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ORIGINAL ARTICLE

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Occupational integration of adults with severe haemophilia (INTHEMO): A study based on the FranceCoag registry

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Abstract

Introduction: Health of people with severe haemophilia (PwSH) improves thanks to the advancements in haemophilia care, giving them more opportunities in occupational integration. However, there is little literature on the occupational integration of PwSH.

Objectives: The main objective of our study was to assess the occupational integration of PwSH and to compare it with that of the general population. The secondary objective was to study the association between individual characteristics (sociodemographic, clinical and psycho-behavioural) and occupational integration of PwSH.

Methods: A multicentre, non-interventional, cross-sectional study was conducted in 2018–2020 on PwSH, aged over 18 and under 65 years and included in the FranceCoag registry. Measurements included indicators of occupational integration, sociodemographic, clinical and psycho-behavioural characteristics. The indicators of occupational integration were compared with those of the general population, using indirect standardization. The data of the general population were available from the National Institute of Statistics and Economic Studies (INSEE). Determinants of occupational integration were explored using structural equation modelling.

Results: Of 1262 eligible people, 588 were included. PwSH had a lower employment rate than the general population (standardized ratio, .85; 95% CI, .77–.94). There were more PwSH at tertiary education level than expected (standardized ratio, 1.38; 95% CI, 1.17–1.61). HIV infection, poor physical health and mental health concerns were associated with a higher risk of unemployment in PwSH.

Conclusion: Employment rate of PwSH is lower than that of the general population despite their higher education level. Target interventions focusing on determinants of difficult occupational integration could be helpful for PwSH.

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KEYWORDS
adult, employment, haemophilia A, haemophilia B, occupations

1 | INTRODUCTION

Haemophilia is a rare and inherited disorder affecting mainly men, characterised by bleeding due to a deficiency in clotting factors.[1] Severe haemophilia is characterised by spontaneous bleeding. Untreated severe haemophilia can cause serious haemorrhagic events such as intracranial haemorrhage, intraspinal haemorrhage, hemoperitoneum and hemarthrosis. However, improvements in haemophilia care (i.e., substitutive therapies) allow people with severe haemophilia (PwSH) to have a near-normal life expectancy,[2,3] so they can reach adulthood and live with a chronic disease. Therefore, they can have more opportunities in occupational integration.

Studies initiated by HERO (Haemophilia Experiences, Results and Opportunities), an international and multidisciplinary research project providing a greater understanding of life with haemophilia, yielded some results on the employment of people with haemophilia (PwH).[4–6] These studies provided findings on PwH of 10 countries. A survey on the whole sample of the HERO project (675 participants) in 2014 showed that the employment rate of PwH was 60% (excluding people in full-time education).[4] A study on demographics, comorbidities and health status of US young adults with haemophilia (18–34 years) in 2015 showed that the unemployment rate was 19% (141 participants), while this number in the general US population was 6% for males aged 20 years or older.[5] However, no formal statistical comparison was conducted in these two studies to confirm this difference in the employment rate and no differentiation was made between people with mild, moderate and severe haemophilia in employment-related results. In another study on treatment outcomes, quality of life, and impacts of haemophilia relationships in young PwH, haemophilia was assumed to be one of the factors influencing career options and fulfilling responsibilities at work, but no results were provided to support these assumptions.[6] Joint pain, physical limitations and mental health issues (stress, anxiety, depression) were also very common among participants of the HERO project,[5] but the effect on the employment was not studied. Other potential determinants such as age, education level, viral infections and prejudice were mentioned in other studies on Dutch PwH.[7,8] However, similar to the study of HERO, the association of these determinants with the employment was not analysed. Although, there are few descriptive results on the employment of PwSH in the literature, their occupational integration is under-studied and its determinants have not been explored.

Our INTHEMO project aimed to assess the occupational integration of PwSH and to compare it with that of the general population. The secondary objective was to study the association between individual characteristics (sociodemographic, clinical, and psycho-behavioural) and occupational integration of PwSH.

2 | MATERIALS AND METHODS

2.1 | Study design and study population

This study was designed as a multicentre, non-interventional, cross-sectional study, involving 29 Haemophilia Treatment Centres (HTC) in France.

Eligibility criteria were PwSH A or B (FVIII or FIX < 1%, respectively), aged over 18 and under 65 years, included in the FranceCoag registry (an exhaustive national cohort of PwH in France),[9] followed by one of the participating centres (2 HTC) with available home addresses, affiliated to the French social system, having no troubles in comprehension, reading or writing and consenting to participate in the study. People withdrawing their consent to participate and people who did not answer the occupational integration items were excluded. The non-participants were people who did not meet all the eligibility criteria and people who were excluded.

The study was approved by the French Ethical Research Committees (CPP Nord-Ouest I - RCB n°2017-A02930-53) and French Data Protection Authority (CNIL), whose principles are in line with those of the General Data Protection Regulation (GDPR). It was conducted in accordance with the applicable privacy requirements and ethical principles outlined in the Declaration of Helsinki. Trial registration number is NCT03301376.

