Results of a questionnaire survey in patients with hemophilia

Hemophilia patient treatment status and awareness of coagulation factor products

Blood Product Subcommittee
Biologics Committee, EFPIA Japan

●European Federation of Pharmaceutical Industries and Associations, Japan (EFPIA Japan)

EFPIA Japan was established in 2002, and represents 24 R&D-based European pharmaceutical companies operating in the Japanese market. We are the voice of the European innovative pharmaceutical industry in Japan. Our mission is to contribute to the welfare of the Japanese population through the provision of innovative pharmaceuticals and vaccines without delay.

EFPIA Japan has played active roles in reviewing, proposing and raising awareness to address various issues related to the pharmaceutical industry. (Homepage: http://efpia.jp/)

●Blood Product Subcommittee (BPSC)

The Blood Product Subcommittee (BPSC) is part of the Biologics Committee along with the Vaccine Subcommittee and the Biological Products Subcommittee. BPSC aims to establish a stable supply process for "Plasma Derived Products" manufactured from human blood and for essential products in medical care, and for any plasma related recombinant products that are manufactured with the world's m~ost advanced technology.

Objective and methods of the survey

In recent years, the safety against infectious diseases has been increasing with coagulation factor preparation used for the treatment of hemophilia, and recombinant products together with plasma-derived preparations have been widely used. Routine prophylaxis with blood coagulation factor products, in addition to on-demand treatment for bleeding episodes, has been widely used and increased the quality of life (QoL) of patients.

As hemophilia treatment environment evolves, BPSC considered it worthwhile to investigate hemophilia patient treatment status and awareness of coagulation factor products and the data for future activities. As part of this effort, BPSC conducted this questionnaire survey in hemophilia patients.

The results of the questionnaire survey enable you to compare hemophilia treatment information and awareness that patients have among the patients participated in the survey. The results may provide interesting information also to patients who did not participate in the survey. BPSC hopes that the survey would serve as one of the useful sources for patient exchanges and meetings.

The questionnaire survey was conducted in the period between 1 August 2014 and 31 March 2015. At the beginning, the survey was conducted online with the cooperation of the National Hemophilia Network of Japan. In order to obtain more responses, a paper-based survey was added in January 2015.

A request to participate in the survey both for the online survey and for the paper-based survey, was distributed to patients via healthcare professionals by three pharmaceutical companies participated in BPSC. Paper-based responses were sent directly to the EFPIA Japan Office by the patient or their family members. The survey was conducted anonymously and no personal identifiers were collected.

1) Responses were collected from 112 participants (82% with Hemophilia A and 17% with Hemophilia B).
2) 89% of the participants received home infusion therapy. The percentage of those who did not receive home infusion was low in the Kyushu region (many were pediatric patients), and in the Tohoku region (many were adult patients).
3) In the case of bleeding, 75% responded that they took injection as early as possible. On the other hand, 60% of the respondents did not necessarily observe instructions given by their doctors, and 20% tended to save the drug consumption.
4) In general, appropriate dose was administered in the case of bleeding in joints.
5) While 87% received routine prophylaxis therapy, the dose and frequency fell below the levels recommended by the guidelines in some respondents.
6) Both for genetically recombinant products and for plasma-derived products, the respondents were highly interested in safety and stable supply.
7) The respondents were more concerned about copayment in the future and increased medical expenses, than about the prices of coagulation factor products.

〈Details of the survey results〉

1. Attributes of the hemophiliac patients surveyed

A total of 112 respondents participated in the survey. Of these respondents, 66% were patients and 34% were parents of patients.

82% of the 112 respondents were hemophilia A patients or parents, and 17% hemophilia B. One did not know the type of his hemophilia (was not informed of the type by his doctor or did not remember). All the 112 participants were male.

As shown in Figure 1-1, responses were collected from patients from a wide range of age groups from small children to aged adults (aged 0 to 69 years). Adults (aged 23 to 50 years), excluding students, accounted for 36%, the largest among all the age groups, followed by patients aged 51 years and above (24%).

Locations of residence of the patients were shown in Figure 1-2. While responses were collected from patients and parents across the country, many responses were collected from the Kanto (37.5%) and Kinki (24.1%) regions, which accounted for a majority (62%).
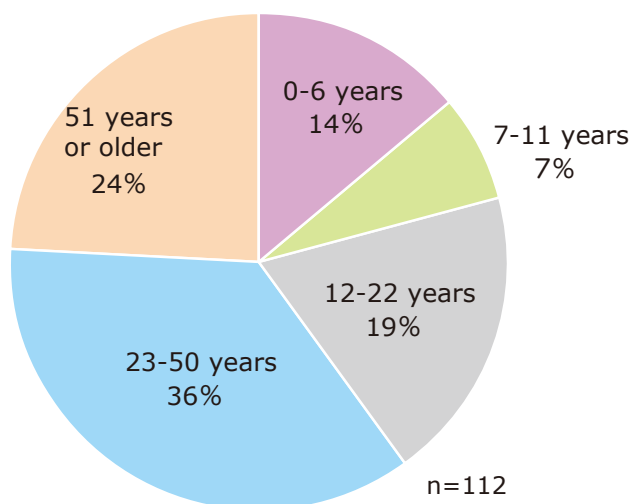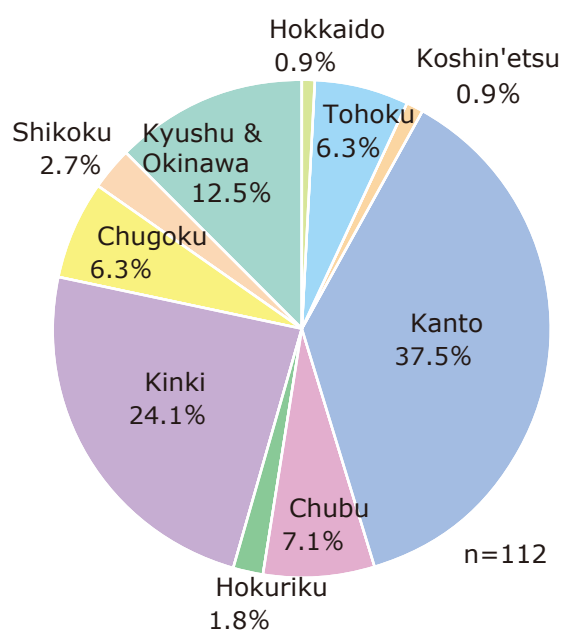

