



Comparison of the measurement properties of the PROBE and EQ5D-5L on the pain assessment

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Background

- Hemophilia is an inherited bleeding disorder characterized by congenital defect of coagulation protein (or coagulation factor)
 - Blood does not clot properly
- Bleeding into joints and muscle is a common feature
- People living with hemophilia may experience
 - Acute pain caused by acute joint and soft tissue bleeding
 - Chronic pain secondary from chronic joint bleeding and joint damage

Gringeri A, et al. Haemophilia 2014; 20:459–463.

Background

- 89% of adults with hemophilia state that pain interferes with their lives
- Pain may impact physical health, well being and social engagement.
- Therefore, pain is a critical aspect of hemophilia.
- However, to date, there was no standardized pain measurement in people living with hemophilia.

Garrido C, et al. Hemophilia. 2012;18:177.

Rambod et al. Int J Community Based Nurs Midwifery. 2016 ; 4(4): 309–319.

Methods-participant enrollment and data collection

- Participants were enrolled through patient organizations from 2016-2017
- Inclusion criteria
 - PWH or participants without bleeding disorders
 - Age > 10 years
 - To be able to complete the questionnaire by themselves
- Study procedure and data collection
 - Participants were instructed to answer the questionnaire either paper- or web-based version
 - All questionnaires were collected via either paper or on-line versions by patient organizations and then transferred to McMaster University for data management

Methods-PROBE questionnaire

- PROBE is a patient-led research initiative with the main objective to develop a standardised questionnaire to assess health status in people living with hemophilia
- PROBE questionnaire (29 questions in 3 major domains)
 - General health problems
 - Hemophilia-related problems
 - Health-related quality of life
- PROBE has been validated in both people living with hemophilia and participants without bleeding disorders

Chai-Adisaksopha C, et al. BMJ Open 2018;8:e021900.

PROBE items on pain assessment

- During the past 12 months, have you experienced acute pain?
 - ☐ Yes
 - ☐ No

If yes, when did your acute pain occur?
(Please check all that apply)

- ☐ Walking
- ☐ Stair climbing
- ☐ Nighttime (such as waking you up/keeping you awake)
- ☐ Resting
- ☐ Weight bearing
- ☐ Playing (including playing with children) or participating in sports / exercising
- ☐ After falling or a trauma
- ☐ Other (Describe): _____

If yes, when did your acute pain occur?
(Please check all that apply)

- ☐ General activity
- ☐ Mood
- ☐ Walking ability
- ☐ Normal work (including both work outside the home and housework)
- ☐ Attending school
- ☐ Relations with others
- ☐ Sleep
- ☐ Enjoyment of life
- ☐ Playing (including playing with children) or participating in sports / exercising
- ☐ Lifting
- ☐ Other (Describe): _____

PROBE items on pain assessment

- During the past 12 months, have you experienced chronic pain?
 - ☐ Yes
 - ☐ No

If yes, when did your chronic pain occur?
(Please check all that apply)

- ☐ Walking
- ☐ Stair climbing
- ☐ Nighttime (such as waking you up/keeping you awake)
- ☐ Resting
- ☐ Weight bearing
- ☐ Playing (including playing with children) or participating in sports / exercising
- ☐ After falling or a trauma
- ☐ Other (Describe): _____

If yes, when did your chronic pain occur?
(Please check all that apply)

- ☐ General activity
- ☐ Mood
- ☐ Walking ability
- ☐ Normal work (including both work outside the home and housework)
- ☐ Attending school
- ☐ Relations with others
- ☐ Sleep
- ☐ Enjoyment of life
- ☐ Playing (including playing with children) or participating in sports / exercising
- ☐ Lifting
- ☐ Other (Describe): _____

