INTRODUCTION

According to the World Health Organization (WHO) Global Hepatitis report in 2017, approximately 257 million people or 3.5% of the global population are living with chronic hepatitis B virus (HBV) infection, whereas 71 million people or 1% of the global population are living with chronic hepatitis C virus (HCV) infection. Apart from that, viral hepatitis accounted for 1.34 million deaths in 2015, among which 887 000 deaths were due to HBV-related liver complications and 399 000 deaths were due to HCV-related liver complications. Left untreated, HBV and HCV infections can lead to liver cirrhosis (LC) (720 000 deaths) and hepatocellular carcinoma (HCC) (470 000 deaths). These long-term complications are life-threatening and accounted for 96% of deaths due to viral hepatitis.
Compared to the WHO Global Hepatitis report on viral hepatitis, the number of deaths due to HCC had been increasing in Japan since 1975. This number of deaths started to increase consistently until it reached its peak of 34,637 per year in 2002, but it decreased gradually until it reached <30,000 per year in 2014. Although mortality has been decreasing annually, HCC still ranks as the fourth common cause of death due to malignancy in men and the sixth common cause of death in women in Japan. By its aetiology, HBV contributes 53% and HCV 25% to liver cancer worldwide. But, this is inverted in Japan, where it is estimated that the contribution of HCV is 66%. These figures indicate the importance of managing infected people to meet the WHO goal of eliminating viral hepatitis by 2030.

Since 2000, the Japanese government has pursued an aetiology-based hepatitis and HCC control health policy and strategy based on large-scale epidemiologic or clinicopathological studies. In accordance with the national health policy, the hepatitis epidemiological research groups of The Ministry of Health, Labor, and Welfare (MHLW) in Japan estimate the number of undiagnosed hepatitis virus carriers and patients with hepatitis virus-related disease with respect to sex-specific and age-specific groups using the data collected by the Japanese Red Cross Blood Center in the same year. MHLW declared that the estimated number of hepatitis virus carriers and patients with hepatitis virus-related disease was about 3.0-3.7 million persons in 2000. Based on this estimation, the countermeasures for viral hepatitis infection control and prevention were started and focused on screening.

As a part of the countermeasure system, it is important to estimate the numbers of hepatitis virus carriers and patients in 2011, using results from large-scale epidemiological studies and national reports to determine the actual trends in the numbers of carriers from 2000 to 2011.

The aim of this study was to determine the trend of total numbers of HBV and HCV carriers over the last 11 years by each liver disease state (AC, CH, LC and HCC) and different states of HBV and HCV carriers linked to the society (undiagnosed carrier, diagnosed carriers who are consulting at the hospital, diagnosed carriers who are not consulting at the hospital, newly infected carrier, cured person and death from 2000 to 2011), and according to this figure we can evaluate the effectiveness of the countermeasure against hepatitis and we can also adopt new strategies based on the outcome of current interventions.

### 2.2 Estimates for the number of undiagnosed carriers

The number of undiagnosed HBV and HCV carriers who were unaware of their infection in 2000 and 2011 was estimated by calculating the sum of products of sex-specific, age-specific and area-specific prevalence among 3,485,648 and 2,720,727 first-time blood donors 1996-2000 and 2007-2011 (Appendix 3, 4) respectively, with total population.

\[
\sum_{i,j,k} r_{ijk} \times p_{ik}^t
\]

where \(i, j, k\) denote the index area (\(i = 1\) for Hokkaido, \(i = 2\) for Tohoku, \(i = 3\) for Kanto, \(i = 4\) for Hokuriku/Tokai, \(i = 5\) for Kinki, \(i = 6\) for Chugoku, \(i = 7\) for Shikoku, and \(i = 8\) for Kyusyu), sex (\(j = 1\) for men and \(j = 2\) for women) and age group (\(k = 1\) for 15-19 years, \(k = 2\) for 20-24 years, \(k = 3\) for 25-29 years, \(k = 4\) for 30-34 years, \(k = 5\) for 35-39 years, \(k = 6\) for 40-44 years, \(k = 7\) for 45-49 years, \(k = 8\) for 50-54 years, \(k = 9\) for 55-59 years, \(k = 10\) for 60-64 years and \(k = 11\) for 65-69 years). Symbols \(r_{ijk}\) and \(p_{ik}^t\) denote the carrier rate and total population among the group of area i, sex j, and age k. We assumed that the carrier rate among people aged 70 and older would be the same as that for those aged 60-69 years. (Figure 1).