Fig 1-1 Patient age distribution

Fig 1-2 Locations of residence of patients

1) Implementation of home infusion therapy

The status of home infusion therapy is presented by age groups of the patients (Figure 2-1). The implementation rate of home infusion therapy was 89%, and almost all the patients received home infusion therapy at the age of seven and above. Seven out of 16 patients aged six years or younger did not receive home infusion therapy, while all of the seven patents were aged three years or younger and had receiving injections at home.
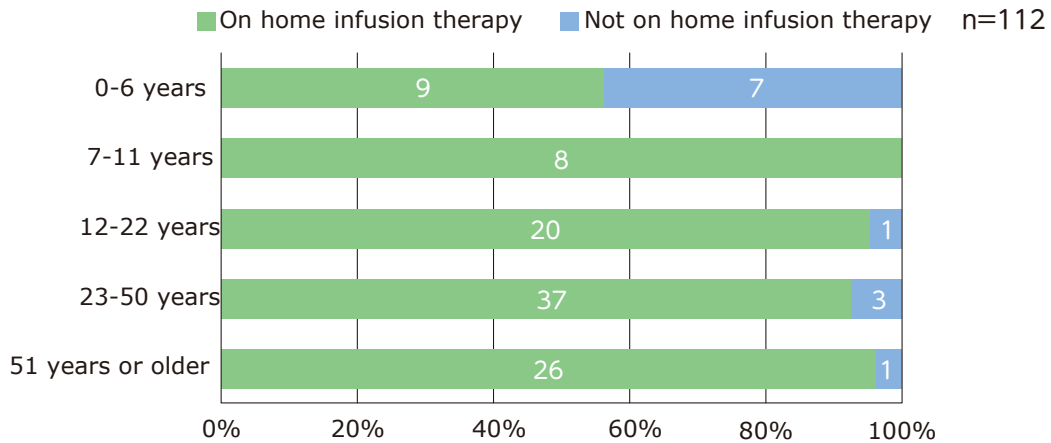
Fig 2-1 Implementation of home infusion therapy by age group

The status of home infusion therapy varied by the location of residence of patients (Fig 2-2). The implementation rate of home infusion therapy was high in most of the regions, but four out of seven in the Tohoku region and four out of 14 in the Kyushu including Okinawa did not receive home infusion therapy. For the four patients in the Kyushu region, it was assumed that the age was the reason for not receiving injections at home where they were younger than three years old. On the contrary, all of the 4 patients who did not receive home infusion therapy in the Tohoku region were adults aged between 17 and 59 years. There may be some reasons, for example, long distance to medical institutions with haemophilia experts, or there may be some problems in access to such medical institutions.
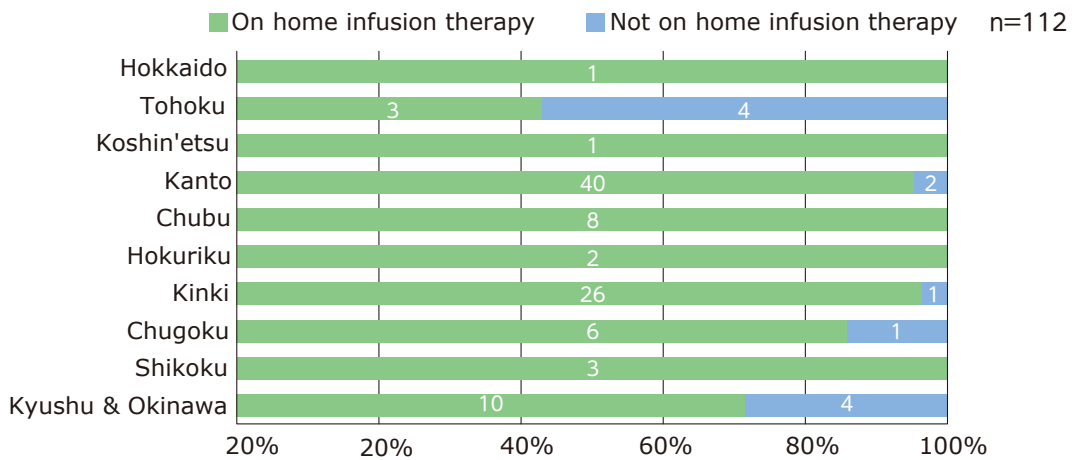
Fig 2-2 Implementation of home infusion therapy by location of residence

The respondents selected precautions they took upon home infusion from multiple options (multiple-choice question). As a result, 75% of the patients with hemophilia A and 75% of those with hemophilia B selected "Take injection as early as possible when bleeding occurs", suggesting that patients and their family members were well informed by healthcare professionals about the importance of early treatment after bleeding. On the other hand, the percentage of the respondents who selected "Adhere to the dose (units) and frequency of injections as instructed by the doctor" fell below 40% both in hemophilia A and hemophilia B patients, which revealed that unexpectedly fewer patients followed doctor's instructions about infusion. Approximately 20% of the respondents answered "Try to minimize the number of injections for hemostasis" or "Try to minimize the dose (units) of injections for hemostasis", showing that the patients tended to reduce the drug consumption (frequency of injections or units) from that instructed by the doctors (Fig 2-3).
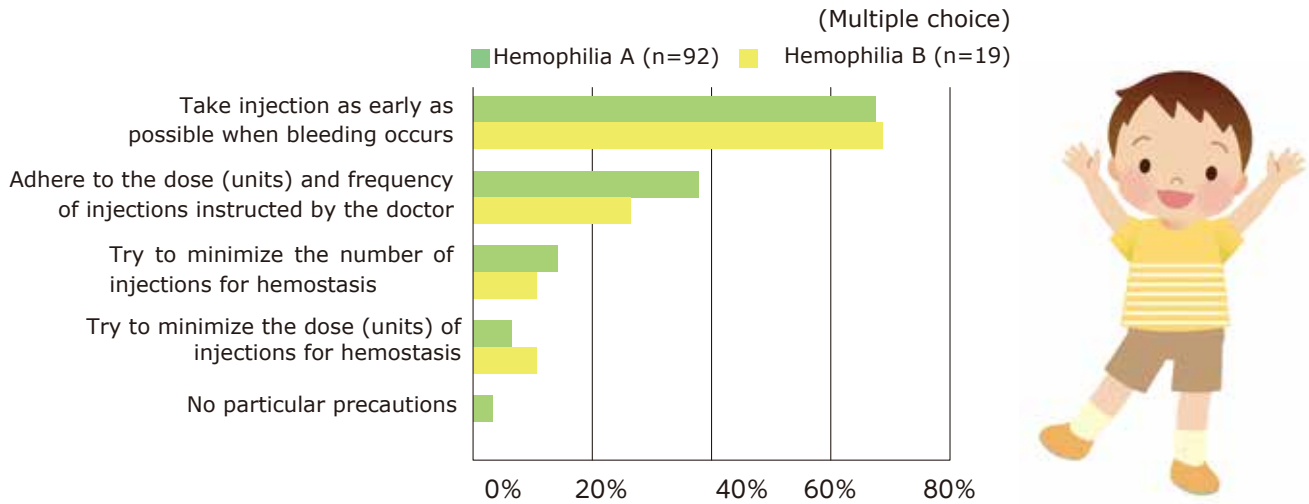