PROBE items on pain assessment

- During the past 12 months did you use any medication for pain?
 - ☐ Yes
 - ☐ No
- If yes, please estimate the percent of the time you used pain medication.
 - ☐ Rarely (1–5% of the time)
 - ☐ Occasionally (6–25% of the time)
 - ☐ Sometimes (26%–50% of the time)
 - ☐ Frequently (51%–75% of the time)
 - ☐ Very frequently (76%–99% of the time)
 - ☐ All of the time (100% of the time)

EQ-5D-5L item on pain assessment

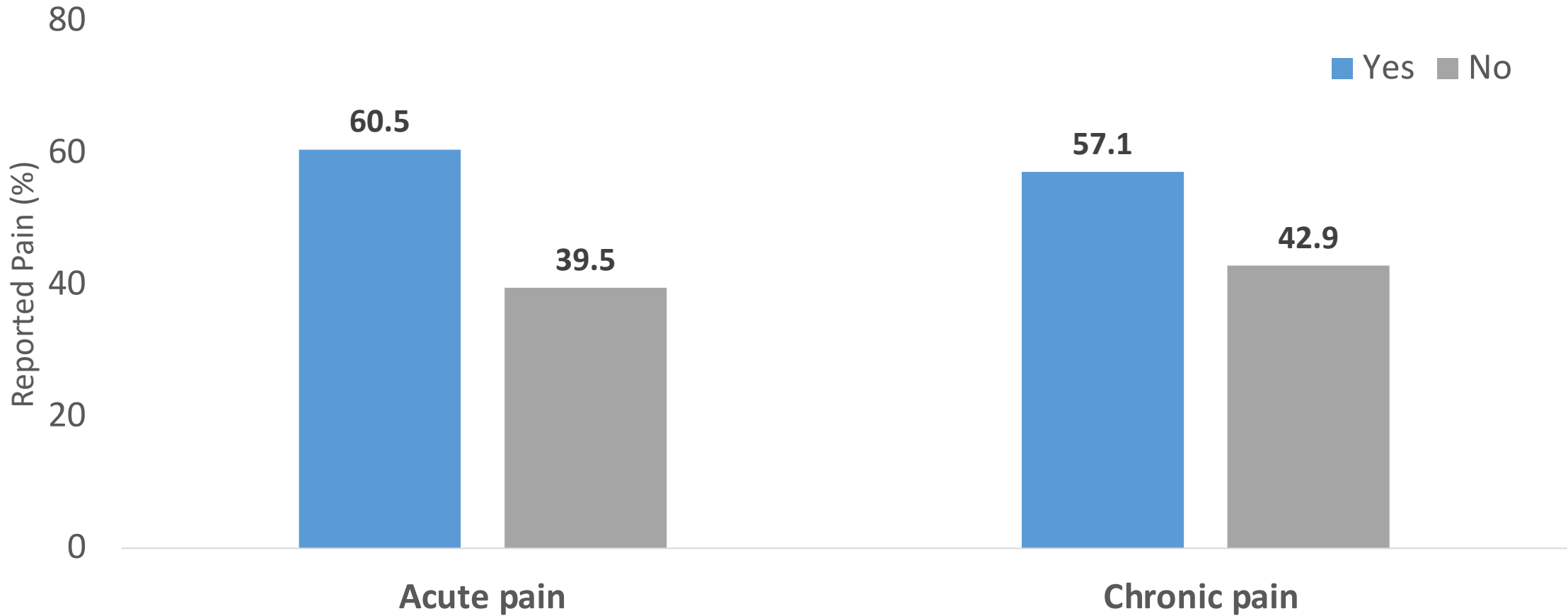
PAIN/DISCOMFORT

- ☐ I have no pain or discomfort
- ☐ I have slight pain or discomfort
- ☐ I have moderate pain or discomfort
- ☐ I have severe pain or discomfort
- ☐ I have extreme pain or discomfort

