was higher in both men (1,302.68 per 100,000 in 2011) and women (987.37 per 100,000 in 2011) aged 20–64 years than in those of other age groups. However, the mortality rate was higher in both men (0.09 per 100,000) and women (0.06 per 100,000) aged  $\geq 65$  years than in those of other age groups.

Regarding hepatitis C, the total number of treated cases increased during the 2008–2011 period (41,223 in 2008; 48,704 in 2011). The prevalence of hepatitis C also increased (84.22 per 100,000 in 2008; 103.26 per 100,000 in 2011). The hepatitis C mortality rate rose steadily over the same period (0.36 per 100,000 to 0.58 per 100,000; a 61% increase). With respect to sex- and age-related data, the prevalence was higher in both men and women aged  $\geq 65$  years than in those of other age groups. Due to the increased prevalence, the mortality rate was also higher in both of men and women aged  $\geq 65$  years than those in other age groups, with differences of 64% and 65%, respectively (Table 1, Fig. 1 and 2).

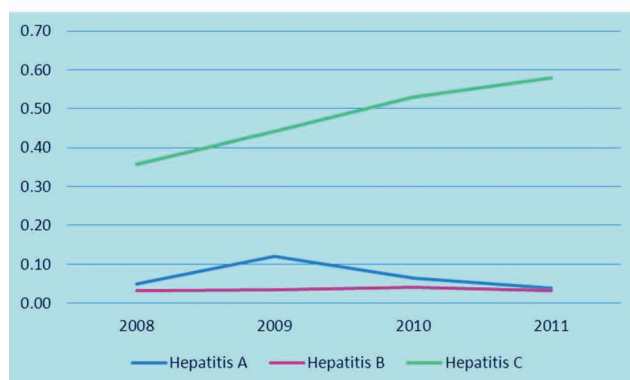
In summary, while the overall prevalence of hepatitis A continuously decreased between 2009 and 2011, those of hepatitis B and C increased during the 2008–2011 period. With regard to the overall trends in mortality rate, that of hepatitis C increased, while those of hepatitis A and B changed little (except for the increase in the mortality of hepatitis A in 2009; Fig. 3.).

The total economic cost of hepatitis A decreased gradually during the 2008–2011 period, with the exception of 2009. The total cost of hepatitis A was US \$62.2 million in 2008, and this more than doubled in 2009; however, it had dropped to US \$45.7 million in 2011 (Table 2, Fig. 4). The total cost of hepatitis A per capita also decreased, from US \$2,540 in 2008 to US \$1,170 in 2011. Direct costs were estimated to be approximately 35% of this total, with indirect costs accounting for the remaining 65% during the observation period (Table 2).

In terms of sex and age group, the economic burden of hepatitis A for men aged 20–64 years (US \$41.8 mil-



A, Prevalence rates



B, Mortality rates

Fig. 3. (Color online) Four-year trends in prevalence and mortality rates of hepatitis A, B, and C (per 100,000 population).

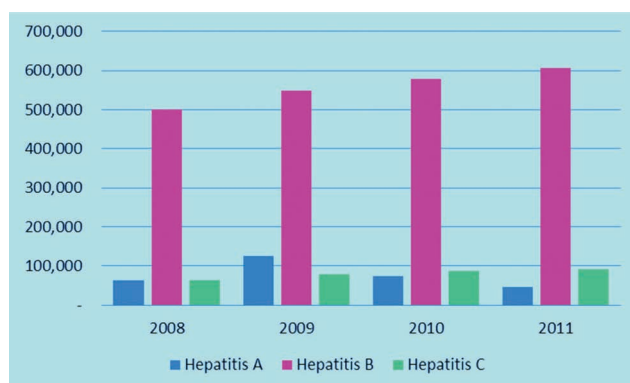


Fig. 4. (Color online) Four-year trends in the economic burdens of hepatitis A, B and C.

lion) was higher than that for women (US \$17.8 million), whereas the costs for women aged  $\geq 65$  (US \$248,000) were approximately 1.7 times the costs for men in the same age group (US \$147,000) in 2008. Overall costs decreased, and similar trends were observed in other years. In 2011, the economic burden of men (US \$32.5 million) aged 20–64 years was higher than that of