Fig 2-3 Precautions taken in home infusion

2）Doses in case of joint bleeds

The initial dose (units/kg) upon joint bleeds ranged from 10-20 IU/kg, 20-30 IU/kg, to 30-40 IU/kg in the majority of the respondents with hemophilia A. The guidelines by Japan Society of Thrombosis and Hemostasis (JSTH) recommends 10-20 IU/kg for mild joint bleeds and 20-40 IU/kg for severe joint bleeds in hemophilia A. The survey proved that the majority of the participants with hemophilia A received the appropriate dose in accordance with the guidelines. Many respondents with hemophilia B also received the appropriate dose in accordance with the guidelines (20-40 IU/kg for mild joint bleeds and 40-80 IU/kg for severe joint bleeds) (Fig 2-4).
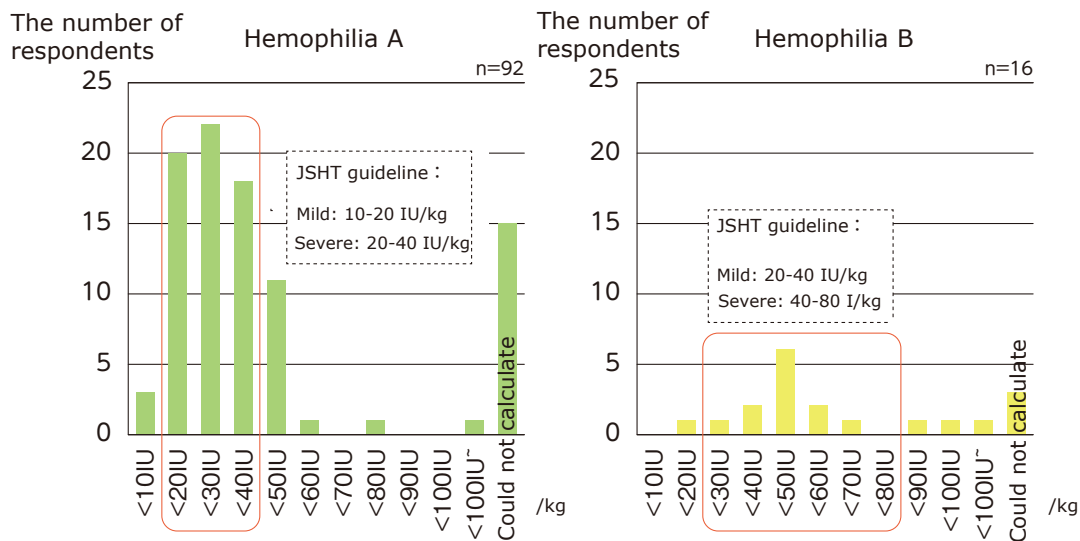

Fig 2-4 The initial dose upon joint bleeds (per kg of body weight)

3. Routine prophylaxis therapy

While the report of the national survey on blood coagulation disorders conducted by the Ministry of Health, Labor and Welfare in 2013 indicated that approximately 50% of hemophilic patients received routine prophylaxis therapy, in this survey, the percentage of the patients who received routine prophylaxis therapy exceeded 85% in all the age groups (Fig 3-1).
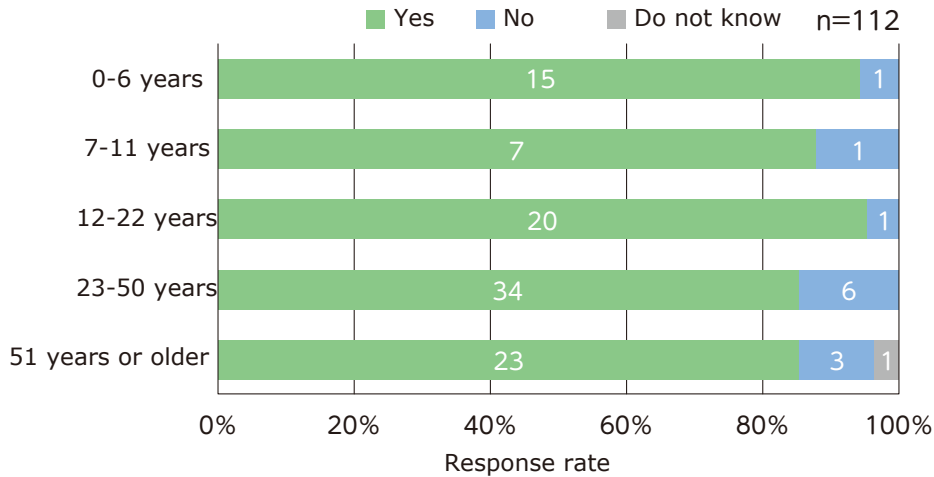