2.2 | Data collection

The inclusion procedure began in April 2018 and ended in February 2020. The indicators of occupational integration, sociodemographic and psycho-behavioural characteristics were collected by a self-administered questionnaire sent to eligible people by post. The clinical characteristics were retrieved from the FranceCoag's database for all eligible people.

2.3 | Measurements

The collected measurements are displayed in Table 1. The indicators of occupational integration were defined according to the National Institute of Statistics and Economic Studies (INSEE) which is responsible for collecting, analysing and disseminating information on the French economy and society.[10] The sociodemographic characteristics were age, sex and residential location (living in or near the city). The clinical characteristics were type of haemophilia, complications, comorbidities,

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TABLE 1 Collected measurements

Indicators of occupational integration	
Occupational status (according to classification of INSEE)	In employment (Employees and self-employed people) Not in employment Unemployed Inactive (Students, retirees, people with disability, people in training, stay-at-home people)
Working time if in employment	Full-time Part-time
Type of contract if in employment	Self-employed Open-ended employment contract Fixed-term employment contract Apprenticeship Interim
Category of occupation if in employment	Farmer Employee Intermediate occupation Executive, senior intellectual worker, accredited professional and equivalent Craftsman, tradesman, business executive
Education level	No diploma/Primary and secondary education Vocational diploma (Certificate of Professional Aptitude, Diploma of Occupational Studies) High school Second-year university or equivalent Bachelor's, Master's, Doctoral degree
Sociodemographic characteristics	Age and sex Residential location (Living in or near the city)
Clinical characteristics	
Type of haemophilia	Haemophilia A Haemophilia B
Complications	History of inhibitors History of intracranial haemorrhage History of major orthopaedic interventions
Comorbidities	HIV Hepatitis B virus (HBV) Hepatitis C virus (HCV) – ever infected If ever infected with HCV, with or without active chronic HCV Cancer Other chronic pathology
Current treatment regimen	On-demand treatment Prophylaxis
Age at start prophylaxis	
Dose of prophylaxis (per year)[a]	High dose Intermediate dose Low dose
Primary prophylaxis	
Psycho-behavioural characteristics	
Short form 12 Health Survey (SF-12)	12-item questionnaire measuring health-related quality of life (HRQoL). Two sub-scales: Physical component summary (PCS) for physical health, mental component summary (MCS) for mental health. Scores range from 0 to 100 with higher scores indicating better HRQoL.
State-Trait Anxiety Inventory, form Y (STAI-Y)	Two sub-scales: Anxiety as emotional state (short version of the STAI-Y State) (6 items), anxiety as personality trait (STAI-Y Trait) (20 items). Scores range from 20 to 80 with higher scores indicating greater levels of anxiety.
Short version of the Center for Epidemiological Studies-Depression (CES-D)	10-item questionnaire. Scores range from 0 to 30 with higher scores indicating greater symptoms of depression.

Abbreviation: INSEE, National Institute of Statistics and Economic Studies.
[a]World Federation of Haemophilia. Guidelines for the management of haemophilia (3rd edition).

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current treatment, age at start prophylaxis and dose of prophylaxis (per year). For the psycho-behavioural aspects, health-related quality of life (HRQoL) was assessed by the Short Form 12 Health Survey (SF-12), measuring two dimensions: physical health and mental health.[11] Anxiety was evaluated by the State-Trait Anxiety Inventory-form Y (STAI-Y).[12] Depression was assessed using the short version of the Center for Epidemiological Studies-Depression (CES-D) scale.[13] All the questionnaires were in validated French versions.

2.4 | Statistical analyses

2.4.1 | Descriptive analysis

Counts and percentages were calculated for categorical variables. Mean values and standard deviations (SD) were calculated for quantitative variables. The normality of distributions of quantitative variables was assessed graphically.

2.4.2 | Comparison between the participants and non-participants

Sociodemographic and clinical characteristics were compared using Chi-squared test (or Fisher's test) for categorical variables, and Student's t-test (or Mann-Whitney U) for quantitative variables. The tests were two-sided.

2.4.3 | Comparison of occupational integration with that of the French general population

The occupational data of the general population were available from the INSEE,[10] stratified by sex and three age ranges (18–24, 25–49 and 50–64 years), except for the education levels with four age ranges (25–34, 35–44, 45–54 and 55–64 years, people aged less than 25 years being excluded). The study sample was divided according to these age ranges. The indirect standardization method was used. Standardized ratios (SR) and their 95% confidence intervals (CI) were calculated.[14] SR higher than 1 means higher number in PwSH than expected in the general population.

2.4.4 | Analyses of the determinants of occupational integration

The association of sociodemographic, clinical and psycho-behavioural characteristics with occupational integration was analysed. Students and retirees were excluded since they were outside the labour force. The evaluation criterion to assess the occupational integration was the "occupational status," which was recoded into a binary variable: in employment versus not in employment (unemployed, people with disability, people in training, stay-at-home people) according to the classification of INSEE. Based on the hypotheses and literary data on haemophilia and other chronic pathologies,[5,6,8,15–18] the potential determinants were age; education level (tertiary education level including second-year university or equivalent and Bachelor's, Master's, Doctoral degree), residential location (living in or near the city), physical health, mental health concerns, complications, comorbidities and current therapeutic regimen.

