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Health status and health-related quality of life of children with haemophilia from six West European countries

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Summary. A multicentre, international, cross-sectional study was carried out in the frame of field testing of the first haemophilia-specific quality-of-life (QoL) questionnaire (Haemo-QoL). The aim of this paper is to describe health status and health care and their impact on QoL in haemophilic children in Western Europe. Children aged 4–16 years with severe haemophilia without inhibitors were enrolled by 20 centres in France, Germany, Italy, the Netherlands, Spain and the United Kingdom. Clinical information was collected by the physicians with a medical documentation form. Health-related QoL (HRQoL) of children was assessed with Haemo-QoL, available for three age groups. Clinical data were available in 318 patients, 85.5% with haemophilia A. The mean age at first bleeding was 11 months, at first joint bleed 25 months. Functional joint impairments were found in 11.3%. Prophylaxis treatment was given to 66.7% of children in whom breakthrough bleeds occurred 0.4 times a month compared to 1.1 bleeds in children receiving on-demand treatment. A significantly higher factor consumption was found only in the two younger age groups of prophylaxis patients compared to on-demand patients. HRQoL was satisfactory in this cohort: young children were impaired mainly in the dimension 'family' and 'treatment', whereas older children had higher impairments in the so-called 'social' dimensions, such as 'perceived support' and 'friends'. Health care of children in Western Europe is progressively improving with a large diffusion of home treatment and prophylaxis. This provides a high level of health status and HRQoL, being better in haemophilic adolescents on prophylaxis.

Keywords: haemophilia, quality of life, health status, prophylaxis, European

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Introduction

Haemophilia is characterized by spontaneous and post-traumatic bleeding; its complications in joints and muscles leads almost inevitably to pain, severe joint damage, disability and a dramatic impairment of health-related quality of life [1]. More than 30 years have been spent from the introduction of modern management of haemophilia: bleeding episodes are now rapidly controlled by plasma-derived and recombinant clotting factor concentrates; haemophilic arthropathy is fought either by preventing it with prophylactic treatment or by repairing the damage with joint replacement surgery [2]. In particular, the availability of safer products and early prophylaxis have greatly improved the management of haemophilic children with a consequent dramatic impact not only on symptoms and survival of these patients but also on their health-related quality of life [3]. However, the healthcare of these patients absorbs a huge amount of economic and human resources [4–6], so that it is essential to frame them in the context of the level of quality of life provided.

Health-related quality of life (HRQoL) is increasingly considered one of the most relevant health outcome measures in medicine [7]. In order to measure HRQoL, generic and disease-specific questionnaires have been developed. While generic instruments measure QoL across health conditions, disease-specific instruments measure quality of life related to a specific disease, being more sensitive to specific treatment and clinical outcomes.

Available data on quality of life in haemophilia evaluated the effectiveness of prophylaxis and home treatment [8–11]. Prophylactic treatment is associated with higher direct treatment costs, but is expected to lower costs in the course of lifetime of a person with haemophilia by reducing its complications such as pain and impairment, and therefore disability and handicap. Studies have shown that prophylactic treatment improved quality of life in terms of reduced hospitalization rates, fewer joint bleeds and less time off school or work, but these studies were carried out mainly in adults or in single countries [8–11]. However, it is still unclear how QoL and health status are related in children and adolescents in Europe. The aim of the study is to describe health status and healthcare of children with haemophilia and their impact on HRQoL. The current analysis was based on a European study (Haemo-QoL study) carried out in connection with the validation of a QoL questionnaire for haemophilic children/adolescents and their parents [12].

Methods

A multicentre, international, cross-sectional, observational study has been carried out in the frame of the field testing of a haemophilia-specific QoL questionnaire. The aim of this paper is to describe clinical conditions of haemophilic children in Western Europe, modality of treatment and their effects on HRQoL.