Fig 3-1 Routine prophylaxis by age group

Reasons for not receiving routine prophylaxis were asked in 13 respondents (seven with hemophilia A, four with hemophilia B, and one with unknown type of hemophilia) who did not receive routine prophylaxis therapy (Fig 3-2). Four patients with hemophilia A and three with hemophilia B answered "Because of infrequent bleeds". Three (Two hemophilia A and one unknown) answered "Troublesome to receive routine prophylaxis", which is based on the patient's own judgement. On another front, the survey revealed that two respondents answered "My doctor did not recommend or explain about routine prophylaxis". While this is due to the doctor's discretion, not the patient's, there should be some room for improvements in providing information to patients in more easily understandable ways.
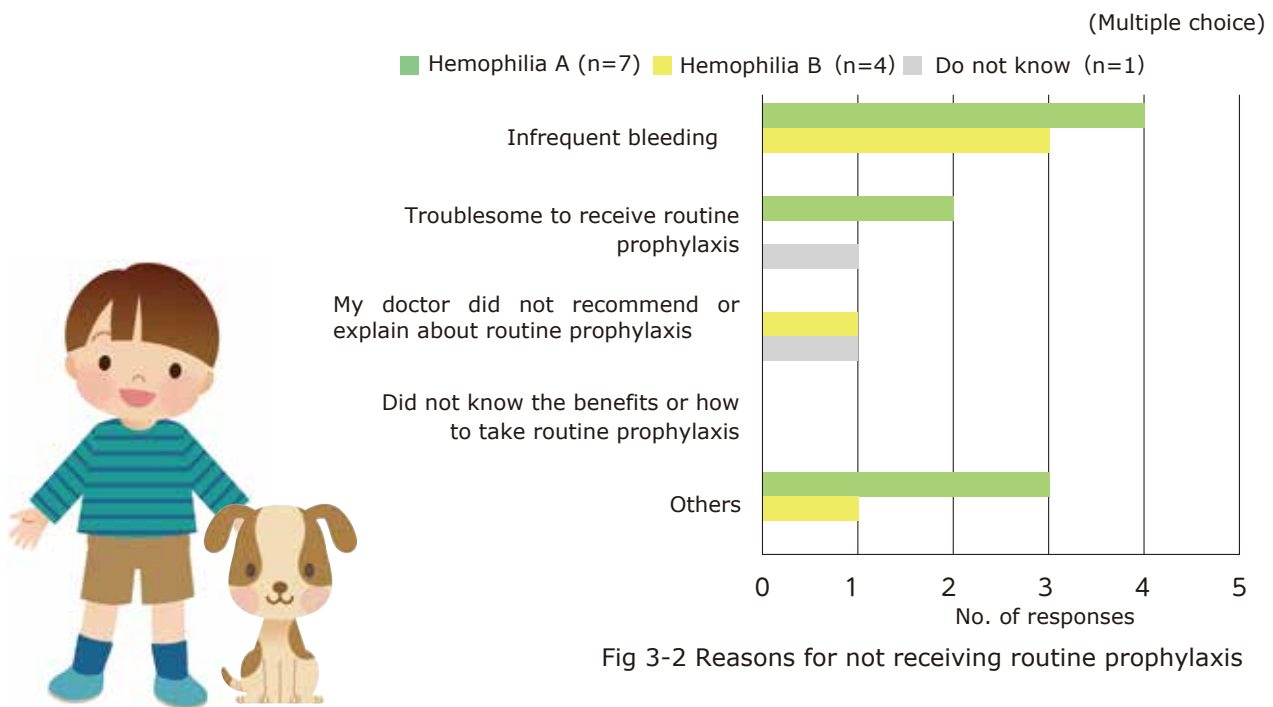
(Multiple choice)

Fig 3-2 Reasons for not receiving routine prophylaxis

The survey showed that many patients believed that "routine prophylaxis should be widely used to maintain joint health". Also, a considerable number of the patients answered that "injections before physical activities (e.g., sport events, school excursions) should be more actively recommended", or "routine prophylaxis should be proactively promoted to small children". No one answered that "routine prophylaxis is not desirable due to increased consumption of drug products."

On another front, some respondents answered that "routine prophylaxis should be limited to patients with frequent bleeds", which emphasized the need to look at communications between health care professionals and patients (Fig 3-3).
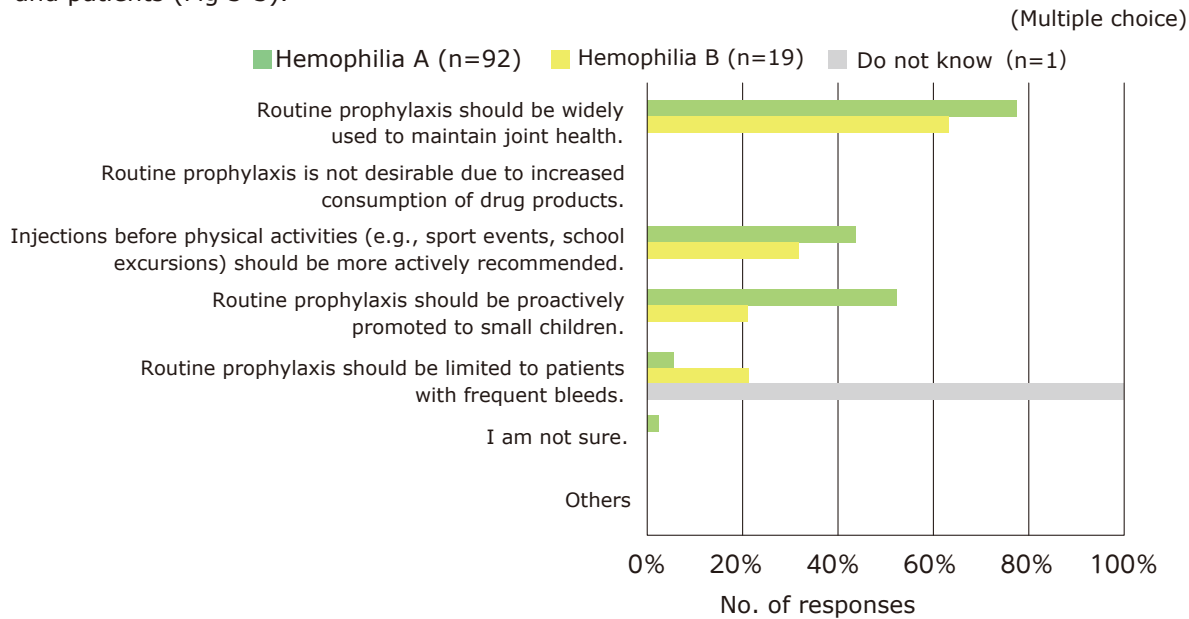

