

Health-Related Quality of Life Over 2 Years Following Valoctocogene Roxaparvovec Adeno-Associated Virus Gene Transfer For Severe Hemophilia A: Results From GENE8-1

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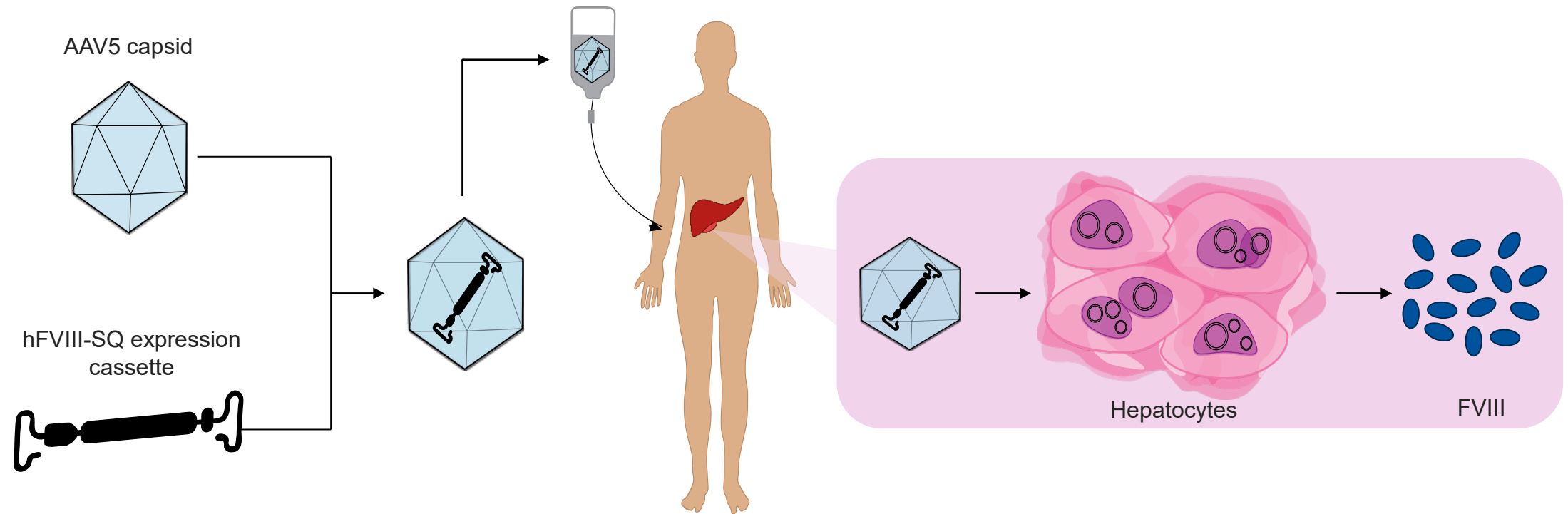
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Director, Officer, Employee	Service on the board of the World Federation of Hemophilia, USA
Shareholder	
Honoraria	
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Consultant	BioMarin Pharmaceutical Inc, Genentech/Roche, Kedrion, CSL Behring, and uniQure

Valoctocogene roxaparvovec gene transfer for severe HA



GENEr8-1 phase 3 study¹

- 134 adult men with severe HA
 - No inhibitors
 - No detectable antibodies to AAV5 capsid
- 6×10^{13} vg/kg valoctocogene roxaparvovec IV infusion
- 132 HIV-negative participants (mlTT population)
- Endpoints
 - Annualized bleeding rate (primary)
 - FVIII activity (secondary)
 - Exogenous FVIII use (secondary)
 - **Quality of life (secondary and tertiary)**

Baseline Characteristics	mlTT (N = 132)
Age at enrollment, years (mean \pm SD)	31.4 \pm 10.1
Male sex	132 (100)
Race and ethnicity ^a	
White	94 (71.2)
Asian	19 (14.4)
Black or African American	15 (11.4)
Hawaiian or Pacific Islander	1 (0.8)
Not provided ^b	3 (2.3)
Hispanic or Latino ethnicity	7 (5.3)
Number of problem joints at study initiation ^c	
0	95 (72.0)
1	17 (12.9)
2	9 (6.8)
3	8 (6.1)
>3	3 (2.3)
BMI, kg/m ² , (mean \pm SD) ^d	25.3 \pm 4.6

^aRace and ethnic group were reported by the participants. ^bDue to patient privacy laws. ^cProblem joints were identified by the investigators at baseline and were defined as joints with any of the following symptoms: chronic joint pain, chronic synovitis, hemophilic arthropathy, limited motion, or recurrent bleeding; ^dBMI is the weight in kilograms divided by the square of the height in meters. Data are n (%) unless otherwise indicated. BMI, body mass index; HA, hemophilia A; HIV, human immunodeficiency virus; IV, intravenous; mlTT, modified intent-to-treat; SD, standard deviation.