Univariate analysis. The determinants were compared between people in employment and people not in employment by using Chi-squared test (or Fisher's test) for categorical variables, and Student's t-test (or Mann-Whitney U test) for quantitative variables. The tests were two-sided.

Structural equation modelling (Figure 1). The model was built, based on the hypotheses and literary data[5,6,8,15–18] a priori and the results of the univariate analysis. Higher education level was considered as a potential motivator, while physical limitations, mental health concerns and comorbidities were considered as potential barriers to the occupational integration.

The structural equation model (SEM) was built using diagonally weighted least squares estimation with robust standard errors. The outcome was "being in employment," which was the main evaluation criterion of the occupational integration. The determinants were sociodemographic, clinical characteristics, physical health and mental health concerns. Physical health and mental health concerns were mediators for the association between the other determinants and occupational integration. The first mediator was physical health measured by physical component summary (PCS). The second mediator was "mental health concerns," which was a latent variable manifested by mental component summary (MCS), STAI-Y and CES-D scores. This latent variable was verified by the confirmatory factor analysis (CFA).

Mediation analysis was conducted. To estimate the direct effects of the determinants, logistic regression in SEM was performed. The total indirect effect via two mediators was obtained by adding two indirect effects. To estimate the total effect, the direct effect of the determinant on the outcome was added to the total indirect effect.[19] Odds ratio (OR) and 95% CI were calculated for the effects on the employment. Standardized coefficients (β) were calculated for the associations with physical health and mental health concerns. Figure 1 reports model specification of determinants for occupational integration.

Model fit. Indicators to assess the model fit were Comparative Fit Index (CFI), Tucker Lewis Index (TLI), Root Mean Square Error of Approximation (RMSEA), Standardized Root Mean Square Residual (SRMR), and the relative chi-square equal to chi-square statistic divided by degrees of freedom (χ^2/df). Recommended cut-offs for good fit are CFI $\geq .90$; TLI $\geq .95$; RMSEA and SRMR $< .08$; (χ^2 / df) ≤ 5.[20]

All the statistical analyses were performed with RStudio version 1.3.959 (RStudio, Boston, MA). Rstudio "lavaan" package was used to conduct the SEM.

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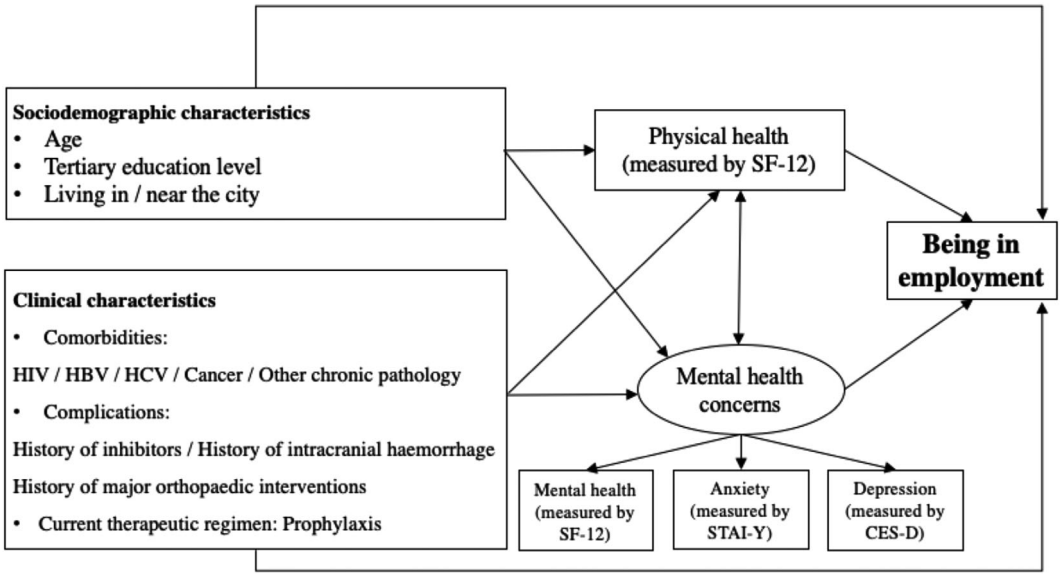

FIGURE 1 Model specification for determinants of occupational integration. Rectangles represent for observed variables, oval for latent variable, single-headed arrows for direct effects, double-headed row for correlation.

3 | RESULTS

3.1 | Participants

There were 1262 questionnaires sent to the eligible people with 589 respondents. One respondent was then excluded due to missing responses concerning the occupational integration items. In total, there were 588 participants and 674 non-participants. Most of them were men (99.3% of all participants) and the mean (SD) age was 41.1 (12.9) years.

Compared to the non-participants, the participants were older (41.1 vs. 36.6 years, $p < .001$) People with history of major orthopaedic interventions participated more frequently in the study than people without, similar to people with HIV, hepatitis B virus (HBV) or hepatitis C virus (HCV) infection. The non-participants started prophylaxis earlier than the participants (22.0 vs. 28.4 years, $p < .001$). The remaining clinical characteristics did not significantly differ between the participants and non-participants (Table 2).