Fig 3-3 Desirable status of routine prophylaxis

Dose in routine prophylaxis

The guidelines recommend 20-50 IU/kg for routine prophylaxis in hemophilia A and 40-80 IU/kg (of recombinant products) in hemophilia B. In this survey, many patients with hemophilia A received routine prophylaxis within the dose range recommended by the guidelines. However, 22 (26%) patients received lower doses than the lowest recommended dose. Among patients with hemophilia B in this survey, only two patients received lower doses than the lowest dose recommended by the guidelines (Fig 3-4). The survey showed that the initial dose for joint bleeds was in accordance with the guideline, but suggested that many patients received lower doses than the recommended doses for routine prophylaxis. Further investigation should be made to understand whether it comes from patients' intention to save the drug consumption or from instruction by doctors.
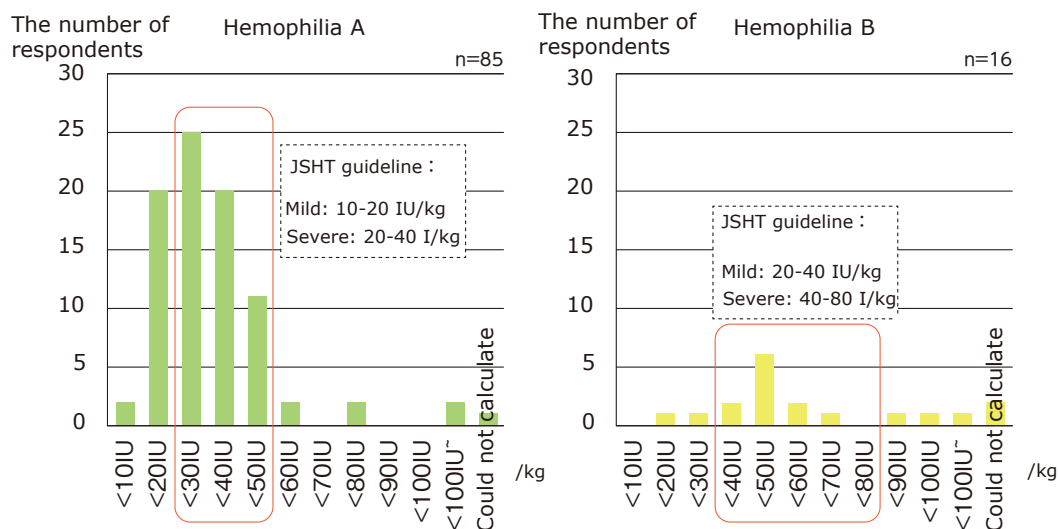

Fig 3-4 Dose in routine prophylaxis (per kg of body weight)

It was observed that injections for routine prophylaxis were given less frequently than recommended by the guidelines (three times a week, or every other day for hemophilia A, and twice weekly or every third day for hemophilia B). The frequency of injection for routine prophylaxis was lower than twice weekly in 32 patients (35%) with hemophilia A and lower than once weekly in five (28%) with hemophilia B (Fig 3-5).
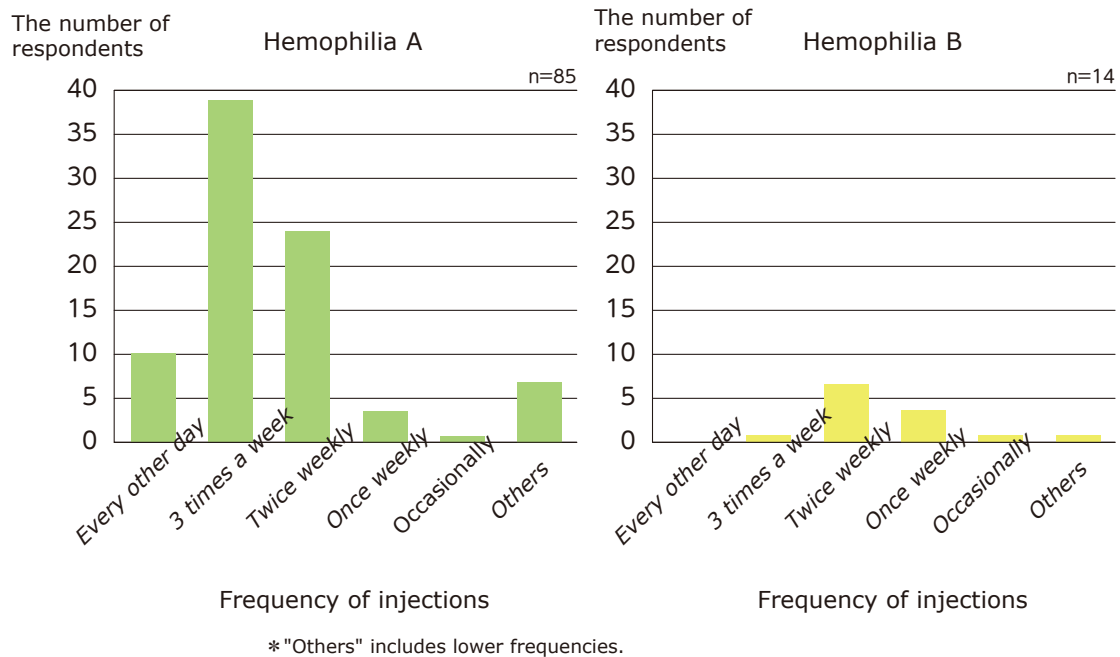
Hemophilia A — The number of respondents — n=85

Hemophilia B — The number of respondents — n=14

Frequency of injections

Frequency of injections

＊"Others" includes lower frequencies.

Fig 3-5 Frequency of injections in routine prophylaxis

4. Products used by the patients

Approximately 78% of the patients in this survey used recombinant products. Recombinant products were used in the majority of the patients both with hemophilia A and hemophilia B, but plasma derived products were often used in the older age group. Eleven respondents (12%) did not know if the product they used was recombinant or plasma derived. More attention should be paid to the way of information sharing - if patients were not interested in the products they used or they were not informed by their doctors (Fig 4-1).

Hemophilia A — n=92

- Plasma derived products only
- Recombinant products only
- Both types
- Unknown

Age	Plasma	Recombinant	Both	Unknown
0-6 years		10	1	4
7-11 years		7		1
12-22 years	2	11	1	2
23-50 years	4	26		4
51 years or older	3	15	1	

Response rate

Hemophilia B — n=19

- Plasma derived products only
- Recombinant products only
- Both types

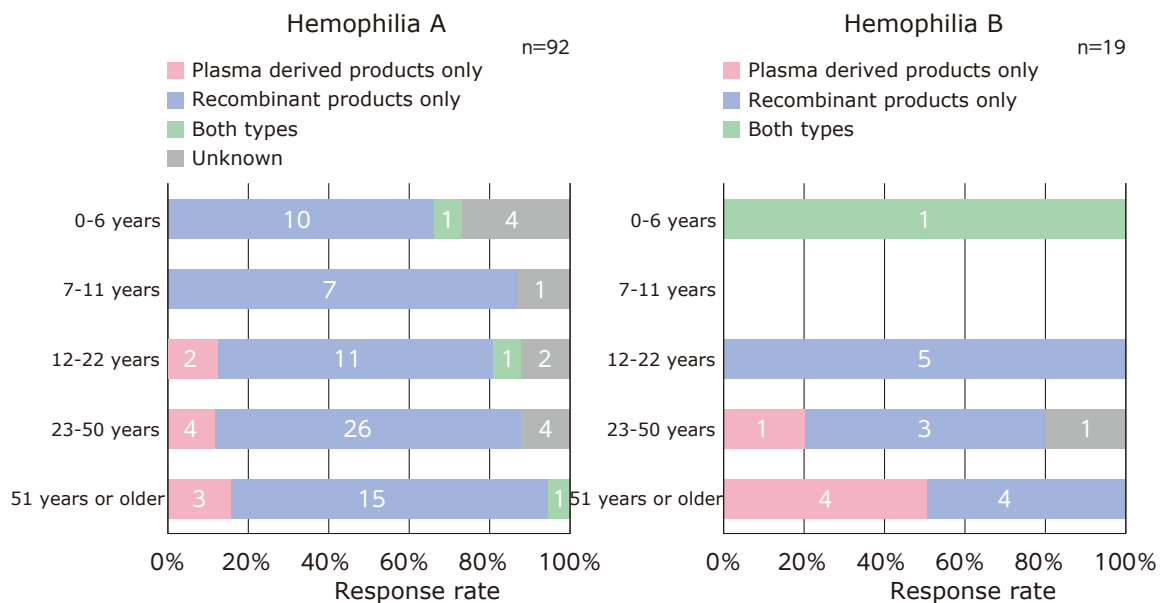| Age	Plasma	Recombinant	Both	Unknown
0-6 years			1	
7-11 years				
12-22 years		5		
23-50 years	1	3		1
51 years or older	4	4		