We also assumed all people whose hepatitis B surface antigen became positive were HBV carriers. At the same time, 70% of those with anti-HCV positivity were assumed to be HCV carriers. The number of undiagnosed carriers based on a clinical diagnosis (asymptomatic carrier, chronic hepatitis, LC and HCC) was estimated as a proportion with respect to the per cent distribution of each clinical diagnosis.

#### 2.2.1 Distribution pattern of the clinical diagnosis of undiagnosed HCV carriers in 2000

The distribution pattern of clinical diagnosis of 906 HCV carriers among blood donors in Hiroshima11,12 (Appendix 1) was used as a baseline.

#### 2.2.2 Distribution pattern of the clinical diagnosis of undiagnosed HCV carriers in 2011

The distribution pattern of the clinical diagnosis of undiagnosed HCV carriers in 2011 was estimated for 11 years using the Markov
model simulation based on the initial distribution of HCV in 2000 (Appendix 1). The transition probabilities were estimated based on 699 HCV carriers in Hiroshima who were firstly diagnosed at the time of their blood donation.13,14

### 2.2.3 Distribution pattern of the clinical diagnosis of undiagnosed HBV carriers in 2000

The distribution pattern of the clinical diagnosis of undiagnosed HBV carriers in 2000 was estimated for 19, 30 and 45 years using the Markov model simulation, in which the time for initial distribution of HBV in all asymptomatic carriers was assumed (Appendix 1). Additionally, the transition probabilities were determined among 938 HBV carriers who were followed up at Narao Hospital.13

### 2.2.4 Distribution pattern of the clinical diagnosis of undiagnosed HBV carriers in 2011

The distribution pattern of the clinical diagnosis of undiagnosed HBV carriers in 2011 was estimated for 11 years using the Markov model simulation based on the initial distribution of HBV in 2000 (Appendix 1). The transition probabilities were assumed based on 938 HBV carriers who underwent follow-up at Narao Hospital.13

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2.3 Estimates for the number of patients

#### 2.3.1 Patients with HBV- and HCV-related disease in 2000

Patients with hepatitis-related disease in 2000 were included in the patient survey.15 The following International Classification of Diseases (ICD) codes were used to categorize the differential diagnosis of liver disease: C22, malignant neoplasm of the liver and intrahepatic bile ducts (HCC); K73, chronic hepatitis; K74.3-74.6, LC; B16-17.0, B18.0-B18.1, viral hepatitis B, except acute hepatitis B; and B17.1, B18.2, viral hepatitis C, except acute hepatitis C.

Proportions of HBV and HCV carriers among each liver disease were assumed to be 13:65 for LC16 and 17:72 for malignant neoplasm of the liver and intrahepatic bile ducts.17 We assumed a proportion of 13:65 for chronic hepatitis, which was the same as LC. In this study, viral hepatitis B and C were assumed as chronic hepatitis B and C, respectively.
2.3.2 | Patients with HBV- and HCV-related disease aged ≤64 years in 2011

Patients aged <64 years were included in the estimation of the number of hepatitis virus-related diseases using medical receipts for insurance claims as follows.\(^7\) We collected the medical claims related to hepatitis virus-related diseases from a database of 582,922-787,075 employees and their family members and summarized the diagnosis individually. Then, we estimated the sex-specific and age-specific 1-year prevalence of each hepatitis virus-related disease. Finally, we estimated the number of patients by the sum of the products of the sex-specific and age-specific 1-year prevalence and total population in Japan.

2.3.3 | Patients with HBV- and HCV-related disease aged ≥65 years and older in 2011

The number of patients aged ≥65 years was included in the patient survey in 2011.\(^7\) The number of patients aged ≥65 years with a malignant neoplasm of the liver and intrahepatic bile ducts, chronic hepatitis, and LC was calculated based on each age-specific group.