3.2 | Occupational integration, education level and comparison to the general population

The observed employment rate was 61.6%. The employment status of the participants was significantly different between age groups ($p < .001$). As compared to the general population, the employment rate was lower (SR, .85; 95% CI, .77–.94) (Table 3).

Education levels of the participants were significantly different between age groups ($p = .003$). As compared to the general population, the percentage of participants having no diploma or with primary/secondary education level was lower (SR, .44; 95% CI, .32–.60), while the percentage of university graduates was higher (SR, 1.38; 95% CI, 1.17–1.61) (Table 4). The participants chose to do intellectual work more often (SR, 1.79; 95% CI, 1.49–2.14) than the general population (Table 3).

Retirement age of PwSH was similar to the legal retirement age in France (61.3 and 62 years, respectively).

3.3 | Determinants of occupational integration

There were 513 participants in this analysis (25 students and 45 retirees were excluded from this analysis since they were outside the labour force, five among 518 eligible people were then excluded due to missing responses concerning education level). Mean PCS score of people in employment was higher than that of people not in employment (42.4 vs. 35.3, $p < .001$), similar to MCS score (46.8 vs. 43.6, $p = .003$). There were no significant differences in the age at start prophylaxis and dose of prophylaxis (per year) between people in employment and people not in employment ($p = .483$ and $p = .883$, respectively). The results of the univariate analysis are reported in Table 5.

In the SEM, the CFA showed that "mental health concerns" was a latent variable manifested by: Mental health of SF-12, anxiety of STAI-Y State and STAI-Y Trait, depression of CES-D. Their standardized factor loadings were .80, .84, .90 and .91, respectively. Physical heath measured by SF-12 and the variable "mental health concerns" were slightly correlated ($r = -.11$, $p = .013$). Indicators verifying the good fit of the model were CFI = .918; TLI = .973; RMSEA = .043; SRMR = .048; (χ^2 / df) = (85.249/45) = 1.894.

The outcomes of the SEM are presented in Figure 2 and Table 6. For educational attainment, people with tertiary education level (OR, 1.94; 95% CI, 1.49–2.53) were more likely to be in employment. For HRQoL, people with better physical health were more likely to have a job (OR, 1.03; 95% CI, 1.02–1.04). People with more mental

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TABLE 2 Characteristics of the participants and non-participants

	Non-participants n (%) / Mean (SD)	Participants n (%) / Mean (SD)	*p*-value
People with severe haemophilia, n	674	588	
Age, years	36.6 (11.4)	41.1 (12.9)	<.001
Type of haemophilia			.198
Haemophilia A	575 (85.3)	486 (82.7)	
Haemophilia B	99 (14.7)	102 (17.3)	
History of inhibitors			.388
No	542 (80.4)	484 (82.3)	
Yes	132 (19.6)	104 (17.7)	
History of intracranial haemorrhage			.964
No	645 (95.7)	563 (95.7)	
Yes	29 (4.3)	25 (4.3)	
History of major orthopaedic interventions			.001
No	353 (52.4)	255 (43.4)	
Yes	321 (47.6)	333 (56.6)	
HIV			.007
No	566 (82.5)	449 (76.4)	
Yes	118 (17.5)	139 (23.6)	
HBV			<.001
No	536 (79.5)	402 (68.4)	
Yes	138 (20.5)	186 (31.6)	
HCV (ever infected)			<.001
No	371 (55.0)	215 (36.6)	
Yes	303 (45.0)	373 (63.4)	
If ever infected with HCV			.004
With active chronic HCV	96 (32.0)	80 (21.7)	
Without active chronic HCV	204 (68.0)	288 (78.3)	
Not available	*3*	*5*	
Cancer			.453
No	663 (98.4)	575 (97.8)	
Yes	11 (1.6)	13 (2.2)	
Other chronic pathology			.039
No	577 (85.6)	478 (81.3)	
Yes	97 (14.4)	110 (18.7)	
Age at start prophylaxis, years	22.0 (14.3)	28.4 (16.3)	<.001
Current therapeutic regimen			.682
On-demand treatment	210 (31.6)	193 (32.8)	
Prophylaxis	455 (68.4)	395 (67.2)	
Dose of prophylaxis (per year)			.272
High dose	161 (46.3)	144 (46.9)	
Intermediate dose	167 (48.0)	136 (44.3)	
Low dose	20 (5.7)	27 (8.8)	
Not available	*107*	*88*	

(Continues)

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TABLE 2 (Continued)

	Non-participants n (%) / Mean (SD)	Participants n (%) / Mean (SD)	*p*-value
Primary prophylaxis			<.001
No	219 (48.7)	225 (65.0)	
Yes	231 (51.3)	121 (35.0)	
Not available	*5*	*49*	

Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus.

