The Impact of Bleeding Disorders on the Socioeconomic Status of Adult Patients

Results of a comparative single centre cohort study

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Summary

The impact of inherited bleeding disorders on the socioeconomic status (SES) of affected individuals is not clear. The SES of adult patients with congenital bleeding disorders (PWBD) from a centre in Germany (age 42.3 ± 15.0 years) was compared to that of a gender- and age-matched control group of patients with thrombophilia or a thrombotic event (PWT). Patients completed a questionnaire including aspects of SES, impact of the disease on their lives, and health-related quality of life (HRQoL). Forty-five patients were enrolled in each group; 71 % of PBWD had a severe form of the bleeding disorder (FVIII/IX activity < 1 % or VWD type 3), and 60 % of all PWBD were treated on-demand. PWBD had a lower monthly income ($p = 0.029$) and a worse occupational status ($p = 0.047$) than PWT, but there was no difference regarding the project-specific SES index. PWBD also reported a worse HRQoL in the physical summary component score of the SF-36 ($p < 0.001$). More PWBD (69.8 %) reported a high impact of the disease on their lives than PWT (33.3 %, $p < 0.001$). In summary, PWBD had a worse occupational status, monthly income, health behaviour, HRQoL, and impact of the disease on their lives compared to PWT, but not a significantly different SES in general.

Keywords

- haemophilia
- von Willebrand disease
- socioeconomic status
- quality of life
- outcomes

Zusammenfassung

Der Einfluss angeborener Blutungsneigungen auf den sozioökonomischen Status (SES) der Betroffenen ist unklar. Der SES von Patienten mit angeborener Blutungsneigung (PWBD) aus einem Zentrum in Deutschland (Alter 42,3 ± 15,0 Jahre) wurde mit dem einer alters- und geschlechts-gematchten Kontrollgruppe von Patienten mit Thrombophilie oder einem thrombotischen Ereignis (PWT) verglichen. Die Patienten beantworteten einen Fragebogen zu Aspekten des SES, Einfluss der Erkrankung auf ihr Leben

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Schlüsselwörter
- hämophilie
- von-willebrand-syndrom
- sozioökonomischer status
- lebensqualität
- ergebnisse

und gesundheitsbezogener Lebensqualität (HRQoL). 45 Patienten wurden in jeder Gruppe eingeschlossen; 71 % der PWBD hatten eine schwere Form der Blutungsneigung (FVIII/IX-Aktivität < 1 % oder VWD Typ 3), 60 % aller PWBD erhielten Bedarfsbehandlung. PWBD hatten ein geringeres monatliches Einkommen ($p = 0{,}029$) und einen schlechteren Beschäftigungsstatus ($p = 0{,}047$) als PWT; es fand sich kein Unterschied bezüglich des projektspezifischen SES-Index. PWBD hatten eine schlechtere körperliche HRQoL ($p < 0{,}001$). Mehr PWBD (69.8 %) berichteten einen starken Einfluss der Erkrankung auf ihr Leben als PWT (33.3 %, $p < 0{,}001$). Es zeigten sich signifikante Unterschiede zwischen PWBD und PWT bezüglich Beschäftigungsstatus, Einkommen, Gesundheitsverhalten, HRQoL und Einfluss der Erkrankung auf ihr Leben, nicht jedoch bezüglich des generellen SES.

The impact of inherited bleeding disorders such as haemophilia and von Willebrand disease (VWD) on the socioeconomic status (SES) of affected individuals has not been sufficiently addressed. Major problems in haemophilia are repeated joint bleeds, which may lead to haemophilic arthropathy with significant impact on school education and professional career. Before modern factor replacement therapy, the possibility of enjoying a full social life was limited.[1] With prophylaxis, younger haemophiliacs have less joint damage,[2] but it is not clear how this influences their social status.