Patient recruitment

Twenty-eight centres in six European countries were asked to participate (France, Germany, Italy, the Netherlands, Spain and the United Kingdom). Patients with haemophilia A and B were enrolled by each centre when they met the following criteria: age ranging from 4 to 16 years, severe factor VIII or factor IX defect (factor VIII $\leqslant$ 1% or lower than 2%, if a clinically severe history of bleeding was present), absence of inhibitors, HIV-1 seronegativity, capacity to understand the questions and informed consent signed by parents or by a family carer.

Medical documentation

Investigators were asked to fill in a medical documentation form for each patient collecting information on health status and modalities of treatment.

Concerning the patient's health status, investigators were asked to provide details about type of haemophilia, level of factor defect, previous history of inhibitor development and treatment for immune tolerance induction, number of joint bleeding events that required treatment in the previous year, presence of target joints, defined as those joints with several bleeds irrespectively of the bleeding frequency, presence of joint impairment, chronic pain and concomitant diseases. Finally, patients were evaluated optionally according to the WFH orthopaedic joint score [13].

Information concerning treatment modalities consisted of type of treatment administration (home treatment, hospital treatment, self-administration, administration by parents, physician or nurses), type of product (plasma-derived or recombinant), factor consumption in the previous year and type of treatment. The latter was defined as continuous prophylaxis when factor concentrate was administered at least twice a week for at least 45 weeks a year; intermittent prophylaxis when it lasted for less than 45 weeks a year; and on-demand treatment when clotting factor concentrate was administered mainly when a bleeding occurred. Patients who underwent intermittent prophylaxis or who were

prophylactically treated less than twice a week were considered in the on-demand group. Continuous prophylaxis was subdivided into two groups: primary prophylaxis when it had started within the second joint bleeding event or the second year of age, secondary prophylaxis when it had started later. Moreover, investigators were asked to report the number of breakthrough bleeding events in the previous 12 months.

Haemophilia-specific QoL questionnaire

A first haemophilia-specific QoL questionnaire (Haemo-QoL) for three age groups was developed and tested psychometrically in a pilot study [14]. The Haemo-QoL was then modified after field testing [12] and the revised version was used for the purposes of this paper.

An interview version for smaller children (age group I: 4–7 years) was available with 21 items pertaining to eight dimensions ('physical health', 'feelings', 'view', 'family', 'friends', 'others' 'sport and school/kindergarten', 'treatment'). For the schoolchildren aged 8–12 years (age group II) the self-administered questionnaire consisted of two additional domains ('perceived support', 'dealing') with overall 64 items; for adolescents (age group III: 13–16 years) it was expanded with two further additional domains ('relationships', 'future') and consisted of 77 items.

The 'physical' dimension includes questions concerning pain and bleeding, etc.; in the dimension 'feeling' it was asked how children feel related to their haemophilia; questions about how children perceive themselves are included in the dimension 'view'; the interaction in the family was questioned in the dimension 'family'; the dimension 'friends' contains questions about the interaction with friends; questions about how children perceive the support they receive from others pertain to the dimension 'perceived support'; in the 'sport and school' dimension children were asked about their school/kindergarten life; the dimension 'dealing' contains questions about how children deal with their haemophilia; questions in the dimension 'treatment' concern treatment issues; in the dimension 'others' the interaction with others is of interest. The two additional dimensions 'future' and 'partnership' asked about specific issues, such as the view of the future and the possibility of having a girlfriend.

Because there were different numbers of items between the dimensions and in the different age groups, the values were transformed to a scale from 0 to 100 to allow comparison between the answer patterns across the age groups and to compare the impairments in the different dimensions. High values indicate high impairments in HRQoL.

Results

Of 28 centres who were asked to participate, 20 contributed to the study: six centres in France, four in Germany, three in Italy, two in the Netherlands, four in Spain and one in the United Kingdom. Overall 339 children with haemophilia with an average age of 10 years (range interval: 4–16 years) were enrolled. Eight patients were excluded because they did not meet the inclusion criteria. An additional 13 patients were not included in the analysis because the medical documentation was not available. Of 318 assessable patients, 95 were in age group I (4–7 years), 118 in age group II [8–11,13] and 105 in age group III (13–16 years).