Table 2. Four-year trends in the economic burden of hepatitis A, B, and C in Korea: numbers of outpatients, direct/indirect/total costs, and total costs per capita<sup>1)</sup>

Year	Sex	Age group	Hepatitis A						Hepatitis B						Hepatitis C					
			No. <sup>2)</sup>	Days <sup>3)</sup>	Direct costs	Indirect costs	Total costs	Per <sup>4)</sup> capita	No.	Days	Direct costs	Indirect costs	Total costs	Per capita	No.	Days	Direct costs	Indirect costs	Total costs	Per capita
2008	Men	≤ 19	2048	6436	910	368	1278	0.91	22657	4496	3081	4621	7702	0.60	548	199	131	20	151	0.47
		20–64	19884	97300	13549	28238	41788	3.22	627032	86478	133566	237344	370909	1.94	57849	25251	14538	25542	40081	2.44
		≥ 65	216	804	102	45	147	0.99	31783	4456	5012	778	5789	0.49	19872	3180	3215	507	3721	0.75
	Women	≤ 19	1319	5008	695	282	977	0.15	13731	2791	1682	2878	4560	0.11	258	106	67	10	77	0.47
		20–64	13337	59915	8244	9540	17785	5.70	346699	41480	59861	45345	105207	0.97	47688	12882	10718	4559	15277	1.14
		≥ 65	231	1305	176	71	248	1.41	37914	7864	6143	1060	7203	0.49	23772	5474	3877	693	4570	0.76
	Subtotal		37035	170768	23677	38545	62222	2.54	1079816	147565	209345	292026	501371	1.32	149987	47092	32546	31331	63877	1.55
	Men	≤ 19	3905	11259	1563	649	2212	0.80	24541	5035	3445	3305	6750	0.47	555	160	157	18	174	0.51
		20–64	46829	184497	26696	62041	88737	3.01	746411	100261	174748	218007	392755	1.84	69655	31694	20568	24761	45329	2.49
		≥ 65	414	757	121	46	167	0.58	39000	6363	6871	1001	7872	0.58	24241	3499	4195	599	4793	0.86
2009	Women	≤ 19	2599	7876	1115	452	1567	0.11	16085	3140	1938	2105	4043	0.09	284	54	62	8	70	0.38
		20–64	30514	104326	15037	18551	33588	4.61	416811	50675	80091	47819	127909	1.03	57047	17668	15096	7299	22395	1.47
		≥ 65	496	1714	232	97	329	0.98	47126	9099	8524	1282	9806	0.57	29482	7464	5208	894	6102	0.88
	Subtotal		84757	310429	44763	81836	126600	2.31	1289974	174573	275616	273519	549135	1.28	181264	60539	45285	33578	78863	1.70
	Men	≤ 19	3055	6122	938	4499	5437	2.43	22251	4755	3448	6010	9458	0.74	658	145	211	19	230	0.70
		20–64	30246	98178	15224	32333	47557	2.39	739618	96248	182031	234595	416626	2.00	68180	32488	22101	28757	50858	2.89
		≥ 65	375	622	100	39	138	0.52	41083	6495	7860	1044	8903	0.63	23208	4290	4303	622	4925	0.89
	Women	≤ 19	2001	4152	643	249	892	0.09	14123	3143	1835	2977	4812	0.11	333	88	106	10	116	0.70
		20–64	21664	58131	9409	9407	18816	2.89	422513	46793	86229	40726	126955	1.01	58826	15712	17293	6981	24274	1.61
		≥ 65	426	1219	167	70	237	0.69	49538	10224	9743	1382	11125	0.62	30481	6871	5637	880	6517	0.90
	Subtotal		57767	168424	26481	46597	73078	1.87	1289126	167658	291146	286734	577879	1.37	181686	59594	49650	37269	86919	1.89
2011	Men	≤ 19	1813	3870	571	231	802	0.57	20523	4582	2922	7660	10582	0.90	714	104	185	18	202	0.53
		20–64	18913	56982	9355	23172	32527	2.69	776529	75832	202135	231153	433288	1.99	71092	29144	22811	29355	52166	2.85
		≥ 65	174	295	51	18	69	0.50	44318	6044	9127	1076	10203	0.68	24122	3560	4663	600	5263	0.89
	Women	≤ 19	1317	2927	439	174	613	0.10	12814	3414	1566	397	1964	0.05	376	40	81	9	89	0.41
		20–64	12894	33838	5441	6085	11526	3.06	450032	43247	97493	41458	138950	1.04	61942	16210	18719	7266	25985	1.61
		≥ 65	247	597	85	35	120	0.62	53485	10651	11384	1472	12856	0.67	31975	6248	6140	874	7014	0.90
	Subtotal		35358	98509	15942	29715	45658	1.17	1357701	143770	324627	283216	607843	1.39	190221	55306	52598	38121	90720	1.86