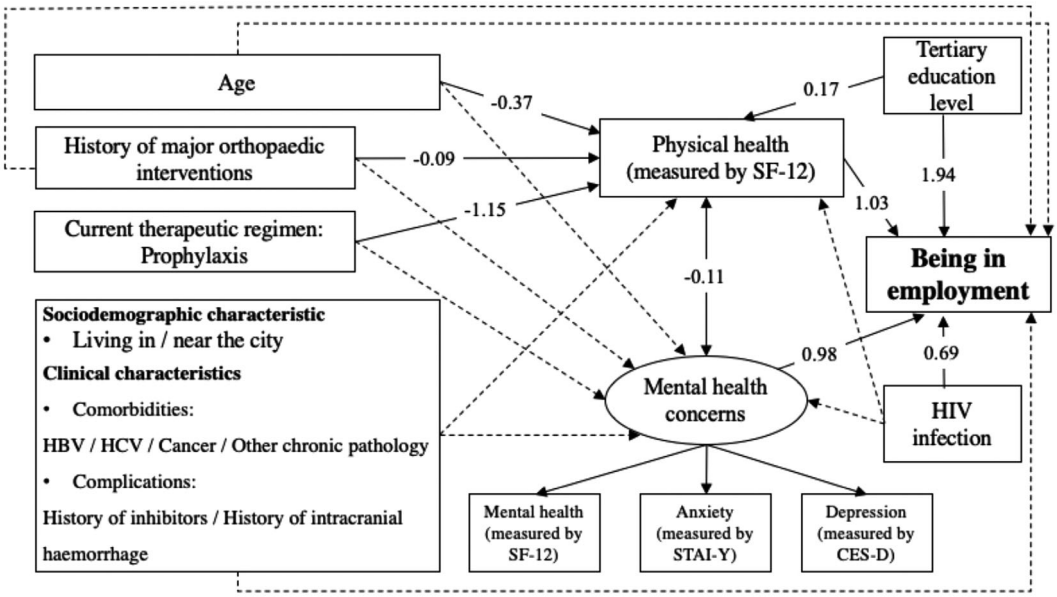

FIGURE 2 Outcomes of structural equation model. Associations with physical health and mental health concerns are presented by standardized coefficients (β). Effect on occupational integration is presented by odd ratios. Dashed arrows represent for non-significance.

health concerns were less likely to be in employment (OR, .98; 95% CI, .97–.99). Current use of prophylaxis did not have direct effect on occupational integration, but it had a negative indirect effect through mediators, that is, physical health and mental health concerns (OR, .91; 95% CI, .84–.99). HIV infection had a negative effect on occupational integration (OR, .69; 95% CI, .50–.94). No significant effects on occupational integration were found in the residential location, complications and other comorbidities including HBV and HCV infections.

4 | DISCUSSION

Employment situation of PwSH is under-studied and determinants of occupational integration have not been explored. In the present project, the employment rate of PwSH was found to be lower than expected despite their higher education level, with HIV infection, poor physical health and mental health concerns as barriers to occupational integration, while high education level as a motivator.

4.1 | Occupational integration of PwSH

The employment rate of PwSH was lower compared to the general population after adjusting for the different age distributions. This outcome is consistent with the findings of previous studies on PwH in Europe.[8,21] Hartl et al. reported that fewer PwH were employed or in training than their controls in Austria (64% vs. 90%, $p < .001$), but the number of participants in haemophilia group and control group was small (53 and 104, respectively) and people with mild, moderate and severe haemophilia were not differentiated.[21] Plug et al. showed the employment rate of PwSH to be lower than that of the general population in the Netherlands (67% vs. 73%).[8] Similarly, the *2008 Quality of life survey for French people with haemophilia* showed that the observed employment rate was 52% among adult participants, while it was 68.1% in the general population.[22,23] However, no formal statistical comparison was conducted in this survey.

Contrary to the employment situation of PwSH, their education level was higher than that of the general population. Previous studies also revealed an equivalent or higher education level for PwH in

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TABLE 3 Occupational integration of PwSH compared to the French general population

	Whole study population	18–24 years		25–49 years		50–64 years		SR	95% CI
		Study population	General population	Study population	General population	Study population	General population		
Participants, n	588	79		335		174			
Occupational status, %									
In employment	61.6	49.4	31.5	73.4	85.4	44.3	65.4	.85	.77–.94
Unemployed	10.0	15.2	8.3	11.9	7.0	4.0	4.6	1.55	1.18–2.00
Inactive	28.4	35.4	60.2	14.7	7.6	51.7	30.0	1.32	1.12–1.53
Working time if in employment, %									
Full-time	86.1	90.0	84.0	85.5	94.1	86.7	89.2	.94	.83–1.05
Part-time	13.9	10.0	16.0	14.5	5.9	13.3	10.8	1.76	1.29–2.34
Type of contract if in employment, %									
Self-employed	12.7	5.2	2.7	12.9	10.8	15.8	17.3	1.10	.80–1.47
Open-ended employment contract	75.2	47.4	44.6	77.2	77.9	82.9	76.4	1.00	.88–1.12
Fixed-term employment contract	5.6	13.2	28.4	5.8	8.5	1.3	5.0	.56	.34–.86
Apprenticeship	3.7	26.3	17.4	1.2	.3	0	0	1.72	.92–2.95
Interim	2.8	7.9	6.9	2.9	2.5	0	1.2	1.02	.49–1.88
Category of occupation if in employment, %									
Farmer	.8	0	.2	.3	1.1	2.6	2.6	.55	.11–1.60
Employee	44.7	59.5	37.6	45.6	25.3	35.1	27.0	1.65	1.40–1.92
Intermediate occupation	2.8	0	23.6	3.2	27.8	2.6	21.8	.11	.05–.20
Executive, senior intellectual worker, accredited professional and equivalent	34.2	13.5	6.2	33.1	20.5	48.1	20.4	1.79	1.49–2.14
Craftsman, tradesman, business executive	7.8	8.1	1.4	6.8	6.0	10.4	9.5	1.24	.82–1.79
Manual labourer	9.7	18.9	30.5	11.0	18.9	1.2	18.2	.48	.41–2.60