Health status

Of 318 assessable patients, 85.5% had haemophilia A and 11.6% haemophilia B, with a factor level of 1% or less (= 0.01 IU dL^{-1}) in 86.5% of them. A history of inhibitor was present in 52 children (16.4%), without any difference in the three age groups. Of these, 37 children (71.2%) underwent an immune tolerance induction treatment, most of them in age group I (85.0%). The mean peak titre of the inhibitor was 147 BU (range 0.5–2640.0); 60.5% of these patients had been high responders (peak titre > 5 BU).

The mean age at the first bleeding was 11 months (median 9, range 0–88), while the age at the first joint bleed was 25 months (median 21, range 0–96). On average the children had had 7.8 bleeds in the past 12 months (median 2, range 0–120); no difference between age groups was found. Less than five joint bleeds in the previous 12 months were reported in two-thirds of the children (67.0%), being similar in all age groups. Half the children were reported to have a target joint (50.3%): 61.0% of the oldest children (age group III) had a target joint ($n = 64$) in comparison to 37 children (38.9%) in age group I (χ^2 test, $P < 0.01$). The most involved target joint was the ankle ($n = 88$), followed by the elbow ($n = 51$) and the knee ($n = 51$), some patients suffering from recurrent bleeding in more than one joint.

A small proportion of patients (11.3%) was suffering from functional joint impairments ($n = 36$), with a significant increase in the older age groups (χ^2 test, $P < 0.018$). Chronic pain was reported in 3.1% of the children ($n = 10$): no difference was found between the groups.

Table 1. Treatment modalities in children with severe haemophilia (figures in parenthesis indicate the number of patients with that particular feature).

	Σ ($n = 318$)	I ($n = 95$)	II ($n = 118$)	III ($n = 105$)
Home treatment				
No ($n = 63$)	19.8%	29.9%	16.1%	14.6%
Yes ($n = 252$)	79.2%	69.1%	83.1%	84.5%
Missing data ($n = 3$)	0.9%	1.0%	0.8%	1.0%
Treatment administration*				
Self-administration	34.1%	7.7%	29.9%	58.6%
Mother administered	67.1%	75.4%	74.2%	52.9%
Father administered	36.1%	52.3%	36.1%	24.1%
Other relatives administered	4.0%	3.1%	4.1%	4.6%
Treatment/physician				
At centre	11.3%	16.5%	8.2%	10.5%
At home	2.8%	5.2%	1.6%	1.9%
Both	1.8%	5.2%	0.8%	–
Treatment/nurse				
At centre	17.8%	22.7%	20.5%	9.5%
At home	11.7%	10.3%	10.7%	13.3%
Both	8.0%	10.3%	7.4%	6.7%
Catheter implantation				
No ($n = 273$)	85.8%	79.4%	87.3%	90.3%
Yes ($n = 40$)	12.6%	20.6%	11.9%	5.8%
Missing data ($n = 5$)	1.6%	–	0.8%	3.9%
Type of product				
Plasma derived ($n = 75$)	24.2%	16.5%	27.2%	28.3%
Recombinant ($n = 235$)	75.8%	83.5%	72.8%	71.7%
Treatment scheme				
Prophylaxis ($n = 212$)	66.7%	68.4%	68.6%	62.9%
On-demand ($n = 101$)	31.8%	30.5%	30.5%	34.3%
Missing data ($n = 5$)	1.6%	1.1%	0.8%	2.9%

*Multiple answers were possible.

The most frequently reported concomitant disease was HCV infection in 19 children, being present in 18 children of age group III and absent in age group I. Developmental delay was found in four patients and neuromuscular disease in one patient. None of the patients had malignancy.

Table 1 shows the treatment modalities of the enrolled children. The majority of all 318 patients were treated at home (79.2%), with a significant difference between the age groups (χ^2 test, $P < 0.02$). One-third of patients (34.1%) self-administered the product, especially the oldest children (58.6%); mothers were the most involved relatives in their home treatment (67.1%). An indwelling central venous catheter was implanted in 12.6% of the children, significantly more often in young children (χ^2 test, $P < 0.01$). Approximately three-quarters of the children (75.8%) were treated with recombinant products in comparison to plasma-derived products (24.2%). Two-thirds of assessable children ($n = 212$) were on prophylaxis, 31.8% received on-demand treatment ($n = 101$).