Proportions of HBV and HCV among each liver disease were assumed to be 14.71 for LC and chronic hepatitis\(^9\) and 17.72 for a malignant neoplasm of the liver and intrahepatic bile ducts.\(^10\) We assumed that chronic viral hepatitis B (ICD code: B18.0-18.1) and C (ICD code: B18.2) were chronic hepatitis B and C, respectively. The proportion of patients aged ≥65 years among all patients with viral hepatitis B and C was the same as that for those with chronic hepatitis.

2.4 | Estimates for the number of unconsulted or ceased carriers in 2011

This was estimated by subtracting the numbers of the 4 groups (undiagnosed carriers, patients, cured carriers and deaths) in 2011 from the total number of carriers (undiagnosed carriers and patients) in 2000.

2.5 | Estimates for the number of new infections from 2000 to 2011

These incidences were estimated by summing the product of sex-specific and age-specific incidence rates among 219,292 and 218,797 blood donors during 1994-2004 in Hiroshima with respect to the total population\(^7\):

\[ \sum_{j,k} i_{jk} \times P_{jk} \]

where \(j, k\) denote the index of sex and age groups. Symbols \(i_{jk}\) and \(P_{jk}\) denote the incidence rate and total population among the groups of sex \(j\) and age \(k\), respectively.

2.6 | Estimates for the number cured from 2000 to 2011

We assumed that no one with HBV infection was completely cured. For HCV, this statistical report was used for the number of interferon (IFN) treatments: “Issued record of application for government-subsidized medical expense of hepatitis IFN

**TABLE 1** Estimated number of persons with persistent HCV or HBV infection at 2000

| At 2000 | Total | AC | CH | LC | HCC |
|---------|-------|----|----|----|-----|
| HBV (L-U) | 1 317 752-1 467 752 | 1 120 344-1 259 811 | 139 677-143 676 | 33 387-35 387 | 24 345-28 878 |
| Undiagnosed (L-U) | 1 217 752-1 367 752 | 1 120 344-1 259 811 | 68 677-72 676 | 15 987-17 987 | 12 745-17 278 |
| Under 39 y | 253 551 | 232 691 | 19 594 | 1064 | 203 |
| 40-64 y | 714 201 | 655 209 | 42 417 | 11 590 | 4985 |
| Over 65 y (L-U) | 250 000-400 000 | 232 444-371 911 | 6666-10 665 | 3333-5333 | 7557-12 090 |
| Patients | 100 000 | 0 | 71 000 | 17 400 | 11 600 |
| HCV (L-U) | 1 694 954-2 194 954 | 464 373-672 238 | 1 088 401-1 363 682 | 87 609-98 845 | 54 571-60 189 |
| Undiagnosed (L-U) | 1 184 954-1 684 954 | 464 373-672 238 | 706 401-981 682 | 10 809-22 045 | 3371-8989 |
| Under 39 y | 125 663 | 50 852 | 74 811 | 0 | 0 |
| 40-64 y | 759 291 | 288 802 | 466 422 | 4068 | 0 |
| Over 65 y (L-U) | 300 000-800 000 | 124 719-332 584 | 165 169-440 449 | 6742-17 978 | 3371-8989 |
| Patients | 510 000 | 0 | 382 000 | 76 800 | 51 200 |
| Total(L-U) | 3 012 706-3 662 706 | 1 584 717-1 932 049 | 1 228 079-1 507 358 | 120 097-134 233 | 78 916-89067 |
| Undiagnosed (L-U) | 2 402 706-3 052 706 | 1 584 717-1 932 049 | 775 079-1 054 358 | 26 797-40 033 | 16 116-26 267 |
| Under 39 y | 379 214 | 283 543 | 94 405 | 1064 | 203 |
| 40-64 y | 1 473 492 | 944 011 | 508 839 | 15 658 | 4985 |
| Over 65 y (L-U) | 550 000-1 200 000 | 357 163-704 495 | 171 835-451 114 | 10 075-23 311 | 10 928-21 079 |
| Patients | 610 000 | 0 | 453 000 | 94 200 | 62 800 |