On the one hand, social status can be determined by an individual's own achievements. On the other hand, social status is influenced by the inherited position of an individual – called ascribed status.[3,4] SES is often measured as a combination of education, income, and occupation. Socioeconomic factors and social class are fundamental determinants of human functioning, including development, well-being, and physical and mental health.[5] Different methods have been suggested to measure SES.[6]

Studies assessing social status in adults with haemophilia have evaluated marital, educational, and occupational status;[7] those in children and adolescents have focused on academic achievements[8,9] and perceived placement within the school community.[10] More recent studies involving haemophilia patients still showed a higher rate of unemployment and occupational disability compared to the general male population in the Netherlands[11] or to matched controls in Austria.[7]

Patients born after the broad availability of prophylaxis showed better results,[11,12] a finding also supported by a Scandinavian study.[13] This effect is particularly evident in the educational achievements of a North American haemophilia cohort.[14] So far, no comparative data has been published involving German Haemophilia patients.

In a previous study, we have explored the impact of social factors on treatment outcomes in patients with bleeding disorders (PWBD).[15] The specific aim of the current study was to compare the SES of PWBD with that of an age- and gender-matched control group comprised of patients with thrombophilia or a thrombotic event (PWT) from the same German treatment centre and living in the same region of Northern Germany.

Study Design and Methods

This study was conducted at the Haemophilia Treatment Centre (HTC) of the University Medical Centre Hamburg-Eppendorf, Germany. Patients ≥ 18 years with congenital bleeding disorders (i.e. haemophilia A or B or VWD type 3) visiting the centre for routine check-up were invited to participate in the study. A control group of PWT, matched for gender and age, was chosen to avoid selection bias regarding social status. As a control group, we aimed to recruit patients who had not been affected by a disease from early childhood on, but who visited our outpatient clinic.

Since patients visiting the HTC in Hamburg are coming from different counties in Northern Germany (i.e. Hamburg, Schleswig-Holstein, Niedersachsen, and Mecklenburg-Vorpommern), it was inappropriate to compare their SES with that reported for the normal population of the county of Hamburg. The study was approved by the local ethics committee (reference number, PV3783).

All participants provided written informed consent in accordance with the Declaration of Helsinki. Patients were recruited from August 2011 through May 2013.

All participants were asked to complete questions including the following aspects:

- socio-demographic characteristics (e.g. marital status, employment status, school education, income, partnership, children),
- HRQoL,
- life satisfaction,
- perceived impact of the disease on the patient's life,
- physical activity,
- pain, and
- concomitant diseases.

In addition, clinical data were collected from patient charts (PWBD: e.g. type and severity of haemophilia, annual bleeding rate, joint status; PWT: type of thrombophilia or thrombotic event and whether patients received anticoagulants).

HRQoL was assessed using the generic SF-36 questionnaire. The SF-36 quantifies physical and social functioning and the ability of individuals to fulfil their physical and emotional roles[16] and consists of 36 items pertaining to 8

domains, which can be summarized to a physical component score (PCS) and a mental component score (MCS).[17] High values imply a good HRQoL (range 0–100).

Life satisfaction was assessed by a five-point Likert scaled general question ranging from „not at all satisfied“[1] to „very satisfied“.[5]

SES was determined by the following socio-demographic characteristics as described before:[15]

- school graduation,
- professional education,
- employment, and
- income of the patient as well as
- school graduation of the patient's mother and father.

A social status index was created using the following formula based on which three groups of social status could be categorised (low, medium, and high):

Social Status Index =

$$\frac{\sum(school\_graduation + professional\_education + employment + income)}{\left(\sum(school\_graduation\_mother + school\_graduation\_father)/2\right)}$$

The impact of the disease on patients' lives was classified as high or low based on the number of different aspects affected as has been previously described.[15] Patients were asked to state for 6 different aspects (i.e. school and professional education, childhood, choice of job, career, social contacts, and leisure activities) whether they have been affected by the disease. According to the median split, high impact was classified by more than one and low impact by one or less impacted aspects of their lives.