Source: INSEE, 2019 Employment survey.
Abbreviations: CI, confidence interval.; PwSH, people with severe haemophilia; SR, standardised ratio.

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TABLE 4 Education level of PwSH compared to the French general population

	Whole study population	25–34 years		35–44 years		45–54 years		55–64 years			
		Study population	General population	Study population	General population	Study population	General population	Study population	General population	SR	95% CI
Participants, n	509	137		136		132		104			
Education level, %											
No diploma/Primary and secondary education	8.5	3.6	14.1	11.2	15.2	8.4	20.7	11.7	28.2	.44	.32–.60
Vocational diploma	23.0	21.2	19.5	16.4	22.2	27.5	32.1	28.2	36.1	.76	.63–.92
High school	19.8	21.9	22.5	19.5	20.4	15.3	15.0	23.2	11.8	1.10	.90–1.34
Second-year university or equivalent	17.2	15.3	13.2	20.1	16.3	19.8	13.4	12.6	9.6	1.28	1.03–1.58
Bachelor's, Master's, Doctoral degree	31.5	38.0	30.2	32.8	25.6	29.0	18.5	24.3	14.1	1.38	1.17–1.61

Source: INSEE, 2019 Employment survey.
Abbreviations: CI, confidence interval.; PwSH, people with severe haemophilia; SR, standardised ratio.

Europe and the USA.[7,8,15,24–26] The contradiction between high level of education and low employment rate may be explained by several factors such as insufficient physical abilities to compete for employment, for example, people having hemarthroses could have reduced physical mobility leading to difficulties to be employed.[7,26] In terms of career options, employed PwSH were more likely to have white-collar jobs than the general population. These occupations could be more suitable for PwSH, since they are at lower risk of injuries and do not require heavy physical activities. Therefore, career options of PwSH may depend on certain haemophilia-related problems such as limited physical abilities, and also because they have great educational achievements.[6,7]

Compared to the general population, employed PwSH were more likely to have part-time jobs. In the PROBE (Patient Reported Outcomes, Burdens and Experiences) study on part-time employment and early retirement of PwSH,[27] a higher part-time employment rate due to health problems (use of mobility aids, pain, difficulties with activities of daily living, history of joint surgery) was found among PwSH compared to people with no bleeding disorder (31.4% vs. 3.75%, $p < .0001$). It can be assumed that PwSH choose part-time jobs since they have more health concerns than other people, and hypothetically, working part-time could be considered as a good way to stay employed for people with chronic pathologies.[28]

The retirement age of PwSH was similar to the legal retirement age in France (61.3 and 62 years, respectively), while previous studies on socioeconomic status of PwH in Austria and Germany[21,29] found that PwH had early retirement due to their health or disease.

Negative effect of HIV infection on employment was observed, whereas no significant effect on physical health was found. Plug et al. showed that HIV infection among Dutch PwH was associated with a higher risk of occupational disability or reduced work performance.[8] Additionally, the occupational integration of people with HIV seemed to be complicated due to prejudices and stereotypes, rather than physical burden.[30]

Mental health concerns and poorer physical health were found to have negative effect on occupational integration. Very few studies have been dedicated to mental problems and occupational situation of PwH. Previous studies on HRQoL and psychosocial aspects of PwH[5–7,15] did not analyse the association between mental health concerns (stress, anxiety, depression) and employment, but they showed that these concerns were common among PwH, and potentially had a negative impact on work performance, leading to occupational instability. In the HERO project, physical limitations due to joint pain and functional impairment were reported to decrease employability and work performance.[4,6,25,31] Employed people still experienced haemophilia-related restrictions in job performance such as pain and frequent absence.[8,32]

Physical health and mental health concerns were not only the determinants of occupational integration but also mediators of sociodemographic and clinical characteristics. People receiving prophylaxis had a lower physical health compared to people receiving on-demand treatment, and current use of prophylaxis had negative indirect effect on occupational integration through physical health and mental health

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TABLE 5 Results of the univariate analysis on determinants of occupational integration