1. Ozelo M et al. *N Engl J Med*. 2022;386(11):1013-1025

Quality of life questionnaires

1

EQ-5D-5L

EuroQol 5 Dimension 5 Level

2

Haemo-QOL-A

Haemophilia-specific Quality of Life
Questionnaire for Adults

3

WPAI+CIQ:HS

Work Productivity and Activity
Impairment plus Classroom Impairment
Questions: Hemophilia Specific

4

HAL

Haemophilia Activities List

EQ-5D-5L

5 dimensions

mobility

self-care

usual activities

pain/discomfort

anxiety/depression

5 levels

no problems

slight problems

moderate problems

severe problems

extreme problems

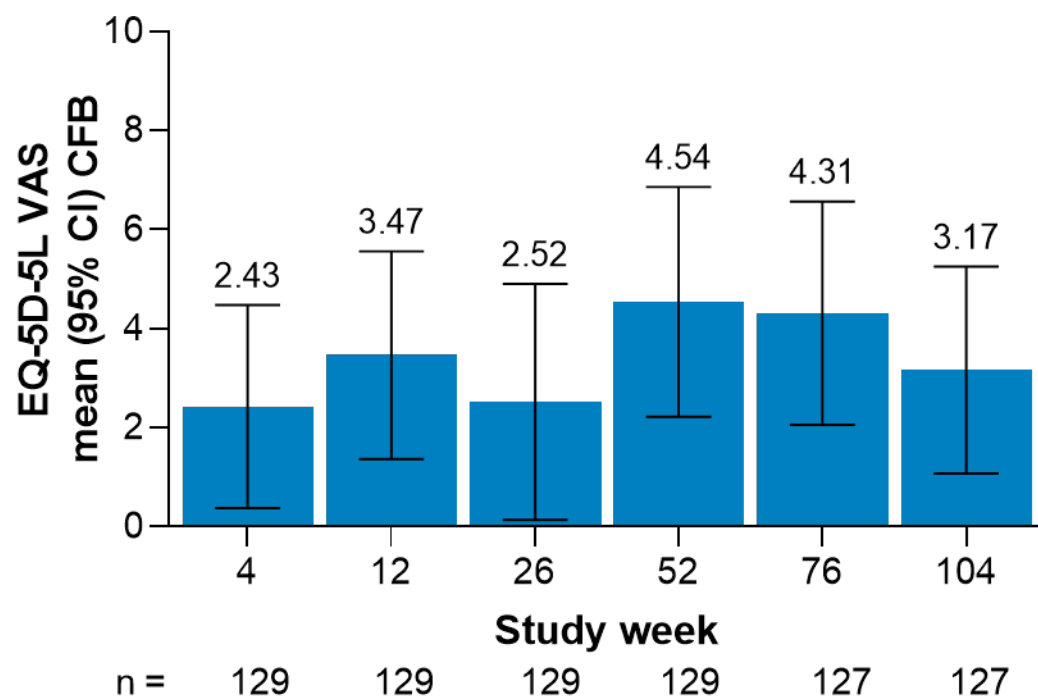


Best health you can
imagine

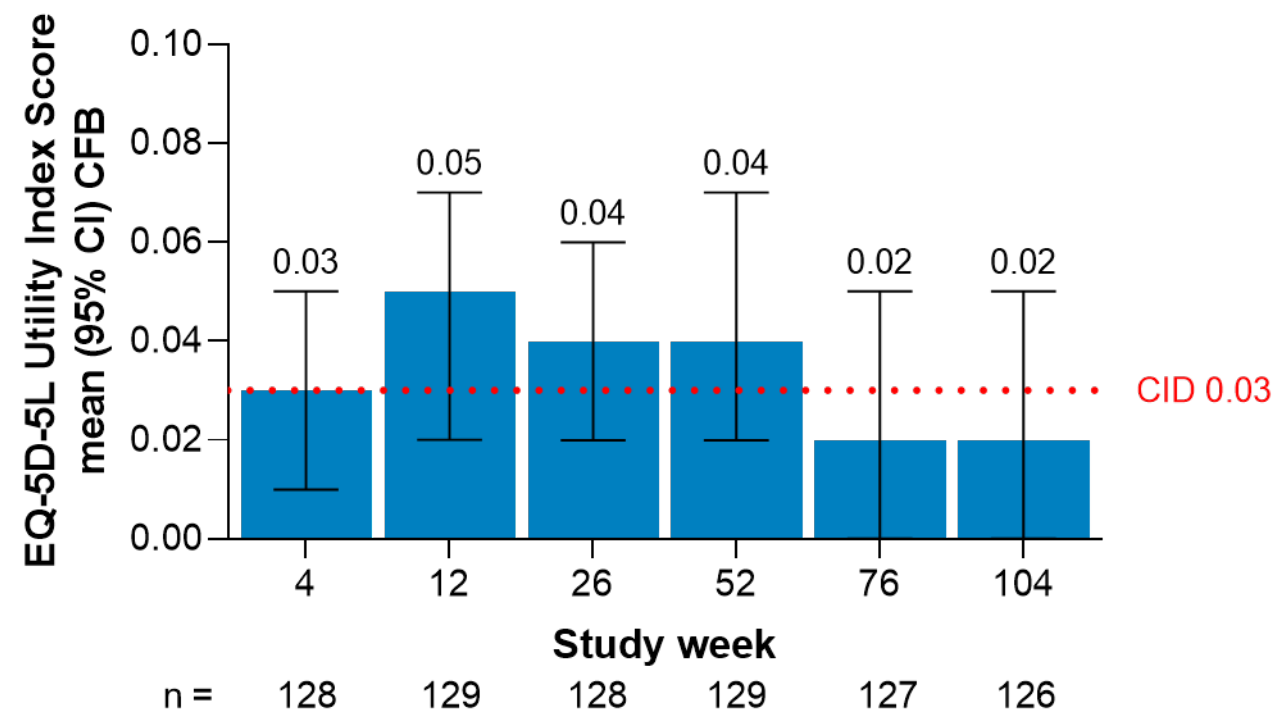
Worst health you can
imagine

EQ-5D-5L VAS and Utility Index scores

EQ-5D-5L VAS



EQ-5D-5L Utility Index Score



Haemo-QOL-A domains

Physical
Functioning

Role
Functioning

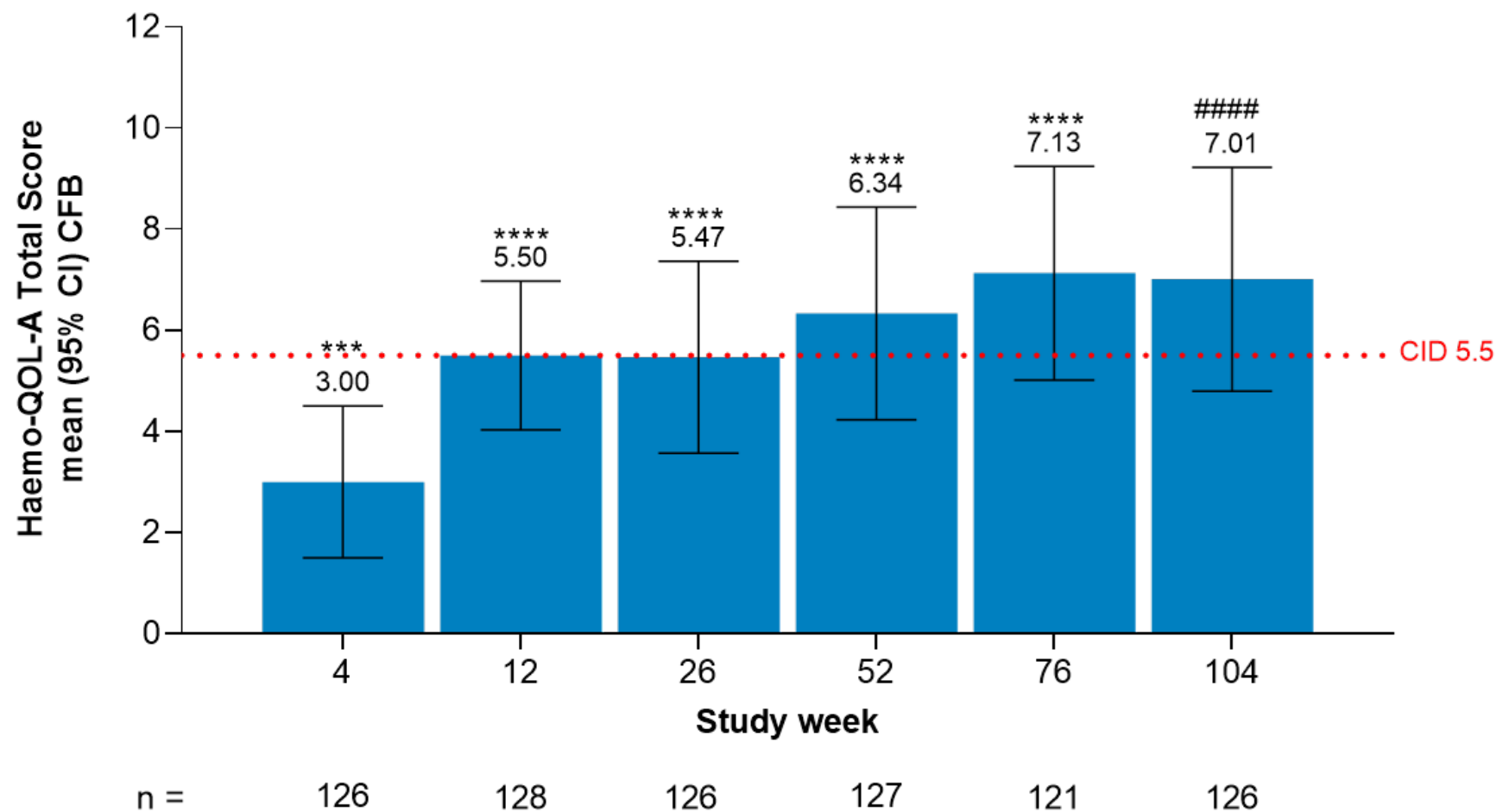
Consequences
of Bleeding

Worry

Emotional
Impact