Pain in the previous three months was evaluated on a visual analogue scale (VAS) ranging from 0 (no pain) to 10 (worst imaginable pain).[18]

Physicians examined the orthopaedic joint status only in PWBD using the World Federation of Haemophilia (WFH) Orthopaedic Joint Score (OJS)[19] with higher values implying higher impairments.

Statistical Analysis

All statistical analyses were conducted using SPSS version 23 (SPSS Inc. Chicago, IL, USA). Continuous variables were presented as mean ± standard deviation (SD), if normally distributed, or as median and range, if not normally distributed. Data were tested for normal distribution with the Kolmogorov-Smirnov test. Differences between groups were examined by Student's t-test or ANOVA (normal distribution) or by Mann-Whitney U-test or Kruskal-Wallis-test (no normal distribution). Categorical variables were analysed using the Pearsońs chi-squared test. A p value of < 0.05 was considered significant.

Results

Description of Study Groups

Socio-demographic characteristics, general clinical data, and health behaviour of PWBD and PWT are shown in ►Table 1. In total, 58 PWBD were recruited.[15] Of these, 45 (77.6 %) were evaluable for a comparative analysis with the age- and gender-matched control group of PWT; all participants were male. The main reason for not being able to analyse all PWBD was the lack of proper controls, because male PWT visiting the treatment centre were generally older than PWBD. None of the screened PWBD or PWT refused study participation.

PWBD and PWT were from the county of Hamburg (19 vs. 22), Schleswig-Holstein (19 vs. 16), Niedersachsen (6 vs. 7), or Mecklenburg-Vorpommern (1 vs. 0) so that regional background was comparable.

Prevalence of pain during the preceding 3 months was not different between the two groups, with 78 % of PWBD and 76 % of PWT reporting pain. However, PWBD reported significantly worse pain intensity than PWT (mean VAS, 4.9 ± 2.1 vs. 3.8 ± 2.1; p = 0.027). With regard to pain localisation, PWBD reported to have pain mainly in joints (57.1 %), while 31 % of PWT had pain in locations other than joints, back or head ($p < 0.001$).

Interestingly, one quarter of PWBD suffered from hypertension compared to only 9.1 % of PWT ($p = 0.043$). Concerning the health behaviour of study subjects, PWBD were more frequently smoking ($p = 0.033$) and were doing less frequently sports than PWT ($p = 0.001$); no difference was found with regard to alcohol intake or drug abuse.

According to their self-reported general health status 23.8 % of PWBD reported a bad health status compared to 9.1 % of PWT (not significant).

Clinical Patient Characteristics

A severe form of the bleeding disorder (plasma FVIII/IX activity < 1 %) was present in 73.7 % and 50 % of patients with haemophilia A and B, respectively (►Table 2a). One patient had VWD type 3. First documented bleeding episode was in median at the age of 3 years (range, 0–22 years); data were only available from 31 PWBD. The majority of all PWBD (60 %) received on-demand treatment, while only 8.9 % were on continuous primary prophylaxis. Of the 32 patients with a severe form of the bleeding disorder, 17 (53 %) received primary ($n = 4$) or secondary prophylaxis ($n = 13$).

Of the 45 PWT, 27 (60 %) had inherited or acquired thrombophilia (i.e. factor V gene mutation Leiden, prothrombin gene mutation G20210A, antithrombin, protein C or protein S deficiency or antiphospholipid syndrome). Forty-two patients (93 %) had previously suffered at least one thromboembolic event with the first event at a median age of 43 years (16–75). Twenty-eight patients (62.2 %) were on anticoagulant treatment at the time of the questionnaire (►Table 2b).