Response rate

Fig 4-1 Drug products used by patients

To the question asking respondents' view to the products they used, many patients both with hemophilia A and hemophilia B chose the answers "Development of Japanese-made recombinant products is desirable" and "Recombinant products should be used more commonly" (multiple-choice question), which presented favorable opinions to recombinant products. Many also chose the answer "Multiple products should be available in the both categories", reflecting their demand for stable supply of coagulation factors and multiple treatment options (Fig 4-2).
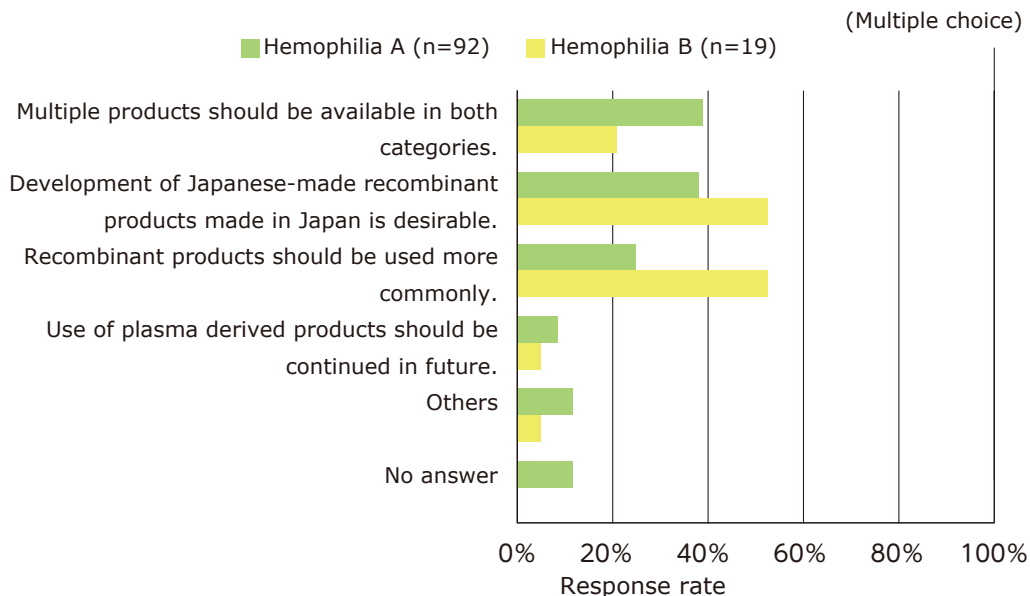
Fig 4-2 View to plasma derived and recombinant products

Many of 19 respondents (12 with hemophilia A and 7 with hemophilia B) who used plasma derived products answered the reason for the product choice as "Using plasma derived products for many years without problems" and "Plasma derived products are derived from blood donation collected in Japan" (multiple-choice question), and five answered it was because "Recommended by my doctor." (Fig 4-3).