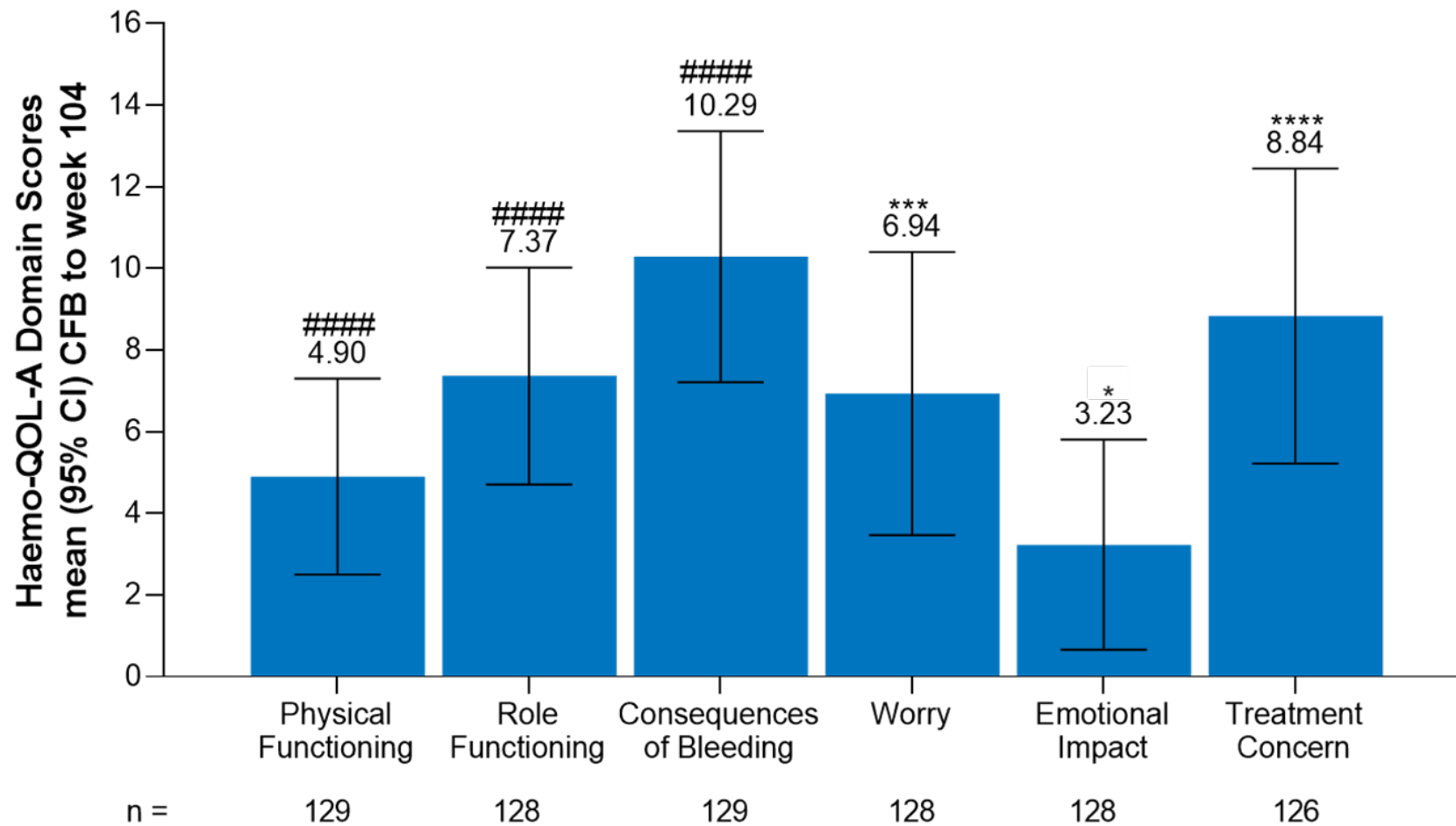
Treatment
Concern

Haemo-QOL-A Total Score



P <0.001 and *P <0.0001 were based on two-sided t-test of CFB vs 0 without controlling for multiplicity. #####P <0.0001 based on two-sided t-test of CFB vs 0 performed as part of a hierarchical testing sequence controlling overall Type 1 error. CFB data are based on participants with data at both time points.
CFB, change from baseline; CI, confidence interval; CID, clinically important