<sup>1)</sup>: Units of cost shown are thousands of dollars (US \$1 = 1160.81 South Korean won, average exchange rate between 2008 and 2011). <sup>2)</sup>: Number of outpatient. <sup>3)</sup>: Days of admission.

<sup>4)</sup>: The burden/per capita calculated episode-based.

Table 3. Four-year trends in economic burden associated with drug expenditure for hepatitis A, B, and C in Korea<sup>1)</sup>

Year	Sex	Age group	Hepatitis A		Hepatitis B		Hepatitis C	
			Drug <sup>1)</sup> expenditure	Per capita <sup>2)</sup>	Drug expenditure	Per capita	Drug expenditure	Per capita
2008	Men	≤ 19	18.37	0.01	733.61	0.06	9.35	0.03
		20–64	373.97	0.03	72520.17	0.38	2825.78	0.17
		≥ 65	6.13	0.04	2185.95	0.19	971.04	0.20
	Women	≤ 19	87.82	0.01	87.82	0.00	3.29	0.02
		20–64	202.51	0.06	28536.44	0.26	2174.49	0.16
		≥ 65	4.34	0.02	2642.85	0.18	1234.45	0.21
	Subtotal		693.13	0.03	106706.84	0.28	7218.39	0.18
2009	Men	≤ 19	33.94	0.01	812.06	0.06	9.62	0.03
		20–64	798.76	0.03	95603.23	0.45	3561.35	0.20
		≥ 65	7.93	0.03	3106.63	0.23	1243.76	0.22
	Women	≤ 19	16.14	0.00	328.05	0.01	2.62	0.01
		20–64	388.49	0.05	39252.56	0.32	2636.27	0.17
		≥ 65	9.52	0.03	3920.48	0.23	1639.64	0.24
	Subtotal		1254.78	0.02	143023.00	0.33	9093.26	0.20
2010	Men	≤ 19	19.63	0.01	749.31	0.06	11.13	0.03
		20–64	483.70	0.02	101728.62	0.49	3732.14	0.21
		≥ 65	4.98	0.02	3691.52	0.26	1220.55	0.22
	Women	≤ 19	9.57	0.00	288.99	0.01	7.36	0.04
		20–64	250.59	0.04	43888.70	0.35	2803.20	0.19
		≥ 65	6.04	0.02	4647.41	0.26	1707.86	0.24
	Subtotal		774.51	0.02	154994.56	0.37	9482.25	0.21
2011	Men	≤ 19	12.18	0.01	726.38	0.06	9.63	0.03
		20–64	330.04	0.03	115120.19	0.53	3753.22	0.20
		≥ 65	2.38	0.02	4464.90	0.30	1293.84	0.22
	Women	≤ 19	7.37	0.00	260.50	0.01	3.93	0.02
		20–64	163.25	0.04	50779.88	0.38	2852.38	0.18
		≥ 65	3.82	0.02	5638.88	0.29	1743.55	0.22
	Subtotal		519.05	0.01	176990.72	0.40	9656.55	0.20

<sup>1)</sup>: Units of cost shown are thousands of dollars (US \$1 = 1160.81 South Korean won, average exchange rate between 2008 and 2011).

<sup>2)</sup>: The burden per capita calculated episode-based.

women (US \$11.5 million) in the same age group, whereas the costs associated with women aged ≥ 65 years (US \$120,000) were higher than those for men of the same age (US \$69,000) in 2011 (Table 2).