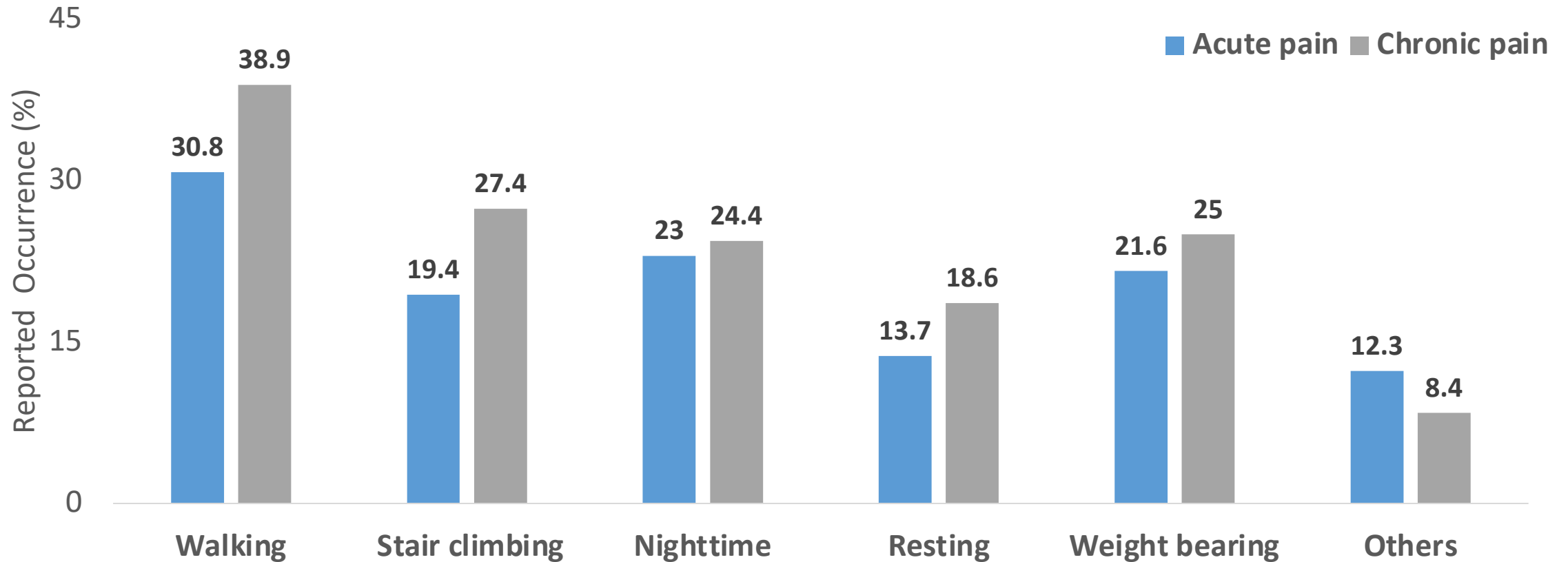
Characteristics of participants

Characteristics	Participants (n=1675)
Age (mean, SD)	37.5 (\pm 17.4)
Sex (male, %)	1,241 (74.2%)
Geographical region	
• Africa	7 (0.4%)
• Western Pacific	333 (19.9%)
• South America	564 (33.7%)
• Europe	490 (29.3%)
• North America	281 (16.8%)
Disease status	
• Hemophilia A	967 (57.7%)
• Hemophilia B	183 (10.9%)
• No bleeding disorder	525 (31.3%)