difference; Haemo-QOL-A, Haemophilia-specific Quality of Life Questionnaire for Adults.

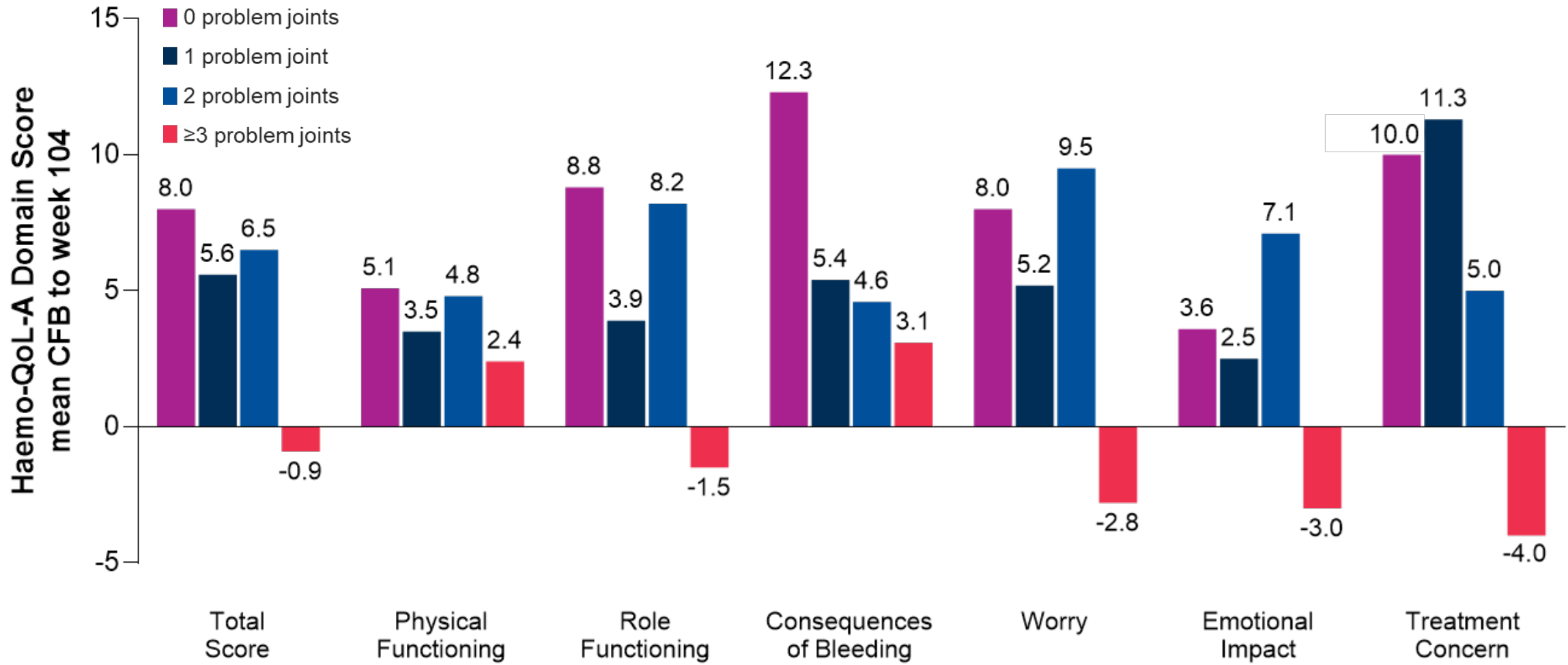
Haemo-QOL-A Domain Scores



*P <0.05; ***P <0.001 and ****P <0.0001 were based on two-sided t-test of CFB vs 0 without controlling for multiplicity.####P <0.0001 based on two-sided t-test of CFB vs 0 performed as part of a hierarchical testing sequence controlling overall Type 1 error. CFB data are based on participants with data at both time points.