Comparison of SES Between PWBD and PWT

PWBD of all types of severity were included, but in general, no significant differences were found between the severity groups with regard to the following outcomes: SES, HRQoL, impact of the disease on patientś lives, life satisfaction; the only difference was seen for the impact of the bleeding disorder on patientś careers ($p < 0.007$), with severe patients (42.9 %) reporting more frequently that their disease

Table 1 Socio-demographic characteristics, clinical data, and health behaviour of patients with bleeding disorders (PWBD) and patients with thrombophilia or a thrombotic event (PWT)

Parameter		PWBD ($n = 45$)	PWT ($n = 45$)	*p*-value
		Mean ± SD	Mean ± SD	
Age (years)		42.3 ± 15.0	43.6 ± 13.9	n. s.
		n (%)	*n* (%)	
Age distribution	18–29 years	12 (26.7)	8 (17.8)	n. s.
	30–44 years	13 (28.9)	15 (33.3)	
	45–64 years	15 (33.3)	17 (37.8)	
	≥ 65 years	5 (11.1)	5 (11.1)	
		Mean ± SD	Mean ± SD	
BMI (kg/m2)		23.8 ± 2.9	25.7 ± 5.4	n. s.
Chronic pain intensity (VAS)		4.9 ± 2.1	3.8 ± 2.1	0.027
		n (%)	*n* (%)	
Pain localisation*	Joints	20 (57.1)	8 (25)	0.001
	Back	1 (2.9)	6 (18.8)	
	Head	0 (0)	1 (3.1)	
	Joint/back/head	14 (40)	7 (21.9)	
	Other	0 (0)	10 (31.3)	
Co-morbidities	Hypertension	11 (25.0)	4 (9.1)	0.043
	Coronary heart disease	2 (4.5)	0 (0)	n. s.
	Stroke	0 (0)	1 (2.4)	n. s.
	Malignant tumour	0 (0)	1 (2.4)	n. s.
	Diabetes	3 (6.8)	2 (4.7)	n. s.
Health behaviour	Smoking	21 (47.7)	12 (26.7)	
	Alcohol intake	32 (72.7)	39 (86.7)	n. s.
	Drug abuse	4 (9.0)	1 (2.2)	n. s.
Sport activities**	No	28 (63.6)	12 (26.7)	0.001
	Yes (no impact[1])	13 (29.6)	22 (48.9)	
	Yes (impact[2])	3 (6.6)	11 (24.4)	

*Two patients with missing data in the group of PWT
**One patient with missing data in the group of PWBD
[1]Swimming, bicycling, gymnastic
[2]Contact or team sport.

had an impact on their careers than mild/moderate patients (7.7 %). Nevertheless, since this was the only difference, we decided to report the following results for the entire PWBD.

Marital status, partnership and number of children were not different between PWBD and PWT. There was also no significant difference with regard to school and professional education, but a trend towards a higher graduation in PWT. A significant difference was found regarding occupational status ($p = 0.047$): 66 % of PWBD were working compared to 84 % of PWT. There was no difference with regard to working hours (full- or half-time) or type of occupation. Similar proportions of PWBD and PWT were retired due to age, while only PWBD were retired due to their disease ($n = 6$) or unemployed ($n = 3$). Monthly income was lower in PWBD ($p = 0.029$, ►Fig. 1).

As a potential confounder for socioeconomic achievements, we also explored the educational status of the study subjects' parents, which showed no significant difference regarding school graduation: 37 % and 36 % of mothers of PWBD and PWT, respectively, had no or the lowest formal qualification; fathers of PWT had a slightly higher graduation than fathers of PWBD (26 vs. 19 % with entry requirements for university and 33 vs. 45 % with no or the lowest formal qualification).

According to the project-specific SES index, no significant difference was found between the groups (►Table 3).