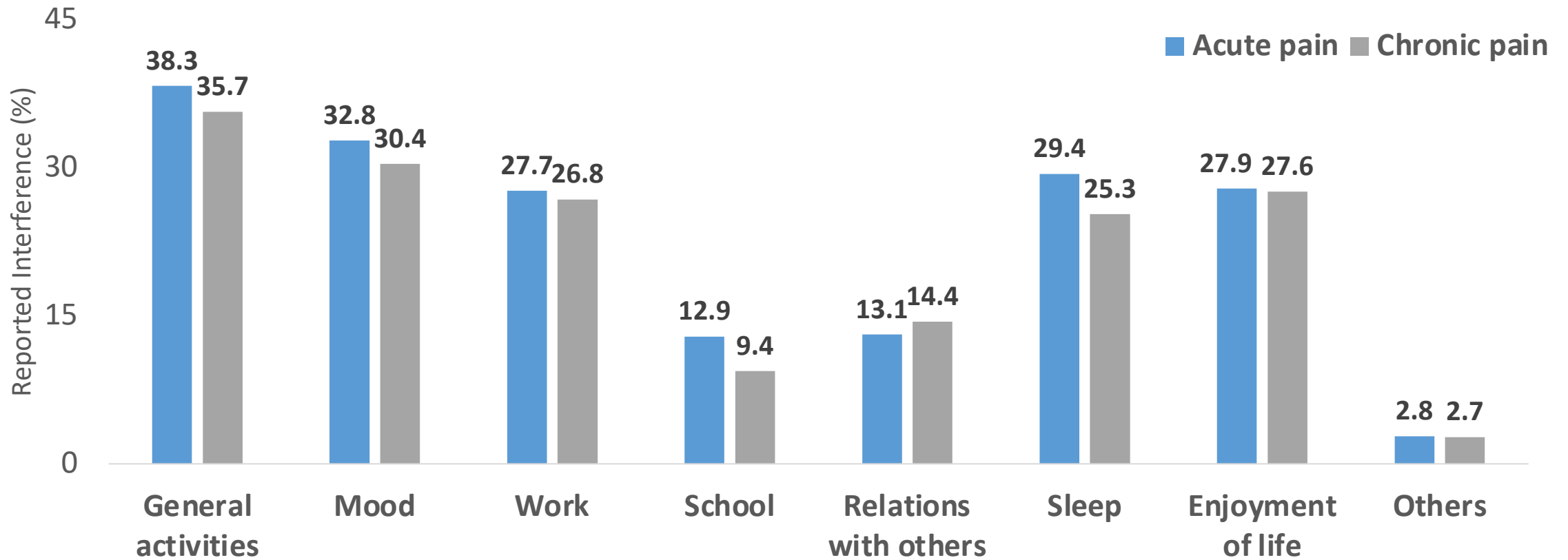
Response to acute and chronic pain items (%)



Occurrence of acute and chronic pain (%)



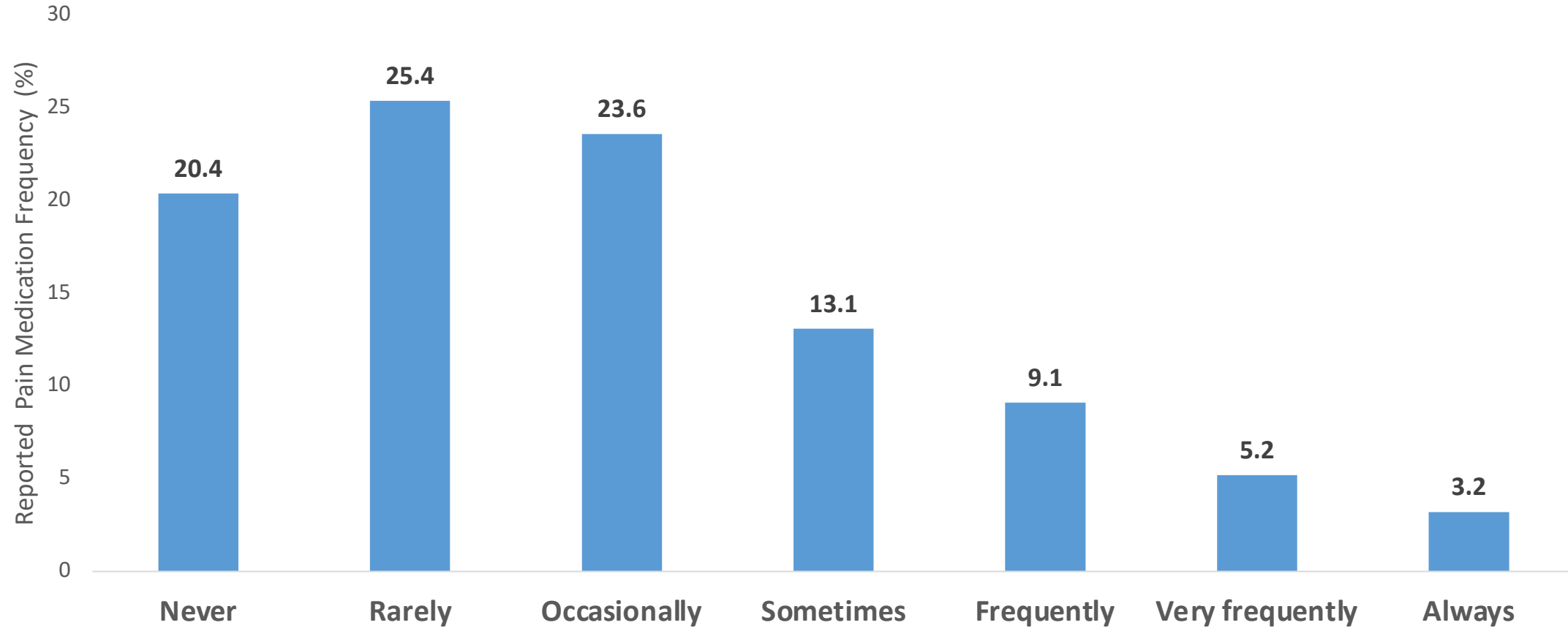
Interference of pain with activities (%)