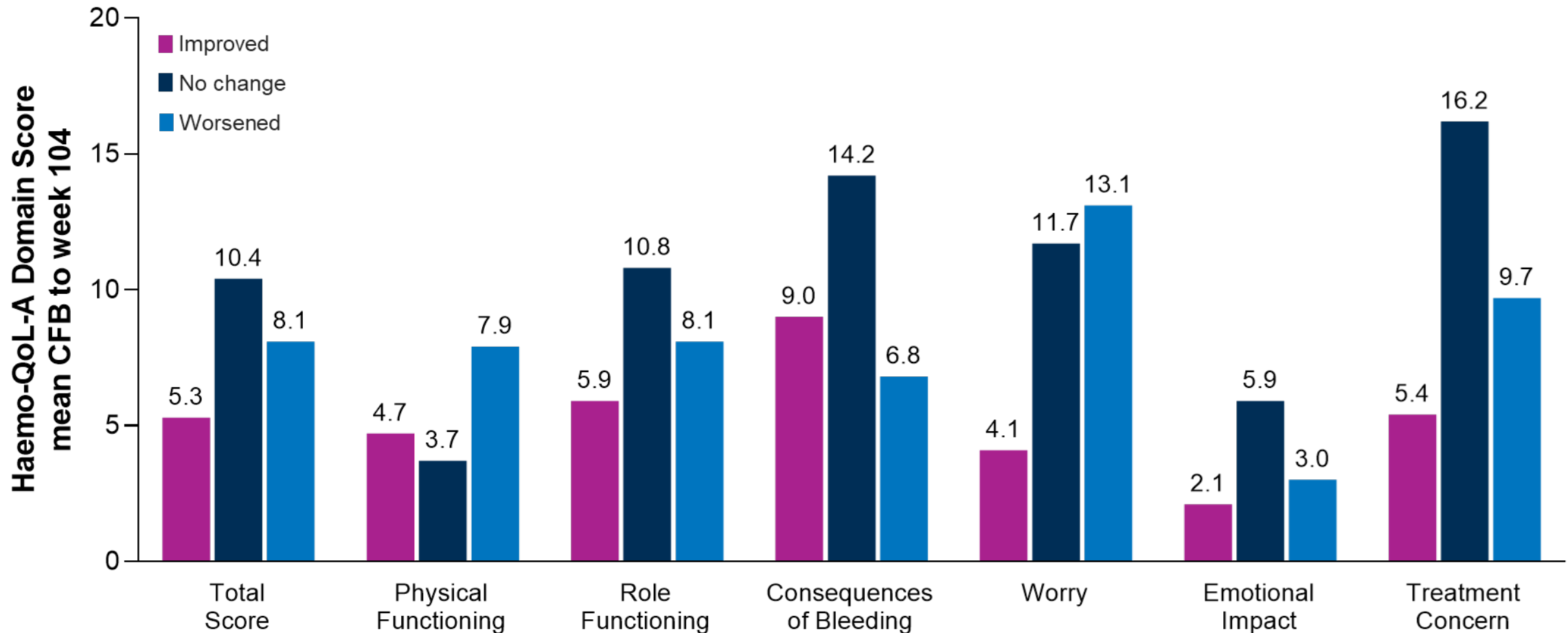
CFB, change from baseline; CI, confidence interval; CID, clinically important difference; Haemo-QOL-A, Haemophilia-specific Quality of Life Questionnaire for Adults