Comparing psychosocial parameters of the SF-36 (►Fig. 2), PWBD reported worse values in the dimensions "'physical functioning", „bodily pain", and „general health perception" than PWT. The 'physical summary component

Table 2a Clinical patient characteristics of patients with bleeding disorders (PWBD) ($n = 45$)

Parameter		*n* (%)
Bleeding disorder ($n = 45$)	Haemophilia A	38 (84.4)
	Haemophilia B	6 (13.3)
	Von Willebrand disease	1 (2.2)
Haemophilia A ($n = 38$)	Severe (FVIII < 1%)	28 (73.7)
	Moderate (FVIII 1–5%)	3 (7.9)
	Mild (FVIII 5–40%)	7 (18.4)
Haemophilia B ($n = 6$)	Severe (FIX < 1%)	3 (50.0)
	Moderate (FIX 1–5%)	2 (33.3)
	Mild (FIX 5–40%)	1 (16.7)
Von Willebrand disease ($n = 1$)	Type 3 (severe)	1 (100)
Type of treatment ($n = 45$)	Trimary prophylaxis	4 (8.9)
	Secondary prophylaxis	13 (28.9)
	Intermittent prophylaxis	1 (2.2)
	On-demand treatment	27 (60.0)
History of inhibitor	Yes	4 (7.0)
viral infections	HIV+	7 (15.6)
	HCV+	28 (62.2)
Target joints	Yes	12 (27.9)
Orthopaedic surgery	Joint replacement	7 (15.5)
	Arthrodesis	4 (8.9)
Parameter		**Median (range)**
No. of annual bleeds	All bleeds	3 (0–34)
	Joint bleeds	2 (0–27)
Orthopaedic joint score		8 (0–38)
No. of target joints		0 (0–3)
Age at first documented bleeding episode		3 (0–22)

Table 2b Clinical patient characteristics of patients with thrombophilia or a thrombotic event (PWT) ($n = 45$)

Parameter		*n* (%)
Type of thrombophilia	Factor V gene mutation Leiden heterozygous	9 (20)
	Factor V gene mutation Leiden homozygous	1 (2.2)
	Prothrombin gene mutation G20210A heterozygous	3 (6.7)
	Antithrombin deficiency	0
	Protein C deficiency	1 (2.2)
	Protein S deficiency	1 (2.2)
	Antiphospholipid syndrome	12 (26.6)
	No inherited or acquired thrombophilia	18 (40)
Site of VTE	No VTE	3 (6.7)
	Distal DVT	5 (11.1)
	Proximal risk-associated DVT	3 (6.7)
	Proximal idiopathic DVT	5 (11.1)
	Pulmonary embolism	7 (15.5)
	Pulmonary embolism and DVT	9 (20)
	Recurrent VTE	13 (28.8)
Anticoagulation	Currently on anticoagulation	28 (62.2)
	Previously on anticoagulation	14 (31.1)
	Never anticoagulation	3 (6.7)
PTS	No PTS	21 (46.7)
	PTS present	8 (17.7)
	No information available	16 (35.5)
Parameter		**Median (range)**
Age at first thrombosis (years)		43 (16–75)
Time since diagnosis of first VTE (months)		19 (2–252)

VTE: venous thromboembolism; DVT: deep vein thrombosis; PTS: post-thrombotic syndrome.

score' (PCS) was also significantly worse in PWBD (41.2 ± 11.5) compared to PWT (50.5 ± 8.6; $p < 0.001$).

The self-reported impact of the disease on different aspects of the patients' lives showed significant differences between PWBD and PWT (►Fig. 3), with more impact on „childhood" ($p < 0.001$), „career" ($p = 0.014$), „social contacts" ($p = 0.002$), and „leisure activities" ($p < 0.001$) in PWBD. 57 % of the PWBD reported an influence of the disease on their school education, and 51 % felt an impact on the choice of their profession. One third of patients perceived to have less career opportunities, mainly because of actual or suspected days lost from work. Based on the classification of high and low impact of the disease on patients' lives, there was a significant difference between PWBD (69.9 %) and PWT (33.3 %; p < 0.001).