In Table 2 the characteristics of prophylactic and on-demand treatment are described. Only 19.8% of children on prophylaxis were on true primary prophylaxis, as defined in the Methods section, whereas the great majority was on secondary prophylaxis. Most of the children (78.7%) were receiving the prophylactic treatment three times a week or more. No differences were found between the age groups. The dosage used per infusion was 34.5 IU kg^{-1}, being significantly higher in younger patients (ANOVA, $P < 0.001$). The average number of breakthrough bleeding events per month was 0.4 (SD = 0.4), being lower in the younger age group.

Data for children who were actually treated on demand are also presented in Table 2. Children on on-demand treatment had on average 1.1 bleeding events per month, ranging from 0.6 in age group I to 1.5 in age group III, this difference being not significant. They received on average 3.2 infusions per month: the difference between the age groups was statistically significant (ANOVA, $P < 0.001$). The average total amount of factor consumption was different between age groups (ANOVA, $P < 0.001$), as expected, as patients' weights and bleeding incidence were higher in the older age group.

Interestingly, the difference in the incidence of breakthrough bleeding events between prophylaxis patients and on-demand patients was statistically

Table 2. Type of treatment, bleeding events and factor consumption in children on prophylactic or on on-demand treatment (figures in parenthesis indicate the number of patients with that particular feature).

	Σ	I	II	III
Patients on prophylaxis				
Type of prophylaxis				
Primary prophylaxis ($n = 42$)	19.8%	26.2%	17.3%	16.7%
Secondary prophylaxis ($n = 167$)	78.8%	70.8%	81.5%	83.3%
Missing data ($n = 3$)	1.4%	3.1%	1.2%	–
Frequency of infusions/week				
Two ($n = 44$)	20.8%	24.6%	22.2%	15.2%
Three ($n = 136$)	64.2%	64.6%	59.3%	69.7%
Every other day ($n = 31$)	14.5%	10.8%	17.3%	15.2%
Missing data ($n = 1$)	0.5%	–	–	–
Dosage IU kg^{-1} ($n = 197$) (mean ± SD)	34.5 ± 18.3	44.6 ± 23.1	33.8 ± 15.5	25.7 ± 9.8
Weeks on prophylaxis ($n = 212$) (mean ± SD)	51.4 ± 2.4	50.8 ± 4.0	51.6 ± 1.2	51.8 ± 0.8
No. of breakthrough bleeding events per month ($n = 51$) (mean ± SD)	0.4 ± 0.4	0.2 ± 0.4	0.4 ± 0.4	0.5 ± 0.4
Factor consumption IU per month ($n = 212$) (mean ± SD)	13 191 ± 9159	12 509 ± 8576	13 479 ± 8.995	13 509 ± 9.983
Patients receiving on-demand treatment				
Number of bleeding events per month ($n = 81$) (mean ± SD)	1.1 ± 1.6	0.6 ± 0.4	1.1 ± 1.2	1.5 ± 2.3
Number of infusions per month ($n = 72$) (mean ± SD)	3.2 ± 2.6	2.0 ± 1.7	2.7 ± 2.2	4.6 ± 2.9
Factor consumption IU per month (mean ± SD)	5815 ± 6753	1568 ± 1271	3926 ± 3.458	10 591 ± 8399

Per month ($n = 90$).

Table 3. WFH score in children with severe haemophilia (figures in parenthesis indicate the number of patients with that particular feature).