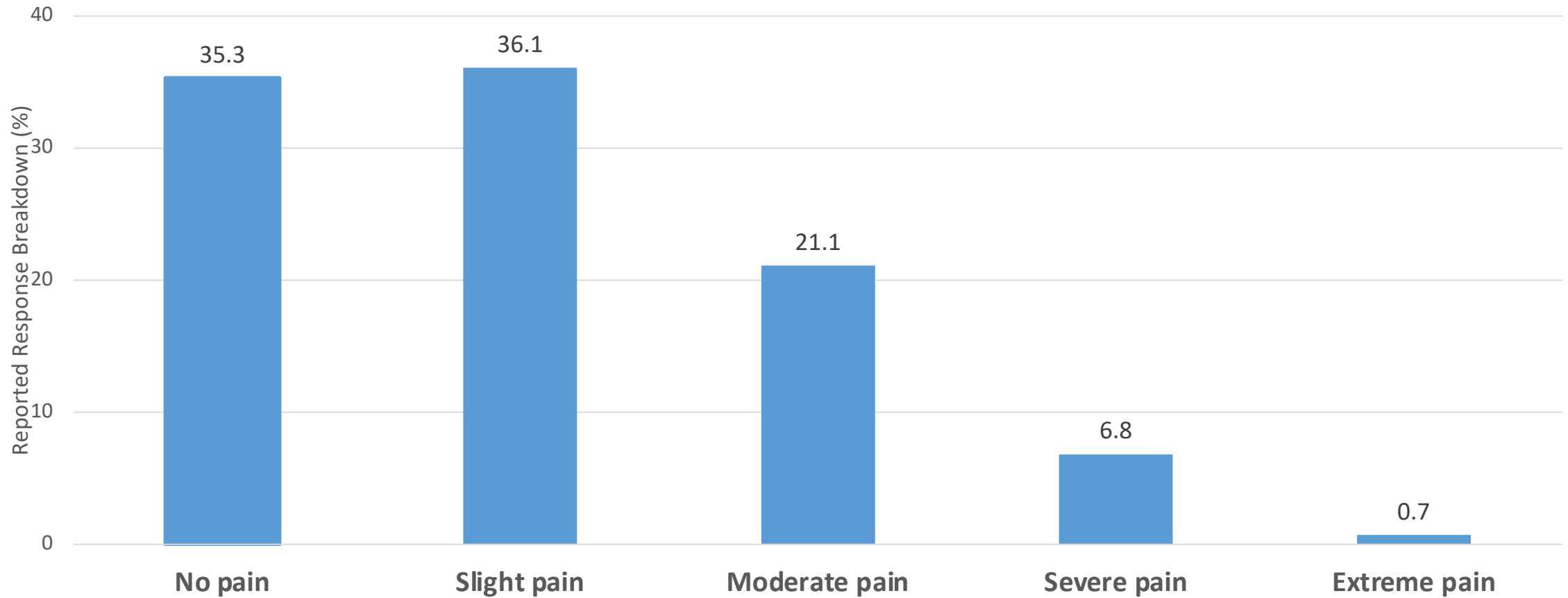
Use of pain medications



Frequency of the use of pain medications



EQ-5D-5L on pain domain (%)