(L-U): Range from lower estimate to upper estimate.
treatment* in 2008-2011.21 (Appendix 2). The complete response (CR) rate was assumed as 60% (distributions of genotypes 1b and 2 were assumed as 70% and 30%, respectively). CR rates for patients with genotype 1b and genotype 2 were 50% and 80%, respectively. The number of cured persons by government-subsidized medical care in 2000-2011 was estimated by the product of the number of IFN treatments in 2008-2011, CR rate and (11/4) which is used to estimate the total number of application forms for medical expenses recorded 4 years to 11 years. Furthermore, the total number of cured persons was estimated to be 1.0-1.5 times the number of cured persons by government-subsidized medical care, with the assumption that the proportion of elderly people in the medical system was 0-33.3%.

2.7 | Estimates for the number of deaths from 2000 to 2011

Numbers of deaths from 2000 to 2011 were estimated using the all-cause mortality and survival rates by the total population and number of deaths available by vital statistics in 2000 and 20052 as follows. Let \( i \) be the index of groups \( (i = 1 \) for carriers younger than 39-year-old in 2000; \( i = 2 \) for 40- to 64-year-old carriers in 2000; \( i = 3 \) for 65 years and older carriers in 2000; \( i = 4 \) for 40-year-old and older patients in 2000), and let \( j \) be the kind of virus \( (j = 1 \) for HBV; \( j = 2 \) for HCV). Let \( m_{i,2000} \) and \( m_{i,2005} \) be mortality in 2000 and 2005. Using the number of \( (i, j) \)-th groups in 2000 \( (p_{i,j,2000}) \), the estimated numbers of deaths until 2011 are calculated by the following formula:

\[
p_{i,j,2000}(1-(1-m_{i,2000}))(1-m_{i,2005})^j.\]

In this estimation, we assumed the following: the age range for all patients is more than 40 years, and the risk ratio of persistent infection of HBV or HCV is 1.

2.8 | Ethical Consideration

No ethical issues occurred in this study, because only census data and published data were used as the data source.

3 | RESULTS

The number of hepatitis virus carriers and patients with hepatitis virus-related disease among the 6 different groups in 2011 was calculated based on an estimate of 3.01-3.66 million carriers in 2000.

The total estimated number of HBV- and HCV-infected persons, including both diagnosed and undiagnosed carriers, in 2000 was 3,012,706-3,662,706 (HBV: 1,317,752-1,467,752; HCV: 1,694,954-2,194,954), but this number decreased to 2,090,128-2,840,128 (HBV: 1,118,627-1,268,627; HCV: 983,879-1,583,879) in 2011. (Tables 1 and 2).

Then, the patients were subdivided into 4 main groups based on age-specific and sex-specific stratification to determine the trend of the natural course of the infection. The numbers of HBV and HCV undiagnosed carriers were estimated to be 2,402,706-3,052,706 (HBV: 1,217,752-1,367,752; HCV: 1,184,954-1,684,954) in 2000 and 811,588 (HBV: 481,470; HCV: 330,118) in 2011. (Figures 2 and 3). However, the numbers of patients were estimated to be 610,000 (HBV: 100,000; HCV: 510,000) in 2000 and 811,588 (HBV: 303,366; HCV: 520,600) in 2011. Furthermore, it is presumed that the number of carriers belonging to the unconsulted or ceased carriers group who did not receive a consultation had increased gradually up to 501,714-1,251,714 (HBV carriers: 145,027-199,125; HCV carriers: 167,923-2,194,954) in 2011. (Tables 1 and 2).

The number of deaths from 2000 to 2011 was estimated to be 375,777-610,200 (HBV carriers: 145,027-199,125; HCV carriers: 750-411,075) (Tables 2). The total number of newly infected persons was 54,645 (HBV infection: 21,184; HCV infection: 33,460) (Tables 2). The total number of newly infected persons after successful anti-HCV therapy was estimated as 2,090,128-2,840,128 (HBV: 1,118,627-1,268,627; HCV: 983,879-1,583,879) in 2011. (Tables 2).