Characteristics	Σ	I	II	III
Swellings				
None ($n = 211$)	94.2%	95.5%	95.1%	92.1%
Swellings present ($n = 12$)	5.4%	4.5%	3.7%	7.9%
Chronic synovitis ($n = 1$)	0.4%	–	1.2%	–
Muscle atrophy				
None or minimal ($n = 219$)	97.8%	100%	97.6%	96.0%
Present ($n = 5$)	2.2%	–	2.4%	4.0%
Axial deformity knee				
Normal ($n = 212$)	95.9%	100%	93.9%	94.6%
8–15° varus or 0–5° valgus ($n = 9$)	4.1%	–	6.1%	5.4%
Axial deformity ankle				
No deformity ($n = 213$)	98.6%	100%	98.8%	97.2%
< 10° valgus ($n = 3$)	1.4%	–	1.3%	2.8%
Crepitus on motion				
None ($n = 203$)	92.3%	100%	92.6%	84.9%
Present ($n = 17$)	7.7%	–	7.4%	15.1%
Range of motion				
Loss of 10% ($n = 179$)	93.2%	100%	94.4%	87.0%
Loss of 10–33% ($n = 13$)	6.8%	–	5.6%	13.0%
Flexion contracture				
≤ 15° ($n = 190$)	96.9%	94.4%	100%	95.6%
> 15° ($n = 6$)	3.1%	5.6%	–	4.4%
Instability				
None ($n = 213$)	96.4%	95.5%	98.8%	94.5%
Present, but not interfering ($n = 8$)	3.6%	4.5%	1.2%	5.5%
WFH orthopaedic joint total score (mean ± SD)	2.19 ± 0.77	2.23 ± 0.60	2.10 ± 0.74	2.25 ± 0.91

different in the whole cohort as well as in each age group (ANOVA, $P < 0.001$). Almost all the patients receiving on-demand treatment (97.8%) experienced at least one bleed in the previous 12 months, in comparison to 60.7% of patients on prophylaxis. The incidence of bleeding episodes per month in the prophylaxis group ($n = 51$) were 0.4 (SD = 0.4) and in the on-demand group ($n = 81$) 1.1 (SD = 1.6). The

total factor consumption per month was significantly higher in prophylaxis patients in comparison to on-demand patients in age group I and II ($P < 0.000$), but no differences were shown between on-demand and prophylaxis patients in age group III (see Table 2).

The distribution of the WFH orthopaedic joint score is described in Table 3, where only the percentage of the given answers is reported. Only few children had joint swelling ($n = 12$), muscle atrophy ($n = 5$), axial deformity in knee ($n = 9$) or ankle ($n = 3$). Crepitus of motion was present in 17 children and showed a significant difference between the groups (χ^2 test, $P < 0.01$). A loss of motion of 10–33% was reported in 6.8% of patients ($n = 13$), being more frequent in older children, age group III (χ^2 test, $P < 0.02$). Of the assessed children 3.1% had a flexion contracture > 15 ($n = 6$) and 3.6% had an instability ($n = 8$) that did not interfere with functioning. The WFH score reached a mean of 2.19 (SD = 0.77) and was similar over the three age groups.

HRQoL

The HRQoL of children with haemophilia was assessed with the recently developed disease-specific questionnaire Haemo-QoL [12], consisting of six to 12 dimensions according to the different age groups, with a smaller number of items for younger children.

As shown in Fig. 1, the youngest children were mainly impaired in the dimension 'family' (M = 34.38, SD = 24.8), which can be related to overprotection by the parents. Young children were only partially impaired in the interaction with 'others' (M = 22.28, SD = 27.4) or concerning their 'treatment' (M = 24.45, SD = 28.1). Children in age groups II and III were perceived not to receive sufficient support from others reported in the dimensions 'perceived support' (II: M = 49.41, SD = 25.23; III: M = 53.00, SD = 23.79) and were impaired in the interaction with their 'friends' (II: M = 43.91, SD = 28.05; III: M = 46.12, SD = 25.06). In addition older children had problems in dealing with their haemophilia as reported in the dimension 'dealing' (II: M = 33.21, SD = 20.36; III: M = 31.92, SD = 19.65).

Clinical data such as type of treatment and number of bleeds were chosen to examine whether they were associated with differences in Haemo-QoL scores. Regarding type of treatment, differences were found in young children (age group I): children on prophylactic treatment were more impaired ($P < 0.01$) in the subscale 'feeling' of the Haemo-QoL. Adolescents (age group III) on prophylactic treatment were less impaired in the subscale 'sport and school' than adolescents receiving on-demand treatment ($P < 0.05$) and showed less impairments in the Haemo-QoL total score ($P < 0.01$) (for further details, see also [14]).