Asked for general life satisfaction, 81.4 % of PWBD reported to be „rather" or „very satisfied" with their lives compared to 86.4 % of PWT, which was not significantly different (mean answer on the 5-point Likert scaled question, 4.02 ± 0.9 vs. 4.25 ± 0.75, PWBD vs. PWT; $p = 0.216$).

Discussion

In this comparative study of PWBD and PWT, we observed a significant difference in occupational status, with less PWBD working than PWT. Only PWBD were unemployed or retired due to their disease, and monthly net-income was lower in PWBD. No differences were found with regard to the social status itself (as defined by our social status index), marital status, partnership, and number of children as well as school and professional education with a trend towards higher achievements in PWT. PWBD reported a stronger impact of the disease on their lives than PWT and showed more significant impairments in the physical aspects of their HRQoL. However, no significant difference was found regarding life satisfaction.

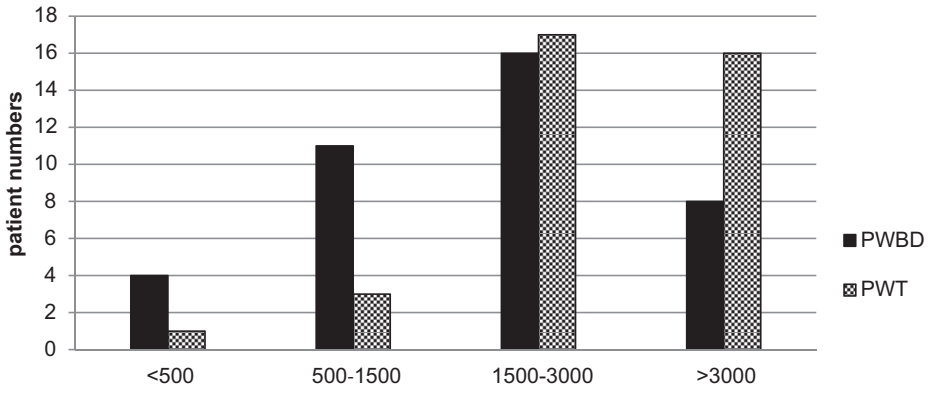

Fig. 1 Differences in monthly net-income (€) between PWBD and PWT. Tested for significance using the Pearson's Chi-squared test ($p = 0.029$).

Previous studies from Austria and the Netherlands reported similar findings, with a higher rate of unemployment and early retirement in haemophilia patients compared to controls.[7,11] Patients with severe haemophilia from the Netherlands were less frequently fulltime working than the general population.[11] In this regard, no differences were found between PWBD and PWT in our study. In contrast to these studies, a more recent publication comparing the Swedish high-dose with the Dutch intermediate-dose prophylactic regimen in younger patients with severe haemophilia (median age 24 years) showed that, compared to the general population, fewer haemophilia patients from both countries achieved a university degree,[20] which is in line with our results. In our cohort, rates of unemployment and early retirement were higher than in controls, while in the above study, unemployment rates were similar (Netherlands) or lower (Sweden) compared to the normal population. These encouraging results might be due to the fact that in this study all patients were on continuous primary prophylaxis compared to only 12.5 % of patients with severe haemophilia in our cohort.

Table 3 Socioeconomic status of patients with bleeding disorders (PWBD) and patients with thrombophilia or a thrombotic event (PWT) according to age groups

Age groups	Socioeconomic status	PWBDn (%)	PWTn (%)
18–29 years	Low	3 (27.3)	3 (37.5)
	Medium	5 (45.5)	3 (37.5)
	High	3 (27.3)	2 (25)
30–44 years	Low	2 (15.4)	1 (6.7)
	Medium	7 (53.8)	5 (33.3)
	High	4 (30.8)	9 (60)
45–64 years	Low	2 (13.3)	1 (5.9)
	Medium	10 (66.7)	10 (58.8)
	High	3 (20)	6 (35.3)
> 65 years	Low	2 (40)	1 (20)
	Medium	3 (60)	3 (60)
	High	–	1 (20)
All	Low	9 (20.5)	6 (13.3)
	Medium	25 (56.8)	21 (46.7)
	High	10 (22.7)	18 (40)