4 | DISCUSSION

In Japan, various national strategies to trace the number of infected person were introduced only after discovery of the specific virus and techniques to detect the virus in humans as early as the 1980s. After 1986, screening for pregnant women was introduced to prevent
mother-to-child transmission of HBV, and then, screening of the HCV virus among blood donors was introduced in 1989. Subsequently, many large-scale epidemiological or clinico-pathological studies have been conducted to clearly understand the relationship between persistent infection of hepatitis virus and HCC, natural course of hepatitis virus infection and actual frequency of newly infected people. The nationwide hepatitis virus screening system was first implemented in 2002 funded by the municipal government, which mainly targeted women aged 40 years and older. Since 2007, regional government has established well-coordinated and collaborated hepatitis treatment systems with regional core centres, specialized institutions for hepatitis treatment and primary care doctors. The alleviation of medical costs, ie the medical expense aid system, was launched in 2008. Moreover, the “Basic Act on Hepatitis Measures” was established to address hepatitis virus infection, and it was adopted by the whole country in 2009. This act is unique and not found in other countries. According to the act, various measures to advance the existing screening system, diagnosis and treatment of liver complication were implemented by various action plans such as hepatitis virus screening for all residents irrespective of age, a medical expense aid system and the establishment of core hospitals for hepatitis treatment in all prefectures.

To get a better control on viral hepatitis, it is important to know the index burden of disease in Japan. Therefore, we have already reported the estimated total number of undiagnosed HBV and HCV carriers in 2000 and 2005; they became the baseline evidences for launching new strategy in Japan. Thereafter, the numbers of carriers and patients in 2011 were determined based on the former estimated value in 2000 and the resultant estimate for 2011 was 2,090,128-2,840,128. Within 11 years, the number of undiagnosed carriers decreased from 2.40-3.05 million in 2000 to 0.777 million in 2011. Compared to 2000, significant decrease in numbers of diagnosed patients and undiagnosed carriers in 2011 indicates that hepatitis virus screening and its surveillance were successfully operating and that the current strategic plans and act were very effective for hepatitis virus prevention and control. But other significant outcomes were found in this study.

Firstly, even the number of undiagnosed carrier was greatly reduced, and the number of patients did not increase obviously and was still lower than expected. The number of unconsulted or ceased carriers in 2011 was estimated to be 0.502-1.252 million. This estimate was unexpectedly high because of many reasons such as unawareness of their positive status due to asymptomatic, forgetfulness of their previous experience with testing or their positive status, a misunderstanding or misbelief about the consequences of the infection or the need for follow-up regardless of treatment, a misunderstanding of the doctor’s advice, default on treatment or death.

Secondly, the number of untreated patients coincidently increased to some extent. It is strongly recommended to improve awareness campaign by using mass media outlets, such as television, websites, pamphlets and radio. In addition, the proper and effective referral
system from the screening centre to the treatment centre (core hospitals) should be upgraded. The follow-up observation of positive carriers throughout their life should be continued by regional health care (a private or primary care doctor). Hence, the operation system of regional core hospital should be upgraded and promoted. Most importantly, the natural disease course should be explained to people, and then, proper counselling and health education should be given to positive carriers after screening. The counselling must encompass how important it is to consult with a hepatologist once and undergo further investigation and a follow-up visit at the designated treatment centre or core hospital. These 2 outcomes are the strong evidence to adopt the new national strategy on viral hepatitis and HCC control in Japan.

In fact, the actual figures of morbidity and mortality of hepatitis virus-related disease can vary by prefecture. In some prefectures (eg the Saga prefecture), the mortality due to HCC is so high that the disease becomes a priority among other public health problems. But