Post hoc analysis by pre-existing problem joints



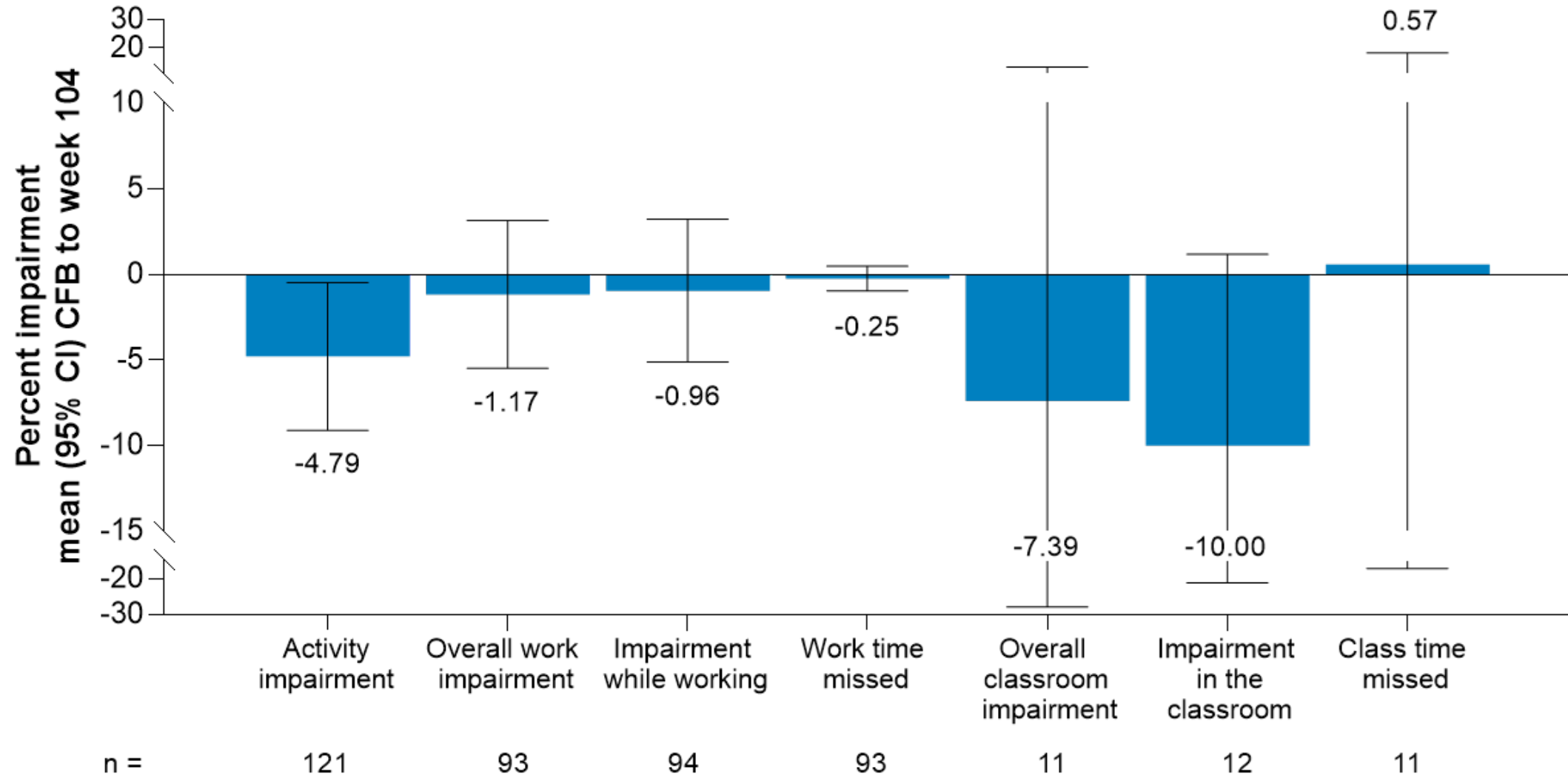
Change in Haemo-QOL-A domain scores were grouped by number of problem joints at baseline. Not all participants completed all domains. CFB data are based on participants with data at both time points. For the “0 problem joints “ group with at baseline, n = 92–96; for the “1 problem joint” group, n = 16–17; for the “2 problem joint” group, n = 8; for the “≥3 problem joint” group, n = 10–11. CFB, change from baseline; Haemo-QOL-A, Haemophilia-specific Quality of Life Questionnaire for Adults.

Post hoc analysis by changes in bleeding rate



Change in Haemo-QOL-A domain scores were grouped by whether annualized rate of treated bleeds improved, worsened, or did not change from baseline to the data cutoff date. All participants with no change in bleed rate had rates of zero before and after gene transfer. Not all participants completed all domains. CFB data are based on participants with data at both time points. For the “Improved” group, n = 80–85; for the “No change” group, n = 35–36; for the “Worsened” group, n = 11. CFB, change from baseline; Haemo-QOL-A, Haemophilia-specific Quality of Life Questionnaire for Adults.