The severity of clinical manifestations of haemophilia was investigated by the number of joint bleeds and major bleeding events. Differences in HRQoL regarding incidence of joint bleeds are reported in this issue [12].

Considering the number of major bleeds, significant but small differences in HRQoL (transformed data) were found in age group I: the 39 children with three major bleeds or more in the previous 12 months had less impairments in their quality of life in comparison to the 38 children with less than three bleeds in the total score (Table 4) and in three

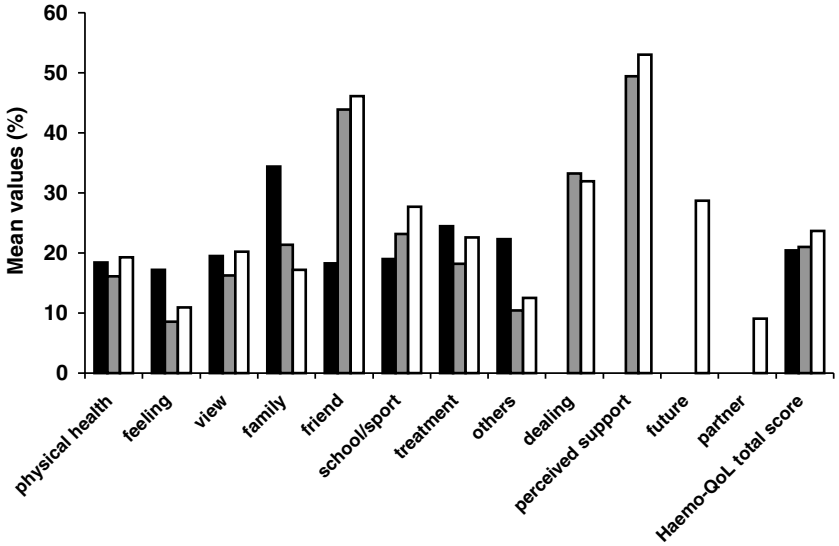

Fig. 1. Mean values (transformed) of the Haemo-QoL dimensions in the three age groups (low values represent low impairments in quality of life and high values high impairments): age group I (black bars), age group II (grey bars) and age group III (white bars).

Table 4. Number of major bleeding events in the previous 12 months and HRQoL (transformed data).

Haemo-QoL	I			II			III		
No. of major bleeds	< 3	≥ 3	*P*	< 3	≥ 3	*P*	< 3	≥ 3	*P*
Physical health	21.71	13.78	n.s.	14.64	16.03	n.s.	13.16	23.91	0.002
Feeling	24.12	11.54	0.041	8.40	8.93	n.s.	9.38	12.37	n.s.
View	10.90	27.08	0.017	16.56	13.62	n.s.	16.69	21.22	n.s.
Family	43.40	27.88	0.004	24.13	21.31	n.s.	13.93	19.02	n.s.
Friend	21.62	15.00	n.s.	38.58	52.03	0.020	44.49	45.48	n.s.
Perceived support	–	–	–	51.72	48.69	n.s.	46.14	58.02	0.028
Others	26.35	16.03	n.s.	11.14	8.33	n.s.	11.31	14.45	n.s.
Sport	18.98	16.67	n.s.	23.69	23.47	n.s.	21.51	32.80	0.014
Dealing	–	–	–	32.66	34.73	n.s.	33.61	30.63	n.s.
Treatment	25.00	21.15	n.s.	18.50	19.69	n.s.	23.07	22.16	n.s.
Future	–	–	–	–	–	–	30.15	28.80	n.s.
Partner	–	–	–	–	–	–	8.46	10.05	n.s.
Total	25.56	16.27	0.006	21.21	21.08	n.s.	21.58	25.74	n.s.

n.s.: Not significant.

dimensions ('feeling', 'view' and 'family'). For age group II a difference was shown in the subscale 'friends': the 43 children with three major bleeds or more were more impaired than the 52 children with less than three major bleeds. The 47 adolescents (age group III) with three major bleeds revealed more impairments in the dimensions 'physical health', 'perceived support' and 'school and sport' than the 35 adolescents with less than three major bleeds.