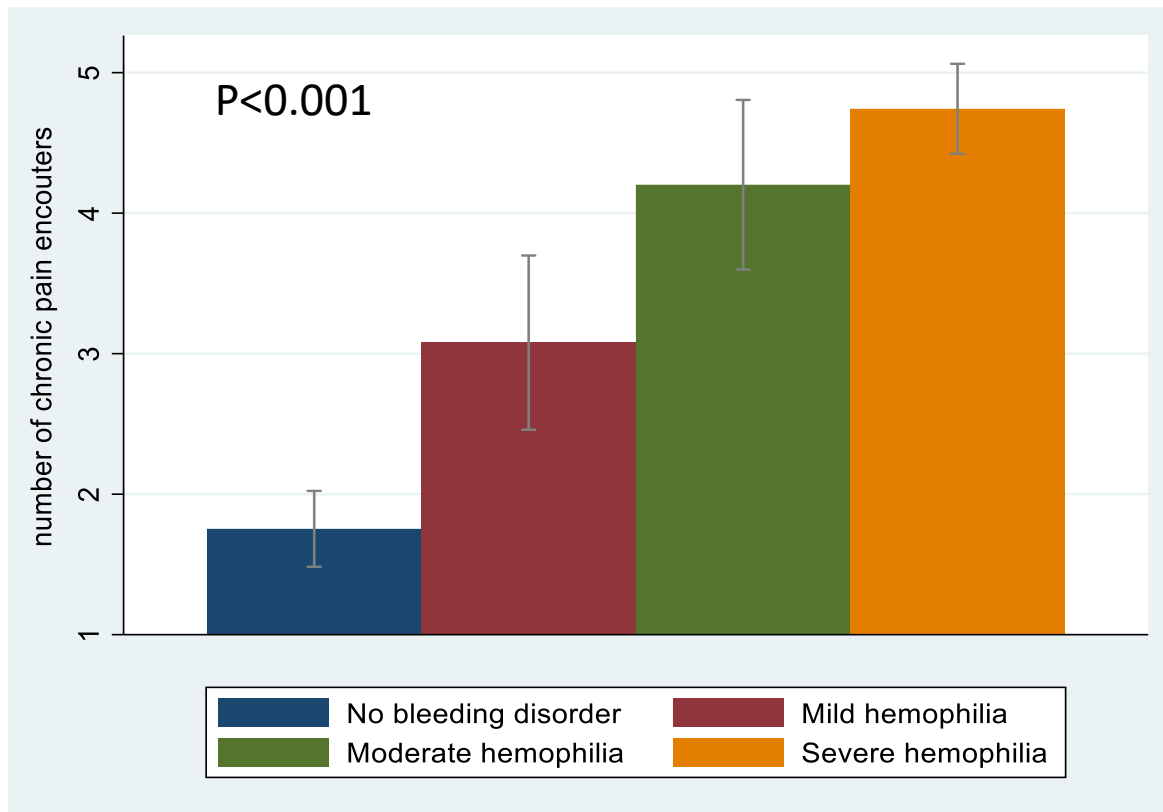


Correlation coefficients of the pain assessment in the PROBE questionnaire and pain domain on EQ5D-5L