Fig 4-3 Reasons for using plasma derived products

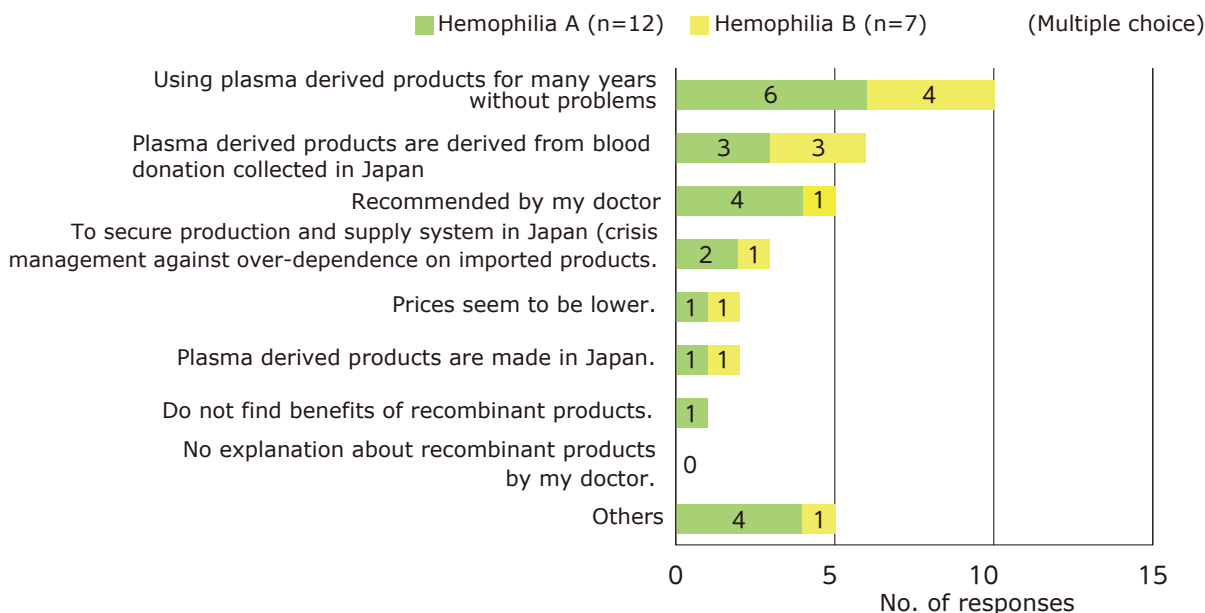On another front, many respondents who used recombinant products stated the reasons for the product choice as "Recommended by my doctor" (60%) and "Recombinant products seem to be safer than plasma derived products" (53%) (Fig 4-4).
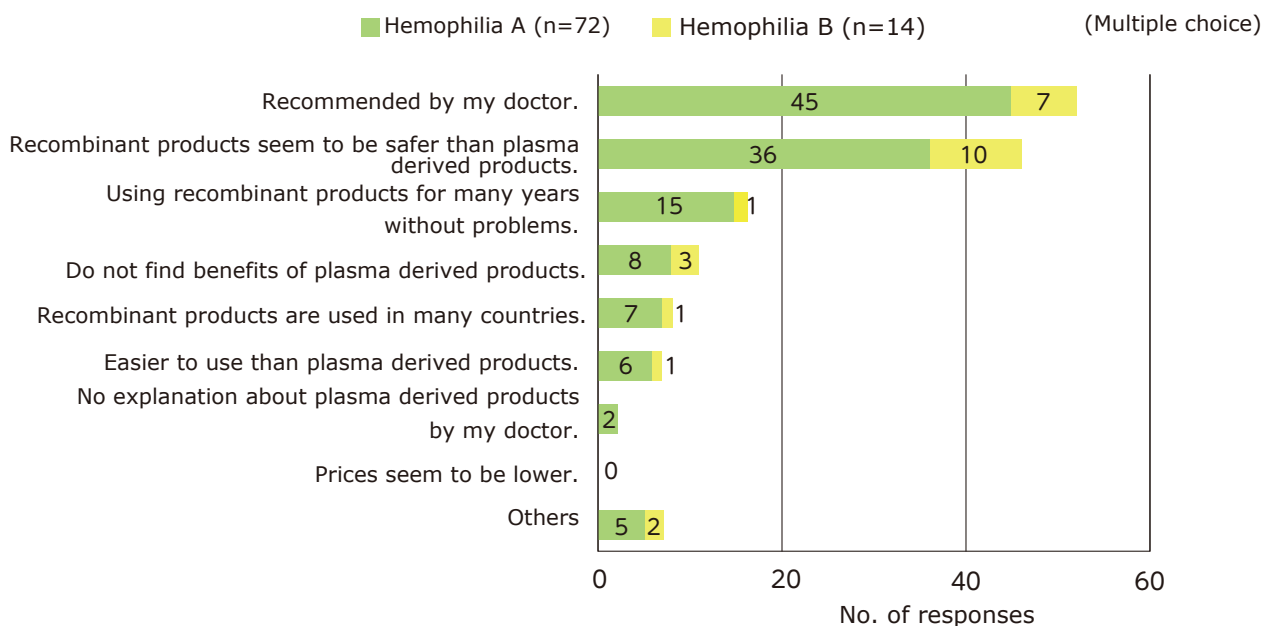
Fig 4-4 Reasons for using recombinant products

The responders were asked to prioritize their expectations for recombinant products and plasma derived products, respectively. Safety ("further enhancement of safety against infections" and "decrease in inhibitor formation") and stable supply were highly prioritized over convenience ("development of more easily reconstitutable products" and "extension of storage period at room temperature") and lower prices (Fig 4-5).

Fig 4-5 Priorities of expectations for recombinant and plasma derived products

5. Recognition about prices

As Fig 4-5 suggested that prices of products were prioritized relatively low by the respondents, and the same tendency was observed with the price related question. Being asked about a difference in prices between recombinant products and plasma derived products, the majority (62%) of the respo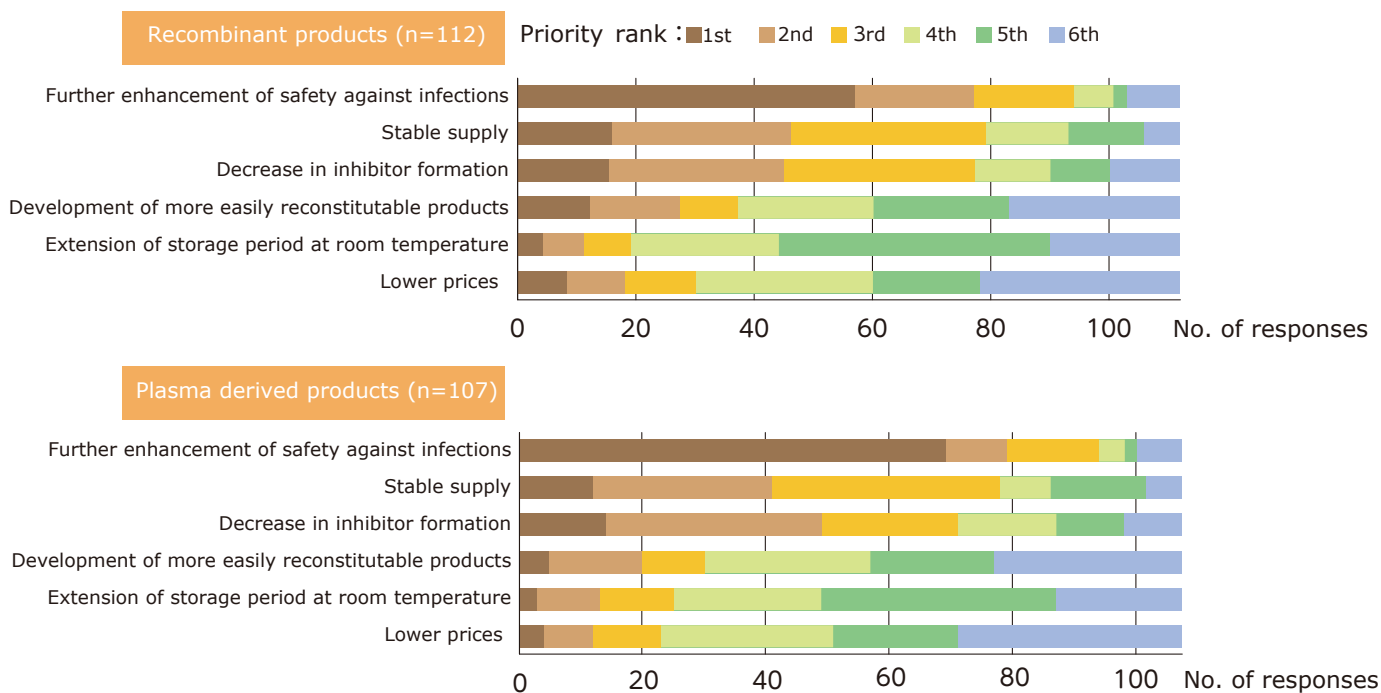ndents answered that they "do not know the price difference between the two categories (multiple-choice question) (Fig 5-1).