A positive effect of prophylaxis on rates of unemployment and early retirement is confirmed by another Scandinavian study that compared Swedish patients on early prophylaxis with Norwegian patients treated on-demand.[13]

More than 50 % of the patients in our cohort reported an impact of their bleeding disorder on several aspects of their lives, including an influence on school education, choice of profession, and career. This is in contrast to Scandinavian data, according to which 86 % of patients reported to have the same opportunities as someone without haemophilia. In that cohort, 79 % of patients were on prophylaxis.[21] Results comparable to those of our study revealed an Iranian study involving 100 haemophilia patients aged 16–67 years (mean age 28 ± 9 years), in which 49 % reported that haemophilia had a negative impact on education.[22]

In our cohort, with one third of patients being < 35 years old, hypertension was more prevalent than in controls, but lower (25 %) compared to the Canadian ARCHER study in haemophilia patients ≥ 35 years (31.3 %)[23] and an Italian study in patients with severe haemophilia ≥ 65 years (71.8 %).[24] One possible explanation could be that patients with haemophilia are less active in sports, which has been shown in our cohort and it could be confounded by the high rate of smoking in that group. That PWBD were more often smoking than PWT which could be due to a perceived protection against cardiovascular disease in PWBD and a higher thrombosis risk of smoking in PWT. By contrast, the body mass index (BMI) was not different between the two groups.

The current study suffers from the relatively small number of enrolled patients (n = 45), which is a common limitation of single-centre studies in haemophilia and additionally due to the fact that not all registered patients appeared to their annual routine visits. Additionally, it was difficult to recruit appropriate PWT in the age range of our patient cohort, since these patients are normally older. We considered male patients with (rather mild) thrombophilia or a thrombotic event (PWT) „healthy enough" to serve as an appropriate control group that is matched not only for age and gender, but also for the region

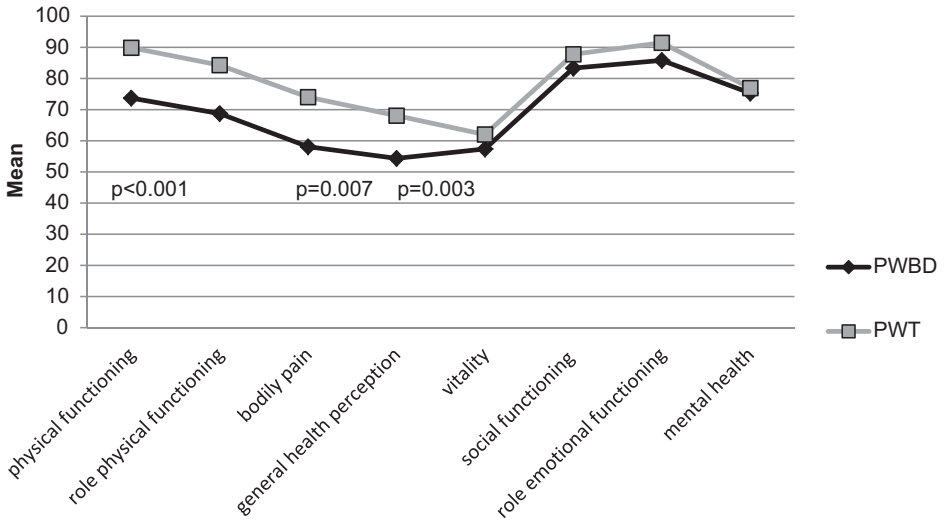

Fig. 2 Differences in health-related quality of life (SF-36) between PWBD and PWT. Differences between groups were analysed by Student's t-test.