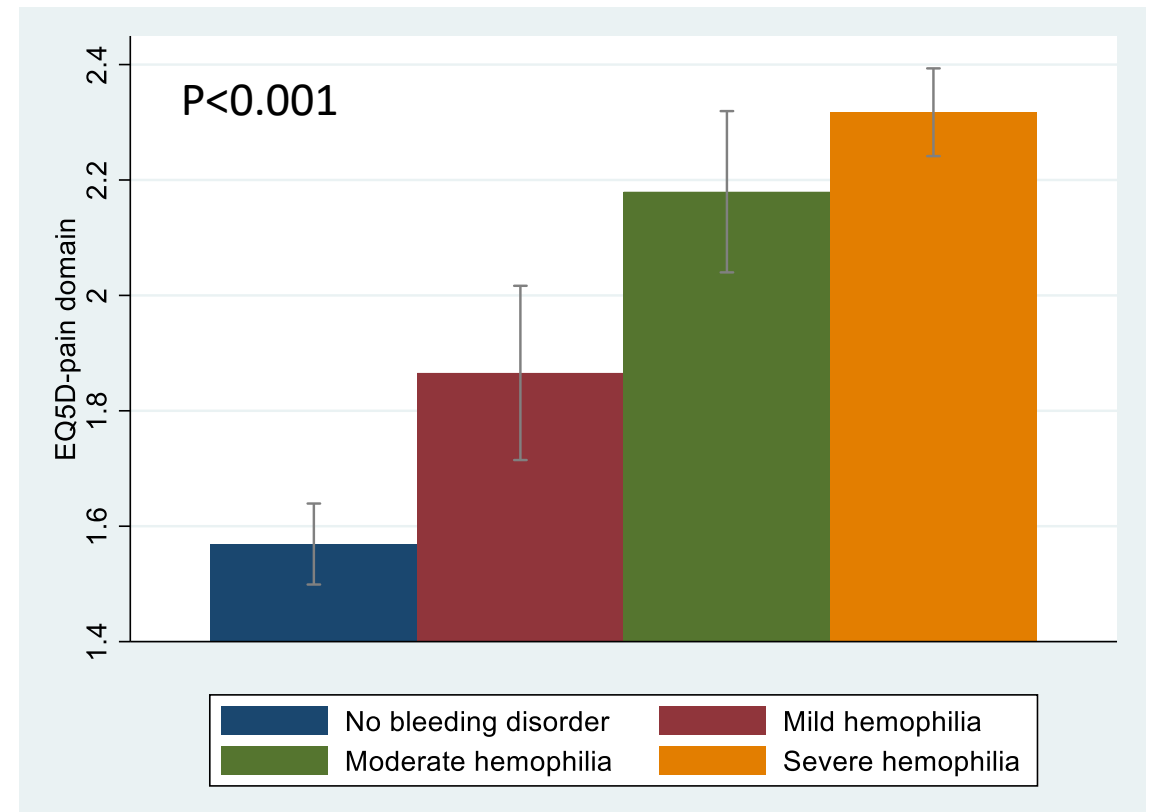
PROBE question	Correlation coefficient	P-value
The occurrence of acute pain (mean counts)	0.43	<0.01
The interfere of acute pain (mean counts)	0.42	<0.01
The occurrence of chronic pain (mean counts)	0.59	<0.01
The interference of chronic pain (mean counts)	0.61	<0.01

The mean number of chronic pain encounters assessed by the PROBE questionnaire

Mean number of chronic pain encounters



Mean pain utility score assessed by the EQ5D-5L



Discussion

- The pain questions on the PROBE questionnaire are well correlated with the pain domain on EQ5D-5L.
- The discriminative property of both tools is found to be excellent to distinguish people with various severity of hemophilia as well as people without bleeding disorders.
- Strength of the PROBE questionnaire on pain assessment
 - It provides more informative data on
 - The use of pain medication
 - Occurrences and interference of acute and chronic pain.