Discussion

This analysis was carried out in the framework of a study designed to develop an instrument to assess health-related QoL in children with haemophilia [12]. To evaluate better the children's quality of life and their determinants, sociodemographic, clinical and psychosocial characteristics were included in the study protocol, using additional standard measures. The analysis of data obtained by these additional measures provided valuable information about clinical status and healthcare of haemophilic children in Western Europe.

The results of this analysis indicated that most of the patients with haemophilia suffer from bleeding in the first year of life, and the first joint bleeding occurs mainly within the second year of life, providing an authoritative confirmation of what has been reported previously by other authors [15]. Furthermore, this information provides further grounds and confirmation of the recommendation to start prophylaxis as soon as possible within the second year of life [16,17].

Surprisingly, half the children of this cohort were reported to have one or more recurrently bleeding joints (target joints), represented in particular by ankles. These findings can be explained by the weak definition adopted by this study ('several bleeds in the same joint') to indicate a target joint, which was independent of the frequency of bleeding events.

As expected, only a very small proportion of patients showed clinical signs of joint involvement, as shown by the WFH orthopaedic joint score. Home treatment seems to be widely present in Western European children, self-treatment being more frequent in older children, and mothers the most active in their children's treatment. An indwelling central venous catheter was implanted in one-fifth of younger children, due to the need for easy venous access for prophylactic treatment. Recombinant products were the most used in these children, even though plasma-derived concentrates were still largely utilized, confirming the observations provided by the European Paediatric Network for Haemophilia Management [17].

Two-thirds of haemophilic children in Western Europe at the time of the analysis were on prophylaxis, even though the prophylaxis met the criteria for primary prophylaxis in only one-fifth of them [16,17]. The study confirms a significant reduction of bleeding incidence in children on prophylaxis compared to children receiving on-demand treatment. By contrast, the total concentrate consumption appears to be similar in adolescents on prophylaxis and on-demand treatment, indicating that prophylaxis absorbs more economic resources at the beginning in small children, but thereafter it leads to a saving of resources in older patients. These findings demonstrate clearly that cost–effectiveness and cost–benefit ratios of prophylaxis must be evaluated after a relatively long period of observation.

HRQoL seems satisfactory in this cohort, as shown by the newly developed haemophilia-specific questionnaire Haemo-QoL, with scores widely below 50 in a range from 0 to 100, high scores being associated with high impairments. Young children appeared to be impaired in the dimension 'family' and 'treatment' which can be explained, for example, by the overprotection of parents assessed in the dimension 'family' or the burden throughout the treatment. Older children had higher impairments in the so-called 'social' dimensions, such as 'perceived support' and 'friends' and also in the dimension 'dealing', which concerns personal adaptation to the disease.

Prophylaxis affected HRQoL: the youngest children were bothered by it, shown particularly by the dimension 'feeling'. By contrast, adolescents showed a higher HRQoL, revealed particularly by the dimension 'school and sport'. This response pattern is confirmed by a slightly lower HRQoL score in smaller children with less major bleeding events, which are clearly associated with prophylactic treatment, whereas HRQoL tested better in adolescents with less bleeding events. These findings indicate strongly that, first, the initial burden induced by prophylaxis in younger children is highly compensated by improvements in HRQoL in older children; secondly, it is essential to evaluate HRQoL and other outcome measures in patients on prophylaxis in the long term.

In conclusion, healthcare of children in Western Europe is improving progressively with a large diffusion of home treatment and prophylaxis. This provides a high level of health status and HRQoL. The newly developed haemophilia-specific QoL questionnaire is sensitive and versatile and discriminates between clinical subgroups and treatments. Even though the study was not designed to evaluate the impact of prophylaxis on HRQoL, it showed a better HRQoL in haemophilic adolescents on prophylaxis. Further specific studies are required to confirm these findings.

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