**TABLE 2**

| At 2011 | Total | AC | CH | LC | HCC |
|---------|-------|----|----|----|-----|
| HBV (L-U) | 1 118 627-1 268 627 | 470 156 + α1 | 260 596 + α2 | 21 167 + α3 | 32 916 + α4 |
| Undiagnosed | 481 470 | 444 206 | 23 318 | 6369 | 7576 |
| Under 39 y | 71 774 | 65 869 | 5547 | 301 | 57 |
| 40-64 y | 209 227 | 191 945 | 12 426 | 3395 | 1460 |
| Over 65 y | 200 469 | 186 392 | 5345 | 2673 | 6059 |
| Patients | 303 366 | 25 950 | 237 278 | 14 798 | 25 340 |
| Under 64 y | 257 066 | 25 950 | 203 278 | 9498 | 18 340 |
| Over 65 y | 46 300 | 0 | 34 000 | 5300 | 7000 |
| Unconsulted or ceased(L-U) | 333 791-483 791 | α1 | α2 | α3 | α4 |
| HCV (L-U) | 983 879-1 583 879 | 119 741 + β1 | 600 134 + β2 | 45 521 + β3 | 50 560 + β4 |
| Undiagnosed | 295 356 | 117 637 | 172 696 | 3591 | 1432 |
| Under 39 y | 32 322 | 13 080 | 19 242 | 0 | 0 |
| 40-64 y | 135 544 | 51 555 | 83 263 | 726 | 0 |
| Over 65 y | 127 490 | 53 002 | 70 191 | 2865 | 1432 |
| Patients | 520 600 | 2104 | 427 438 | 41 930 | 49 128 |
| Under 64 y | 319 000 | 2104 | 282 438 | 14 930 | 19 528 |
| Over 65 y | 201 600 | 0 | 145 000 | 27 000 | 29 600 |
| Unconsulted or ceased(L-U) | 167 923-767 923 | β1 | β2 | β3 | β4 |
| Total(L-U) | 2 090 128-2 840 128 | 589 687 + γ1 | 850 554 + γ2 | 65 780 + γ3 | 82 392 + γ4 |
| Undiagnosed | 776 826 | 561 843 | 196 014 | 9960 | 9008 |
| Under 39 y | 104 096 | 78 949 | 24 789 | 301 | 57 |
| 40-64 y | 344 771 | 243 500 | 95 689 | 4121 | 1460 |
| Over 65 y | 327 959 | 239 394 | 75 536 | 5538 | 7491 |
| Patients* | 811 588 | 27 844 | 654 540 | 55 820 | 73 384 |
| Under 64 y | 563 688 | 27 844 | 475 540 | 23 520 | 36 784 |
| Over 65 y | 247 900 | 0 | 179 000 | 32 300 | 36 600 |
| Unconsulted or ceased(L-U) | 501 714-1 251 714 | γ1 | γ2 | γ3 | γ4 |

Since 2000

| | Total | AC | CH | LC | HCC |
|---|---|---|---|---|---|
| Newly infected | 54 645 | 54 645 |
| HBV | 21 184 | 21 184 |
| HCV | 33 460 | 33 460 |
| Cured HCV | 200 000-300 000 |
| Death | 375 777-610 200 |
| HBV | 145 027-199 125 |
| HCV | 230 750-411 075 |

(L-U): Range from lower estimate to upper estimate; patient*: Excepted number of patients with HBV and HCV coinfection.
the mortality rate may be low in other prefectures. This proves the possible use of the countermeasure system in determining the actual figure of infection, and it helps develop more effective strategic plans based on the prefecture's own needs. Although the strategic plan can vary by prefecture, it must strictly follow the "Basic Act on Hepatitis Measures." Yearly review and evaluation of the existing system and strategic plans can be performed based on the significant outcomes reported according to these countermeasures, and then, any action plans of public health promotion can be decided.

Although the overall number of viral hepatitis carriers in Japan has decreased to some extent, the frequency of HCC is still high among all cancer-related deaths. Most patients with HCC in Japan have underlying viral hepatitis, in which HCV accounts for two-thirds of the patients while HBV accounts for about 15%. To reduce the disease-specific mortality rate related to hepatitis virus, it is recommended to upgrade the promotion of nationwide screening system including screening at risk person, screening of blood donors, haemodialytic patients, recipient of repeated blood transfusion due to haemoglobinopathies such as thalassaemia, continuous medical education and using of newly discovered effective drugs with standard regime, promoting the referral system and core hospitals.