■ Hemophilia A (n=92)　■ Hemophilia B (n=19)　(Multiple choice)

	Hemophilia A	Hemophilia B
Do not know the price difference between the two categories.	62	7
Prices should be lowered for both categories.	29	6
High prices are acceptable for products with higher level of efficacy, safety and convenience.	20	7
Prices of recombinant products seem to be higher than those of plasma derived products.	12	7
Recombinant products should be priced lower than plasma derived products.	7	4
Prices seem to be the same level for both categories.	6	1
Prices of plasma derived products seem to be higher than recombinant products.	4	2
Prices should be set the same for both categories.	2	2
Plasma derived products should be priced lower than recombinant products.	1	1
Others	5	

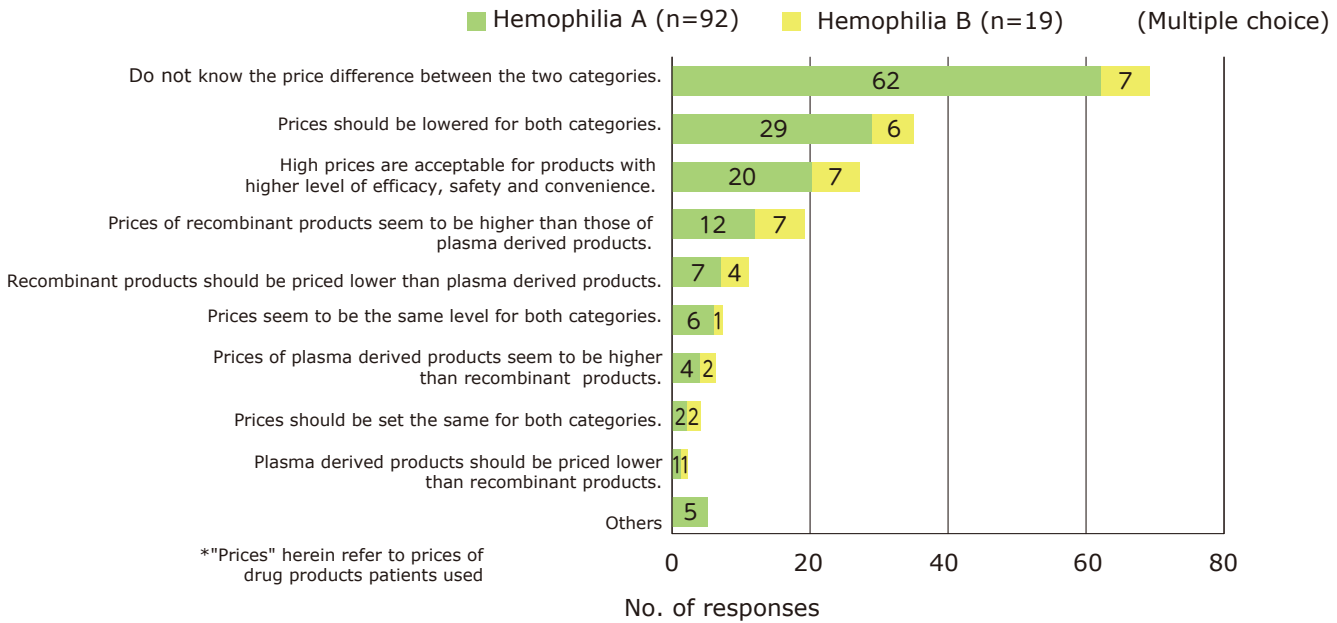*"Prices" herein refer to prices of drug products patients used

No. of responses

Fig 5-1 Recognition about price differences between recombinant and plasma derived products

In addition, to the question about a view to prices, many chose the two answers "Worried that copayment may be increased in the future" (77%) and "Concerned that high prices may lead to increase of medical expenses in Japan" (59%) (multiple-choice question), suggesting that they were more concerned about copayment in the future and increase in medical expenses, than prices of products (Fig 5-2).

■ Hemophilia A (n=92)　■ Hemophilia B (n=19)　(Multiple choice)

	Hemophilia A	Hemophilia B
Worried about copayment may be increased in future.	72	14
Concerned that high prices may lead to increase of medical expenses in Japan.	55	10
High prices may result in saving the drug consumption.	17	
Not interested in prices as I have no copayment.	12	3
Others	8	2

*"Prices" herein refer to prices of drug products patients used
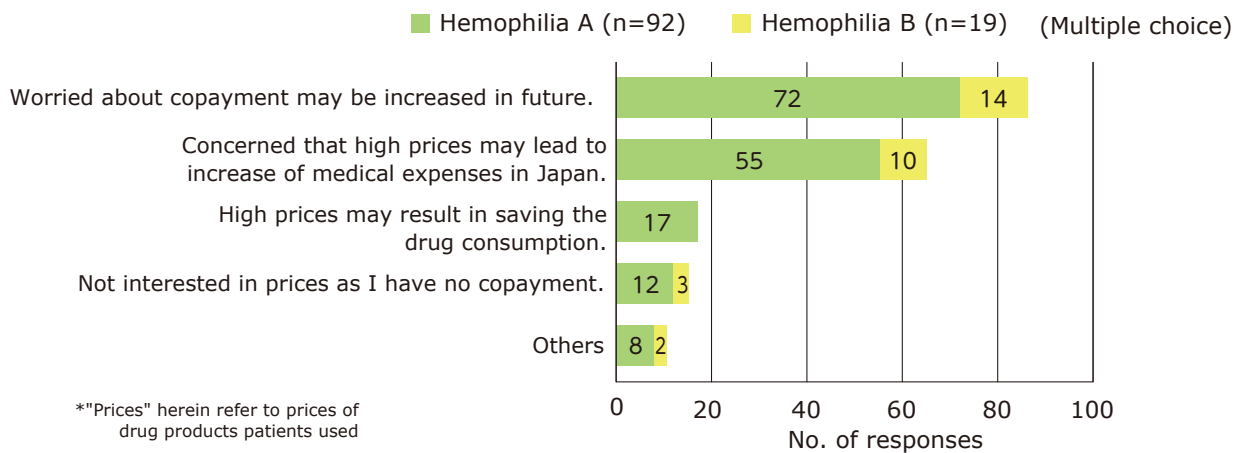
No. of responses

Fig 5-2 View to prices

Blood Product Subcommittee in Biologics Committee of EFPIA Japan extends deep gratitude to the patients and their family members for their participation in this survey.

BPSC will continue to make an effort to understand hemophilia patients and treatment through surveys and awareness activities in collaboration with patient groups including National Hemophilia Network of Japan, and hemophilia care professionals, ultimately to contribute to the improvement in the treatment and QOL of hemophilia patients.

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