	People in employment n (%) / Mean (SD)	People not in employment n (%) / Mean (SD)	*p*-value
Participants, n	359	154	
Sex			>.999
Male	357 (99.4)	153 (99.4)	
Female	2 (.6)	1 (.6)	
Age, years	38.8 (11.2)	42.1 (12.1)	.003
Tertiary education level			<.001
No (below tertiary level)	154 (42.9)	112 (72.7)	
Yes	205 (57.1)	42 (27.3)	
Living in or near the city			.841
No	201 (56.5)	88 (57.9)	
Yes	155 (43.5)	64 (42.1)	
Not available	*3*	*2*	
SF-12			
PCS	42.4 (11.1)	35.3 (11.0)	<.001
MCS	46.8 (10.5)	43.6 (11.5)	.003
STAI-Y			
State	36.6 (12.3)	40.4 (14.9)	.005
Trait	40.3 (10.2)	44.0 (11.1)	<.001
CES-D	7.7 (5.5)	10.1 (6.1)	<.001
Type of haemophilia			.997
Haemophilia A	299 (83.3)	129 (83.8)	
Haemophilia B	60 (16.7)	25 (16.2)	
History of inhibitors			.191
No	301 (83.8)	121 (78.6)	
Yes	58 (16.2)	33 (21.4)	
History of intracranial haemorrhage			.805
No	346 (96.4)	147 (95.5)	
Yes	13 (3.6)	7 (4.5)	
History of major orthopaedic interventions			.025
No	166 (46.2)	54 (35.1)	
Yes	193 (53.8)	100 (64.9)	
HIV			.001
No	287 (79.9)	102 (66.2)	
Yes	72 (20.1)	52 (33.8)	
HBV			.044
No	262 (73.0)	98 (63.6)	
Yes	97 (27.0)	56 (36.4)	
HCV (ever infected)			.025
No	144 (40.1)	45 (29.2)	
Yes	215 (59.9)	109 (70.8)	
If ever infected with HCV			.868
With active chronic HCV	45 (21.4)	25 (22.9)	
Without active chronic HCV	165 (78.6)	84 (77.1)	
Not available	*5*	*0*	

(Continues)

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TABLE 5 (Continued)

	People in employment n (%) / Mean (SD)	People not in employment n (%) / Mean (SD)	*p*-value
Cancer			.057
No	356 (99.2)	149 (96.8)	
Yes	3 (.8)	5 (3.2)	
Other chronic pathology			.101
No	305 (85.1)	121 (78.2)	
Yes	54 (14.9)	33 (21.8)	
Age at start prophylaxis, years	29.2 (16.4)	28.1 (15.4)	.483
Current therapeutic regimen			.124
On-demand treatment	122 (34.0)	41 (26.6)	
Prophylaxis	237 (66.0)	113 (73.4)	
Dose of prophylaxis (per year)			.883
High dose	84 (41.5)	43 (45.3)	
Intermediate dose	79 (49.2)	43 (45.3)	
Low dose	14 (9.3)	9 (9.4)	
Not available	*60*	*18*	
Primary prophylaxis			.892
No	137 (66.2)	64 (64.6)	
Yes	70 (33.8)	35 (35.4)	
Not available	*30*	*14*	

Abbreviations: CES-D, center for epidemiological studies-depression; HBV, hepatitis B virus; HCV, hepatitis C virus; MCS, mental component summary; PCS, physical component summary; SD, standard deviation; SF-12, short form 12 health survey; STAI-Y, state-trait anxiety inventory (form Y).

concerns. Previous studies showed different results on the association between prophylaxis and HRQoL.[31,33,34] In a study of the HERO project, people currently on prophylaxis reported more mobility issues and poorer HRQoL than those having on-demand treatment.[31] Similar to the EQOFIX study on HRQoL of PwH B, people on prophylaxis had lower HRQoL compared to people receiving on-demand treatment.[33] However, in another study on European PwSH, long-term prophylaxis was associated with improvements in HRQoL.[34] This treatment has been available in Sweden since the late 1970s, while in France, PwH started to receive it in the mid 1990s. Swedish people spent a higher percentage of their life on prophylaxis, and they had better ability to do everyday activities, lower annual bleeding rates and lower number of days missed from work/college. A study on long-term outcome of prophylaxis and on-demand treatment for severe haemophilia also found that Dutch people on prophylaxis had better HRQoL than French people having on-demand treatment.[35] Another study on dose of prophylaxis for severe haemophilia showed that Swedish people with high-dose prophylaxis had reduction in bleeding and haemophilic arthropathy compared to Dutch people with intermediate-dose prophylaxis, while there was no significant difference in HRQoL.[36] The different results on prophylaxis may be explained by the burden of the regular infusion of blood-clotting factors which could decrease the HRQoL,[33] the length of the period of using prophylaxis and dose of prophylaxis. However, age at start prophylaxis and dose of prophylaxis were not significantly associated with the employment status and HRQoL (data not shown) in our project. There might also be confounders of the association between prophylaxis and occupational integration, for example the bleeding phenotype, but this data was not available to be explored.

Health problems such as physical limitations, mental health concerns and comorbid conditions were barriers, while having a tertiary education level was a motivator to the occupational integration of PwSH. Although, previous studies on educational attainment of PwH in Europe and the United States did not precisely analyse the association between education and employment, they still considered education to be a crucial element in improving the occupational lives of the participants.[7,15,25]

4.2 | Strengths and limitations

Concerning clinical characteristics, there might be selection bias when more participants had health problems (major orthopaedic interventions, HIV, HBV, HCV) than non-participants and the participants were older than the non-participants.