In addition, prefecture-specific health strategies should be allocated based on the prefecture's basic needs and own resources. The countermeasures should also be continued as parameters or indicators of the efficacy of the selected treatment regime and to observe the natural disease course. The estimation of the total numbers of diagnosed and undiagnosed carriers, and treated patients and unconsulted or ceased carriers in accordance with disease-specific mortality are crucial countermeasures in the prevention and control of hepatitis virus infection. Furthermore, a health policy for the treatment of HBV-positive or HCV-positive carriers through screening should be strengthened to meet the elimination goal of hepatitis virus by 2030.1

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CONFLICT OF INTEREST

There is no declaration of interest.

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**APPENDIX 1**  Age-specific distribution pattern on clinical diagnosis of HCV patients (Mizui\(^{11,12}\)) and HBV estimated by Markov model (Tanaka\(^{13}\))

| Age   | HCV  |  |  | HCC (%) |
|-------|------|---|---|---------|
| ≤39   | 40.4 | 59.5 | 0.0 | 0.0     |
| 40-59 | 38.0 | 61.4 | 0.5 | 0.0     |
| ≥60   | 41.6 | 55.1 | 2.2 | 1.1     |

| Age   | HBV  |  |  |         |
|-------|------|---|---|---------|
| ≤39   | 87.8 | 7.7 | 0.4 | 0.0     |
| 40-59 | 74.0 | 5.9 | 1.6 | 0.2     |
| ≥60   | 54.2 | 2.7 | 1.3 | 0.5     |

**APPENDIX 2**  Number of supporting application for public medical expenses assistance between 2008 ~ 2011 (MHLW\(^{21}\))

| Year   | Interferon (IFN) | Nucleic acid analogue | Triple combination (IFN + Ribavirin + Terakuleville) | IFNfree |
|--------|------------------|-----------------------|------------------------------------------------------|---------|
| 2008 (H20) | 44 731 | | | |
| 2009 (H21) | 26 594 | | | |
| 2010 (H22) | 28 797 | 38 038 | | |
| 2011 (H23) | 16 171 | New: 11 916 | 1550 | |
| Total (2008-2011) | 116 293 | New: 49 954 | 1550 | |
| Estimate (2000-2011) | 319 806 | | | |
| Estimate for cure | | | | |

**APPENDIX 3**  Age-specific prevalence rate of HBsAg among blood donors from 2007 to 2011 (Tanaka\(^{10}\))

| Age in 2011 | Total | HBsAg-positive | Prevalence, % (95% CI) | Men | HBsAg-positive | Prevalence, % (95% CI) | Women | HBsAg-positive | Prevalence, % (95% CI) |
|-------------|-------|----------------|------------------------|-----|----------------|------------------------|-------|----------------|------------------------|
| 16-19       | 275 907 | 233 | 0.084 (0.074-0.095) | 146 229 | 134 | 0.092 (0.076-0.107) | 129 678 | 99 | 0.076 (0.061-0.091) |
| 20-24       | 870 427 | 625 | 0.072 (0.066-0.077) | 503 773 | 373 | 0.074 (0.067-0.082) | 366 654 | 252 | 0.069 (0.060-0.077) |
| 25-29       | 431 363 | 580 | 0.134 (0.124-0.145) | 275 621 | 406 | 0.147 (0.133-0.162) | 155 742 | 174 | 0.112 (0.095-0.128) |
| 30-34       | 263 469 | 600 | 0.228 (0.210-0.246) | 173 371 | 467 | 0.269 (0.245-0.294) | 90 098 | 133 | 0.148 (0.123-0.173) |
| 35-39       | 249 768 | 705 | 0.282 (0.261-0.303) | 162 477 | 552 | 0.340 (0.311-0.368) | 87 291 | 153 | 0.175 (0.148-0.203) |
| 40-44       | 210 825 | 693 | 0.329 (0.304-0.353) | 131 294 | 520 | 0.396 (0.362-0.430) | 79 531 | 173 | 0.218 (0.185-0.250) |
| 45-49       | 140 337 | 524 | 0.373 (0.341-0.405) | 84 149 | 405 | 0.481 (0.435-0.528) | 56 188 | 119 | 0.212 (0.174-0.250) |
| 50-54       | 109 455 | 510 | 0.466 (0.426-0.506) | 60 432 | 346 | 0.573 (0.512-0.633) | 49 023 | 164 | 0.335 (0.283-0.386) |
| 55-59       | 86 364 | 477 | 0.552 (0.503-0.602) | 44 889 | 284 | 0.633 (0.559-0.706) | 41 475 | 193 | 0.465 (0.400-0.531) |
| 60-64       | 66 692 | 413 | 0.619 (0.560-0.679) | 35 001 | 245 | 0.700 (0.613-0.787) | 31 691 | 168 | 0.530 (0.450-0.610) |
| 65-69       | 16 120 | 109 | 0.676 (0.550-0.803) | 8645 | 60 | 0.694 (0.519-0.869) | 7475 | 49 | 0.656 (0.473-0.838) |
| Total       | 2 720 727 | 5469 | 0.201 (0.196-0.206) | 1 625 881 | 3792 | 0.233 (0.226-0.241) | 1 094 846 | 1677 | 0.153 (0.146-0.160) |
### APPENDIX 4  
Age-specific prevalence rate of anti-HCV among blood donors from 2007 to 2011 (Tanaka10)