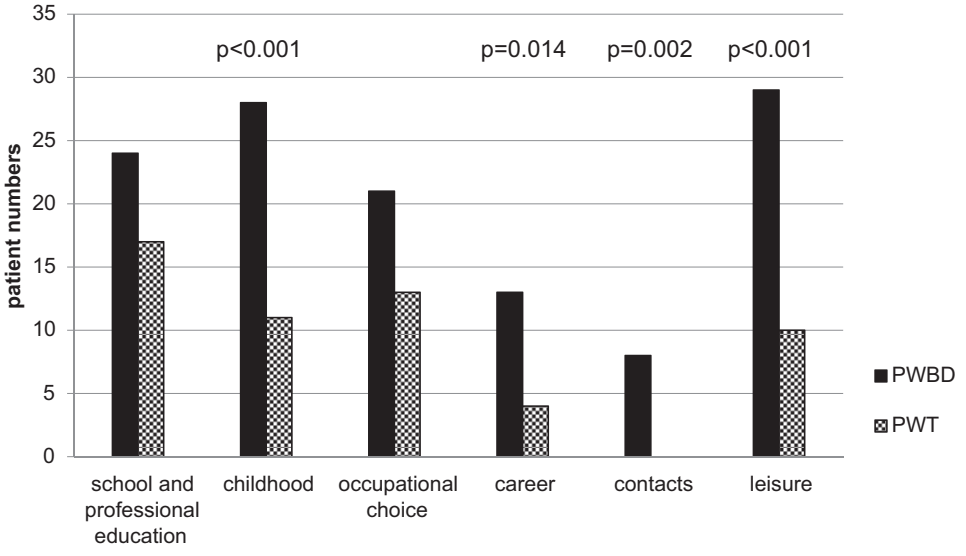

Fig. 3 Impact of the disease on different aspects of the patients' lifes in PWBD and PWT. Tested for significance using the Pearson's Chi-squared test.

of residence in Germany from which the patients with haemophilia were recruited. By choosing PWT as a control group, we wanted to avoid selection bias with regard to social status (as would have been the case when choosing, for example, the patients' peers, hospital personnel, or even healthy blood donors). Our assumption was confirmed by the fact that median age of first manifestation of the disease was 43 years (range, 16–75 years) for PWT compared to 3 years (range, 0–22 years) for PWBD. Other potential control groups like the patient's peers would probably have had a similar social background. Moreover, these controls would have been difficult to approach, since older haemophilia patients in general do not want to speak about their disease with others which, on the other hand, would have been necessary for the recruitment of their peers.

We have chosen a comparison group which was easily accessible and which came from the same region of Northern Germany. Thus, one might argue that the findings of our study cannot be extrapolated to the entire country. However, there is a well-known South-North slope with regard to the SES in our country, and we therefore think that our data are sufficiently representative for the Northern part of Germany.[25,26] In contrast, a comparison to socioeconomic data of the whole German population does not seem appropriate. Such a comparison would require a multi-centre setting including patients from all regions of the country.

Conclusion

PWBD showed a negative perceived and measured impact of the bleeding disorder on their lives: PWBD

- were more frequently unemployed or retired due to their disease,
- had lower monthly income, and
- showed a trend towards lower educational achievements than PWT.

This finding might be due to a low proportion of patients receiving prophylactic factor replacement therapy, emphasising the need for implementation of early and continuous prophylaxis. Future studies involving German PWBD on early prophylaxis are needed to prove the effect of prophylaxis on socioeconomic achievements as a meaningful long-term outcome parameter in haemophilia treatment.

Author contributions

KH designed the study, recruited patients, and contributed to data analysis. KH and SvM drafted the first version of the manuscript. SvM analysed the data. CB critically revised the manuscript. FL oversaw the study, recruited patients, and critically revised the manuscript. All authors approved the final version of the manuscript.

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