The total economic cost of hepatitis B increased rapidly during the 2008–2011 period (from US \$501.4 million to US \$607.8 million; Table 2, Fig. 4). The total costs of hepatitis B per capita increased slightly, from US \$1,320 in 2008 to US \$1,390 in 2011. Indirect costs were estimated to be approximately 53.4% of this total, with direct costs accounting for the remaining 46.6% over the same period (Table 2). In terms of sex and age group, the economic burden of hepatitis B for men aged 20–64 years (US \$370.9 million) was much higher than that for women in the same age group (US \$105.2 million), and the costs for men and boys aged ≤ 19 years (US \$7.7 million) were approximately 1.7 times those for women and girls in the same age group (US \$4.6 million) in 2008. Furthermore, in 2011, the burden associated with men aged 20–64 years (US \$433.3 million) was much higher than that associated with women in the

same age group (US \$139.0 million), whereas the costs associated with women aged ≥ 65 years (US \$12.9 million) were higher than those for men in the same age group (US \$10.2 million) (Table 2).

The total economic cost of hepatitis C increased continuously during the 2008–2011 period, from US \$63.9 million to US \$90.7 million (Fig. 4). The total cost of hepatitis C per capita also increased, from US \$1,550 in 2008 to US \$1,860 in 2011. Direct costs were estimated to be approximately 58.0% of this total, with indirect costs accounting for the remaining 42.0% in 2011 (Table 2). In terms of sex and age group, the economic burden of hepatitis C for men aged 20–64 years (US \$40.1 million) was higher than that for women in the same age group (US \$15.3 million), whereas the costs associated with women aged ≥ 65 years (US \$4.6 million) were higher than those associated with men in the same age group (US \$3.7 million) in 2008. The overall cost increased during the observation period, and similar trends were observed in later years. In 2011, the economic burden for men aged 20–64 years (US \$52.2 million) was



higher than that of women in the same age group (US \$26.0 million), whereas costs associated with women aged  $\geq 65$  years (US \$7.0 million) were higher than those associated men in the same age group (US \$5.3 million) in 2011 (Table 2).

## DISCUSSION

This study estimated the individual economic burdens of hepatitis A, B, and C simultaneously using nationally representative data; namely, NHIS claims, Korea Health Panel, and KOSIS data. To analyze the burden of disease, we estimated the prevalences, mortality rates, and economic burdens of hepatitis A, B, and C. Although the prevalence of hepatitis A more than doubled between 2008 and 2009, the overall prevalence of hepatitis A decreased during the 2008–2011 period. In contrast, the prevalences of both hepatitis B and C increased steadily over the same period. Little difference was found in the mortality rate of hepatitis B, whereas that of hepatitis A decreased gradually alongside the decrease in prevalence. In contrast, the mortality rate of hepatitis C increased over the study period.

The total economic burden of hepatitis A decreased gradually, with the exception of the cost in 2009, when it was more than twice that in the previous year. Despite the unusually high total burden of hepatitis A in 2009, its per capita burden steadily decreased during the 2008–2011 period. In contrast to hepatitis A, the total burden of disease per capita showed increasing trends for hepatitis B and C. Additionally, the per capita direct cost of hepatitis A steadily decreased, whereas that of hepatitis B increased consistently over the same period. In 2011, the economic burden of hepatitis B was approximately 13 and 7 times higher than those of hepatitis A and hepatitis C, respectively. In particular, the higher cost burden of hepatitis B could be attributed to higher direct costs due to the use of oral antiviral drugs for chronic hepatitis B, such as entecavir, which has been covered by NHIS since 2007.

The greatest economic burden of disease per capita was that of hepatitis C, followed by B, and finally A. The per capita burden of hepatitis C was 1.6 times higher than that of hepatitis A, and the per capita burden of hepatitis B was 1.2 times higher than that of hepatitis A. The trends in direct costs per capita were similar to those in the total economic burden, with hepatitis C, followed by B, and finally A. In other words, the most costly disease per person was hepatitis C, even though the total burden of disease was much larger for hepatitis B than for hepatitis A and C. One of the reasons is that some medicines such as interferon- $\alpha$ -2a/ribavirin which is widely used for hepatitis C, are relatively expensive when compared to the medicines for hepatitis A and B (20).