| Age in 2011 | Total | Men | Women |
|-------------|-------|-----|-------|
|             | Donors | Anti-HCV-positive | Prevalence, % (95% CI) | Donors | Anti-HCV-positive | Prevalence, % (95% CI) | Donors | Anti-HCV-positive | Prevalence, % (95% CI) |
| 16-19       | 275 907 | 115 | 0.042 (0.034-0.049) | 146 229 | 60 | 0.041 (0.031-0.051) | 129 678 | 55 | 0.042 (0.031-0.054) |
| 20-24       | 870 427 | 415 | 0.048 (0.043-0.052) | 503 773 | 221 | 0.044 (0.038-0.050) | 366 654 | 194 | 0.053 (0.045-0.060) |
| 25-29       | 431 363 | 339 | 0.079 (0.070-0.087) | 275 621 | 229 | 0.083 (0.072-0.094) | 155 742 | 110 | 0.071 (0.057-0.084) |
| 30-34       | 263 469 | 452 | 0.172 (0.156-0.187) | 173 371 | 346 | 0.200 (0.179-0.221) | 90 098 | 106 | 0.118 (0.095-0.140) |
| 35-39       | 249 768 | 509 | 0.204 (0.186-0.221) | 162 477 | 375 | 0.231 (0.207-0.254) | 87 291 | 134 | 0.154 (0.128-0.179) |
| 40-44       | 210 825 | 547 | 0.259 (0.238-0.281) | 131 294 | 414 | 0.315 (0.285-0.346) | 79 531 | 133 | 0.167 (0.139-0.196) |
| 45-49       | 140 337 | 578 | 0.412 (0.378-0.445) | 84 149 | 436 | 0.518 (0.470-0.567) | 56 188 | 142 | 0.253 (0.211-0.294) |
| 50-54       | 109 455 | 542 | 0.495 (0.454-0.537) | 60 432 | 386 | 0.639 (0.575-0.702) | 49 023 | 156 | 0.318 (0.268-0.368) |
| 55-59       | 86 364 | 439 | 0.508 (0.461-0.556) | 44 889 | 279 | 0.622 (0.549-0.694) | 41 475 | 160 | 0.386 (0.326-0.445) |
| 60-64       | 66 692 | 391 | 0.586 (0.528-0.644) | 35 001 | 232 | 0.663 (0.578-0.748) | 31 691 | 159 | 0.502 (0.424-0.580) |
| 65-69       | 16 120 | 113 | 0.701 (0.572-0.830) | 8645 | 67 | 0.775 (0.590-0.960) | 7475 | 46 | 0.615 (0.438-0.793) |
| Total       | 2 720 727 | 4440 | 0.163 (0.158-0.168) | 1 625 881 | 3045 | 0.187 (0.181-0.194) | 1 094 846 | 1395 | 0.127 (0.121-0.134) |