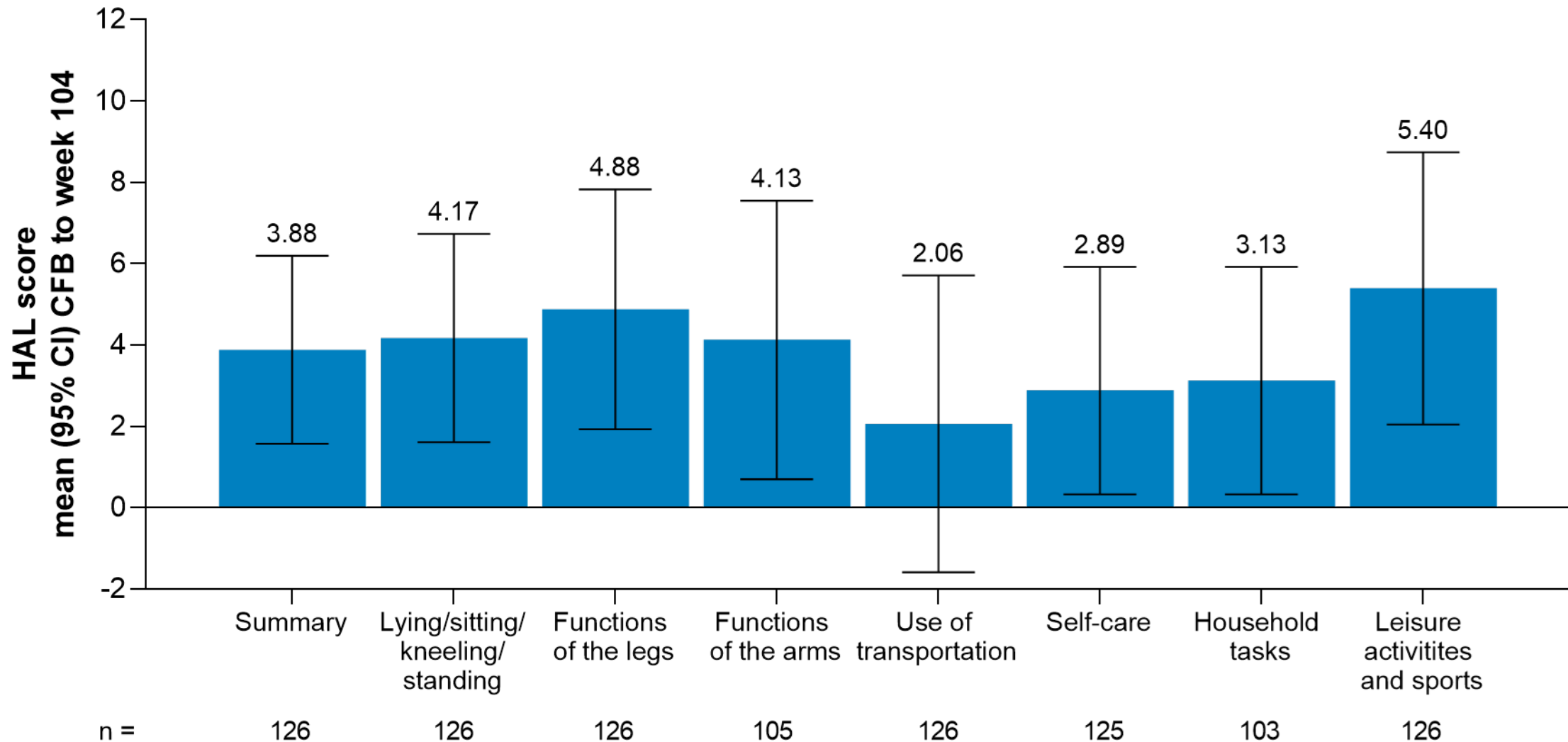
WPAI+CIQ:HS scores



Data presented as mean (95% CI). CFB data are based on participants with data at both time points.

CFB, change from baseline; CI, confidence interval; WPAI+CIQ:HS, Work Productivity and Activity Impairment plus Classroom Impairment Questions: Hemophilia-Specific.

HAL summary and domain scores



Data presented as mean (95% CI). CFB data are based on participants with data at both time points.
CFB, change from baseline; CI, confidence interval; HAL, Haemophilia Activities List.

Conclusions

- Improvements in health-related quality of life were maintained through 2 years post gene transfer
- An annualized treated bleed rate of zero on FVIII prophylaxis did not preclude appreciable, meaningful quality of life improvements for participants after gene transfer
- Participants with pre-existing problem joints attained measurable quality of life improvements following gene transfer
- HAL and WPAI+CIQ:HS scores reflected decreased impairment and increased activity through 2 years post gene transfer

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