Considering sex and age groupings, the prevalences of both hepatitis A and B were higher in men than women, while, the prevalence of hepatitis C was higher for women than in men. The prevalence of hepatitis A was higher for men aged 20–64 years than those in other age groups; hepatitis A in women was most prevalent in those aged  $\leq 19$  years. Regarding hepatitis B, there was higher incidence in both men and women aged 20–64 years than in those of other age groups.

Meanwhile, the mortality rates of hepatitis B and C were higher in both men and women aged  $\geq 65$  years than in those of other age groups. In terms of hepatitis A, the mortality rate in men 20–64 years of age was higher than those in men of the other age groups. Furthermore, although the prevalences and mortality rates of hepatitis B and C were usually higher in women than men, those of hepatitis A were higher in men than in women. The individual burdens of disease for hepatitis A, B, and C were higher for in men aged 20–64 years than in women of the same age group, whereas the disease burden of women aged  $\geq 65$  years were higher than those in men of the same age group for all types of hepatitis infection.

Several previous studies have examined the burden of hepatitis infection in South Korea, mostly focusing on hepatitis B, which is regarded as endemic in the country (21). In 1997, the total economic burden of acute hepatitis B was US \$120.6 million, which was divided into two components, direct and indirect costs. Direct costs (including western-style and traditional medicine, pharmacy, dietary supplements, and nursing care) were US \$68.6 million, and indirect costs (including transportation, time, opportunity costs of inpatient hospital days, job losses, reduced work productivity, and premature death) were US \$49.6 million. Additionally, the direct and indirect costs of chronic hepatitis B were US \$143.0 million and US \$76.4 million, respectively (3). In 2001, the medical cost of chronic hepatitis B was US \$62.7 million. Furthermore, chronic hepatitis B-related diseases have been reported as placing a significant cost burden on the South Korean health system (22). In 2005, the total costs of chronic hepatitis B were US \$456.1 million (23). In this 2005 study, the total cost was divided into direct costs, such as formal and informal medical costs and transportation costs, and indirect costs such as time and productivity loss due to morbidity or premature death; the direct costs were US \$131.9 million and indirect costs were US \$324.2 million.

Few studies have assessed the burdens of hepatitis A and C: this is because the Korean Health Authority has focused on hepatitis B infection and has not recognized the importance of other hepatitis infections. Indeed, the incidence of HAV infection has decreased substantially in developed countries, and outbreaks have been rare in recent decades (24). Nevertheless, the number of cases of hepatitis A progressively increased in South Korea before the early 2000s (25), as improved sanitation and living standards meant that the population had fewer opportunities to develop anti-HAV antibodies through natural infection (26). With regard to hepatitis C, HCV continues to be a major disease burden and is a cause of concern worldwide, especially in developing countries. Although most developed countries have a low prevalence of hepatitis C, the rates still remain high in East Asian countries such as South Korea and Japan (27).

It is useful to compare our results with those of other studies in South Korea that used similar methods, as we will in this way gain an understanding of the relative magnitudes of each disease burden, the economic burden of disease. Hepatitis A, B, and C confer lower economic burdens than major diseases such as cancer, stroke, asthma, epilepsy, and musculoskeletal disease, whose costs are known to range from US \$525.5 million



to US \$6.9 billion (15,17,18,28). However, the total costs of hepatitis A, B, and C (US \$744.1 million) was higher than that of epilepsy (US \$525.5 million, as of 2010) (29) and only slightly lower than that of asthma (US \$786.1 million, as of 2008) (15). However, the economic burdens of colorectal cancer, stroke, and musculoskeletal disease were 4.1, 4.7, and 9.3 times greater than those of hepatitis, respectively (17,28,30). Furthermore, one of the indicators of comparable estimation is the percentage of gross domestic product (GDP). The total economic burden of hepatitis was US \$744.1 million, which represented approximately 0.07% of the Korean GDP (0.004% for hepatitis A, 0.06% for hepatitis B, and 0.01% for hepatitis C).