Conclusions

The PROBE questionnaire is a disease-specific patient reported outcome measure, which will provide more insightful information regarding pain status in PWH.

Collaborating Patient Organizations

- Fundación de la Hemofilia (Argentina) Cordoba Chapter
- Hemophilia Foundation Australia
- Federação Brasileira de Hemofilia (Brazil)
- Canadian Hemophilia Society
- Association Française des Hémophiles (France)
- Deutsche Hämophiliegesellschaft (Germany)
- Magyar Hemofilia Egyesület (Hungary)
- Irish Haemophilia Society
- Federazione delle Associazioni Emofilici (Italy)
- National Hemophilia Network of Japan
- Federación de Hemofilia de la República Mexicana (Mexico)
- Nederlandse Vereniging van Hemofilie-Patiënten (The Netherlands)
- Haemophilia Foundation of New Zealand
- Haemophilia Foundation of Nigeria
- Polish Hemophilia Society
- Federación Española de Hemofilia (Spain)
- The Haemophilia Society (United Kingdom)
- National Hemophilia Foundation (US)
- Asociación Venezolana para la Hemofilia (Venezuela)
- Vietnamese Hemophilia Association

Acknowledgements

- PROBE is an independent investigator led research project with grant / research support from:
 - Bayer
 - Bioverative
 - CSL Behring
 - Novo Nordisk (HERO)
 - Roche
 - Shire
 - Sobi
- Project support: National Hemophilia Foundation (US)

For more information

If you have questions or would like more information about PROBE you may directly contact the PROBE investigator team:

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PROBE Global Aims

- Move advocacy beyond emotion and anecdote to **arguments grounded in evidence**
- Address healthcare payers' desire to better understand **outcomes important to patients**
- Illustrate patient knowledge, perspectives and experience can **contribute to defining and measuring key health outcomes**

www.PROBEstudy.org



Validation



- Identified outcomes patients deem relevant to their life¹
- PROBE validation
 - Feasibility assessed and methodology demonstrated¹
 - Questionnaire face validity, relevance, clarity and completeness tested¹
 - Test-Retest reliability (reproducibility) demonstrated²
 - Core analytic framework (psychometric properties) established³
 - Cross-cultural validation⁴
- 2,101 surveys collected in 24 countries (4/2015 - 2/2017)

¹Skinner, MW, et al. Pilot and Feasibility Studies, 2018 4:58. doi: 10.1186/s40814-018-0253-0; ²Chai-Adisaksopha C, et al. Haemophilia. 2018;00:1–9. doi: 10.1111/hae.13649; ³Chai-Adisaksopha C, et al. BMJ Open 2018;8:e021900.. doi: 10.1136/bmjopen-2018-021900; ⁴Chai-Adisaksopha C, Haemophilia. 2019; 00: 1– 8. <https://doi.org/10.1111/hae.13703>

Comparing outcomes patients deem relevant

- Pain - chronic/acute, interference, occurrence
- Independence - limitations, impact on activities of daily living
- Education - attainment, attendance
- Employment - duration, underemployment, attendance
- Family life - marriage, children
- Mobility - assistance required, impairment
- Current health status (EQ-5D-5L – VAS)

Acknowledgments

Investigators

Principal Investigator

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- Michael Nichol Ph.D., University of Southern California, School of Policy and Planning Development (US)
- Declan Noone, Irish Haemophilia Society (Ireland)
- Brian O'Mahony, Irish Haemophilia Society, Trinity College Dublin (Ireland)
- David Page, Canadian Hemophilia Society (Canada)
- Jeff Stonebraker Ph.D., North Carolina State University, Poole College of Management (US)

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- Sanofi
- Sobi
- Takeda

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- McMaster University

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