This study used self-administered questionnaires to collect data from the participants, which might lead to non-representativeness of the study population due to non-response bias. Nevertheless, the sample size of this study is large, and it is based on an exhaustive national cohort of PwSH in France. In terms of methodology, indirect

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TABLE 6 Effects of the determinants on occupational integration (n = 513)

	Direct Effect OR (95% CI)	TotalIndirect Effect[a] OR (95% CI)	Total Effect OR (95% CI)
Age, years	1.00 (.98–1.02)	.99 (.98–.99)	.99 (.97–1.00)
Education level			
Tertiary education	1.94 (1.49–2.53)	1.13 (1.05–1.22)	2.20 (1.68–2.87)
Residential location			
Living in or near the city	.87 (.68–1.12)	1.07 (.99–1.14)	.93 (.72–1.20)
Physical health	1.03 (1.02–1.04)		
Mental health concerns[b]	.98 (.97–.99)		
Complications			
History of inhibitors	.85 (.61–1.18)	.94 (.88–1.01)	.80 (.57–1.12)
History of intracranial haemorrhage	1.12 (.60–2.07)	.88 (.74–1.03)	.97 (.51–1.89)
History of major orthopaedic interventions	.96 (.73–1.24)	.93 (.87–1.00)	.89 (.68–1.17)
Comorbidities			
HIV	.69 (.50–.94)	1.04 (.96–1.12)	.71 (.52–.98)
HBV	1.02 (.76–1.37)	.96 (.89–1.03)	.97 (.72–1.32)
HCV	.93 (.59–1.44)	1.00 (.91–1.10)	.93 (.59–1.46)
Cancer	.57 (.19–1.71)	.89 (.75–1.05)	.50 (.16–1.55)
Other chronic pathology	1.02 (.71–1.47)	.99 (.91–1.08)	1.01 (.70–1.46)
Current therapeutic regimen			
Prophylaxis	.75 (.56–1.00)	.91 (.84–.99)	.68 (.51–.92)

Abbreviations: CI, confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus.; OR, odds ratio.
[a]Total indirect effect via physical health and mental health concerns.
[b]Latent variable manifested by observed scores of STAI-Y, CES-D and MCS of SF-12.

standardization limits the effect of different age distributions which is important in terms of employment. The impacts of individual characteristics on occupational integration were examined more completely in SEM, allowing to detect some underlying determinants that traditional regressions may not find. Mediation analysis and CFA can also be conducted in SEM, leading to possibility of testing many hypotheses related to occupational integration and higher statistical power than traditional regressions.[37]

This project provides additional information on the occupational integration of PwSH. The determinants of occupational integration found in this project could help caregivers to identify PwSH having more occupational difficulties and to offer career advice. Complementary studies could be carried out for people at high risk of having employment-related problems to deeper investigate the motivators and barriers of the employment such as education level, mental health concerns and prophylactic treatment. Moreover, a longitudinal study could have more possibilities to assess the causality of the relation for factors influencing the occupational integration, and an interventional study could be proposed to assess some supportive strategies for occupational lives of PwSH. Self-management programs and cognitive-behavioural therapy could also be effective for work performance and return to work of people with chronic diseases.[38,39]

5 | CONCLUSION

Deterioration in physical and mental health, as well as HIV infection could be associated with difficult occupational integration and decrease in employability. HCV infection, however, does not appear to affect occupational integration of PwSH. Contrary to the employment situation, education level of PwSH was higher than expected. This is also a determinant of successful occupational integration. Apparently, health and high educational attainment are key factors to job opportunities for PwSH. More support programs targeting the determinants of employment are necessary to help PwSH overcome difficulties in occupational integration.

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CONFLICTS OF INTEREST

The authors have no competing interests.

AUTHOR CONTRIBUTIONS

Ngoc Anh Thu Nguyen, Pascal Auquier, Any Beltran Anzola, Natacha Rosso-Delsemme, Hervé Chambost and Noémie Resseguier conceived the study. The investigators of the French Haemophilia Treatment Centres (R.D., C.F., C.B., AnLi, J.G., A.R., B.W., S.M.C., D.D., AnHa, N.S., A.B.-D., M.T., A.C., B.G., S.B., M.-A.B., A.F., G.M., V.G., P.C., E.D., B.F., M.M., M.P., B.T., S.V., F.G.-V., P.N., B.P., C.O.-C., S.G., A.V., A.L., A.H., P.M., P.-S.R. and H.C.) enrolled participants. The members of the Association française des hémophiles (Nicolas Giraud and Thomas Sannié) contributed with communication actions for participants. The members of the FranceCoag registry (Karine Baumstarck, Mohamed Boucekine, Vanessa Milien, Clemence Tabele, Pascal Auquier and Hervé Chambost) contributed by supplying datasets of the registry. Ngoc Anh Thu Nguyen and Natacha Rosso-Delsemme performed the statistical analyses. Ngoc Anh Thu Nguyen, Pascal Auquier, Any Beltran Anzola and Natacha Rosso-Delsemme wrote the draft of the manuscript. All authors critically reviewed the manuscript, provided input on data interpretation, and approved the final version of manuscript.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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APPENDIX

INTHEMO STUDY GROUP

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