

# Aging and health status in persons leaving with hemophilia and controls without a bleeding disorder

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## INTRODUCTION

People with hemophilia (PWH) have a life expectancy disadvantage as compared to the general population but little is known about the impact of aging on health status and health-related quality of life (HRQL). The aim of the analysis was to assess the characteristics of the association between aging, health status and HRQL in PWH and people with no bleeding disorders (PWNoBD).

## METHODS

A cross-sectional, multinational study was conducted as part of the Patient Reported Outcomes, Burdens and Experiences (PROBE) project. PWH and PWNoBD were asked to complete the PROBE questionnaire. Measures of health status and HRQL were the PROBE score, the EQ-5D-5L utility index, and the EuroQol visual analog scale (EQ-VAS) of global health. The association between these measures and the age of participants was explored using a multivariable model adjusting for sex (all) and disease severity (PWH only) and stratifying by country.

## AFFILIATION

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## RESULTS

**Table 1: Characteristics of the study population**

| People with hemophilia (n = 1157)*      |                   |                   |                   |                   | People with no bleeding disorders (n = 690)  |                   |                   |                   |                   |
|---|-------------------|-------------------|-------------------|-------------------|--|-------------------|-------------------|-------------------|-------------------|
|   | Age category      |                   |                   |                   |  | Age category      |                   |                   |                   |
|   | 18 – 44           | 45 – 64           | 65 – 74           | ≥ 75              |  | 19 – 44           | 45 – 64           | 65 – 74           | ≥ 75              |
| n (%)**                                 | 732 (63)          | 331 (29)          | 73 (6)            | 21 (2)            | n (%)**  | 335 (49)          | 272 (39)          | 71 (10)           | 12 (2)            |
| Income***                               |                   |                   |                   |                   | Income***  |                   |                   |                   |                   |
| Low Middle                              | 65 (9)            | 10 (3)            | 0 (0)             | 0 (0)             | Low Middle   | 12 (4)            | 3 (1)             | 0 (0)             | 0 (0)             |
| Upper Middle                            | 302 (41)          | 40 (12)           | 2 (3)             | 3 (14)            | Upper Middle   | 95 (28)           | 53 (19)           | 15 (21)           | 4 (33)            |
| High                                    | 365 (50)          | 281 (85)          | 71 (97)           | 18 (86)           | High   | 228 (68)          | 216 (79)          | 56 (79)           | 8 (67)            |
| Male (%)                                | 706 (96)          | 317 (96)          | 71 (97)           | 20 (95)           | Male (%)   | 144 (43)          | 116 (43)          | 36 (51)           | 4 (33)            |
| No. Of Comorbidities [Median (range)]   | 1 (0 - 8)         | 1 (0 - 9)         | 1 (0 - 7)         | 1 (0 - 4)         | No. Of Comorbidities [Median (range)]  | 0 (0 - 6)         | 0 (0 - 6)         | 0 (0 - 5)         | 1.5 (0 - 3)       |
| PROBE Score (n = 982) [median (Q1; Q3)] | 0.76 (0.64; 0.85) | 0.68 (0.57; 0.78) | 0.71 (0.64; 0.80) | 0.67 (0.52; 0.84) | PROBE Score (n = 580) [median (Q1; Q3)]  | 0.92 (0.83; 0.98) | 0.90 (0.79; 0.96) | 0.86 (0.79; 0.93) | 0.75 (0.69; 0.89) |
| EQ-5D (n = 1109) [median (Q1; Q3)]      | 0.82 (0.70; 0.92) | 0.75 (0.62; 0.84) | 0.76 (0.63; 0.88) | 0.68 (0.52; 0.86) | EQ-5D (n = 666) [median (Q1; Q3)]  | 0.92 (0.83; 0.98) | 0.94 (0.87; 1.00) | 0.94 (0.83; 1.00) | 0.84 (0.50; 1.00) |
| VAS (n = 1228) [median (Q1; Q3)]        | 0.75 (0.60; 0.90) | 0.70 (0.50; 0.80) | 0.73 (0.60; 0.84) | 0.62 (0.50; 0.80) | VAS (n = 675) [median (Q1; Q3)]  | 0.85 (0.75; 0.90) | 0.80 (0.75; 0.90) | 0.85 (0.80; 0.90) | 0.80 (0.65; 0.88) |
| <b>Hemophilia severity</b>              |                   |                   |                   |                   | <small>*Unless otherwise specified **Row percentage (across age categories), all other percentages are within risk categories. ***This refers to the average per-capita income of the country according to the World Bank<br/>Q1: first quartile; Q2: third quartile; PROBE = patient reported outcomes burden and experience; VAS = visual analogue scale</small> |                   |                   |                   |                   |
| Mild (FL < 0.05 IU/mL)                  | 72 (10)           | 70 (21)           | 23 (32)           | 7 (33)            | 1157 PWH and 690 PWNoBD completed the questionnaire in 33 countries from 2016 to 2019. Eight percent of the PWH and 12% of the PWNoBD were aged ≥65 years.   |                   |                   |                   |                   |
| Moderate (FL 0.01-0.05 IU/mL)           | 136 (19)          | 50 (15)           | 7 (10)            | 8 (38)            |  |                   |                   |                   |                   |
| Severe (FL < 0.01 IU/mL)                | 524 (72)          | 211 (64)          | 43 (59)           | 6 (29)            |  |                   |                   |                   |                   |