During the 2008–2011 period, a noteworthy anomaly was noted in 2009, when the total burden of hepatitis A increased to more than double that in 2008. Meanwhile, the total burdens of hepatitis B and C in 2009 both increased by approximately 37% compared with the previous year. The increased burden of hepatitis A was caused by an increase in the number of patients, which was in turn due to an outbreak in South Korea in 2009 (the number of patients who self-reported to the Korea Center for Disease Control and Prevention in 2009 was almost double that in 2008) (31). The increased total burden of hepatitis B and C could be attributed to increased drug expenditure (Table 3) resulting from new NHIS-covered drugs, such as entecavir, which was covered for medical aid patients beginning in early 2007, and for health insurance patients in late 2009 (32).

The estimated burdens of hepatitis A, B, and C may have been much larger if hepatitis-related chronic diseases, such as cirrhosis and HCC had been considered. For example, the population attributable fraction of HCC has been as 68.1% for HBV and 15.2% for HCV in South Korea (33). Additionally, the burden of cirrhosis was estimated as 63% that of HCC (23). As a result, the burden of HCC was approximately US \$534.9 million (US \$289.8 million in direct costs and US \$245.1 million in indirect costs), while that of cirrhosis was US \$337.4 million (US \$188.0 million in direct costs and \$149.4 million in indirect costs). Taken together, total burden of hepatitis-related diseases was in fact to US \$1.62 billion in 2011 (34).

All hepatitis-related diseases could be managed by an effective health policy, similar to the National Cancer Control Program (NCCP) in South Korea. The NCCP was established at the government level in order to manage the burdens associated with all types of cancer. The program comprised the National R&D Program for the Cancer Control, the National Cancer Registration Program, the National Cancer Screening Program, the Cancer Patient Management Program, the Regional Cancer Center Support Program, and the Financial Aid Program (35). One possible approach to disease management is for the government to phase in management programs for selected hepatitis infections, taking the available budget into account. The total burden of disease, which reflects prevalence and mortality rates, would be a reasonable criterion for selecting diseases to receive such consideration. Therefore, it follows that an effective management policy should be planned and implemented in order to prevent and control the economic burden of hepatitis B in South Korea. In practice, this

could be done using an effective vaccine for hepatitis B. indeed, immunization has been a central strategy for most countries to reduce the burden of hepatitis B (36). By the same token, South Korea already has a national immunization program to prevent hepatitis B infection in children. This program has already been rolled out at no cost to the patient through every community health center, is subsidized by the government at 30% in private hospitals (37), and was made available at no cost to the patient in all clinics beginning in January 2014 (38). For this reason, the prevalence of hepatitis B is decreasing in people aged  $\leq 19$  years; however, the total number of patients with hepatitis B continues to increase. As the total hepatitis B burden will increase with the rising prevalence, it is imperative that effective prevention approaches be implemented on a national level, focusing on hepatitis B carriers and patients and aimed at the appropriate target populations.

This study had some limitation. Firstly, the burden of hepatitis infection may have been underestimated, because the main diagnosis code was used to estimate the incidences, prevalences and mortality rates in this study. Second, the study relied on the accuracy of NHIS claims data, in which the burden of hepatitis was limited to cases where it was the primary diagnosis. Therefore, cases were not taken into account that had hepatitis virus infection listed as a secondary diagnosis. Third, health insurance claims data are in general limited by a coding accuracy issue: when physicians diagnose disease using ICD-codes, the data include potential misclassifications. After all, the original purpose of such data is the claim rather than statistics. Finally, the prevalence of hepatitis may not have corresponded to the other statistics as different data sources were used. For example, the prevalence of hepatitis B in those aged  $\leq 19$  years in this study, which used NHIS claims data, was a somewhat higher than that found in other studies used the KNHANES (39).

In summary, we analyzed the economic disease burden to hepatitis infection in South Korea. This study was important in that we simultaneously considered the burdens of hepatitis A, B, and C, and there have been few previous studies addressing hepatitis C infection. We also showed the trends of each disease based on long-term results. The costs associated with hepatitis A are still high, even though the prevalence is decreasing. Among hepatitis infections, hepatitis B accounts for the greatest portion of the total economic disease burden. However, we should continue to focus on hepatitis C, not only because the economic burden has increased steadily but also because HCV is a leading cause of cirrhosis and HCC, as is HBV.

In conclusion, it is necessary to implement effective prevention and management of hepatitis as the economic burdens of hepatitis B and C increase with rising prevalence.

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**Conflict of interest** None to declare.

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