As expected, the EQ-5D utility index and EQ-VAS did not show a variation with aging in PWNoBD, while in PWH they were reduced respectively by 0.031 (95% confidence interval [CI] 0.021-0.041) and 0.030 (95% CI 0.014-0.047) every 10 years. Aging was associated with a mean reduction in the PROBE score of 0.010 (95% CI 0.004 to 0.017) every 10 years in PWNoBD. PWH showed an additional reduction in the PROBE score of 0.015 (95% CI 0.008 to 0.022) every 10 years.

## CONCLUSIONS

Aging is associated with a steeper decrease in health status and HRQL in PWH than in PWNoBD. PROBE is more sensitive than EQ5D in measuring the association of aging for the specific domains measured in both PWH and PWNoBD.

## DISCLOSURE

PROBE is an independent investigator led research project with grant / research support from: Bayer, CSL, Novo Nordisk, Roche, Sanofi, Sobi, Takeda and collaboration of the US National Hemophilia Foundation and McMaster University.

**Table 2: Results of the multivariable analyses**

| Explanatory variable | PROBE Score n = 1562 |                  | EQ-5D utility index n = 1775 |                  | EQ VAS n = 1803 |                  |
|----------------------|----------------------|------------------|------------------------------|------------------|-----------------|------------------|
|                      | Coeff**              | 95% CI           | Coeff**                      | 95% CI           | Coeff**         | 95% CI           |
| Age                  | -0.0010              | -0.0017; -0.0004 | -0.0003                      | -0.0012; -0.0007 | 0.0000          | -0.0009; 0.0009  |
| Interaction Age*PWH  | -0.0015              | -0.0022; -0.0008 | -0.0031                      | -0.0041; -0.0021 | -0.0030         | -0.0047; -0.0014 |
| Male sex             | 0.0125               | -0.0145; 0.0396  | 0.0129                       | -0.0145; 0.0404  | 0.0061          | -0.0182; 0.0304  |
| NoBD                 | Ref                  | -                | Ref                          | -                | Ref             | -                |
| Mild                 | -0.0282              | -0.0749; 0.0184  | 0.0634                       | -0.0028; 0.1297  | 0.0851          | -0.0001; 0.1702  |
| Moderate             | -0.1241              | -0.1668; -0.0813 | -0.0461                      | -0.1233; 0.0312  | 0.0014          | -0.1011; 0.1039  |
| Severe               | -0.1152              | -0.1582; -0.0722 | -0.0780                      | -0.1524; -0.0036 | -0.0143         | -0.0942; 0.0657  |
| Constant             | 0.9130               | 0.8855; 0.9405   | 0.9166                       | 0.8720; 0.9613   | 0.8161          | 0.7686; 0.8636   |

\*The regression coefficients can be interpreted as the adjusted mean difference in the score. For the PROBE score and VAS, that ranges from 0 to 1, the coefficient times 100 is equal to the percentage variation in the score, with a negative sign indicating a reduction. For EQ-5D utility value, that ranges from -0.594 to 1, the coefficient needs to be reported to a scale 0-100 before being interpreted as a percentage variation.