

Health-related quality-of-life outcomes 4 years after treatment with valoctocogene roxaparvovec

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Introduction

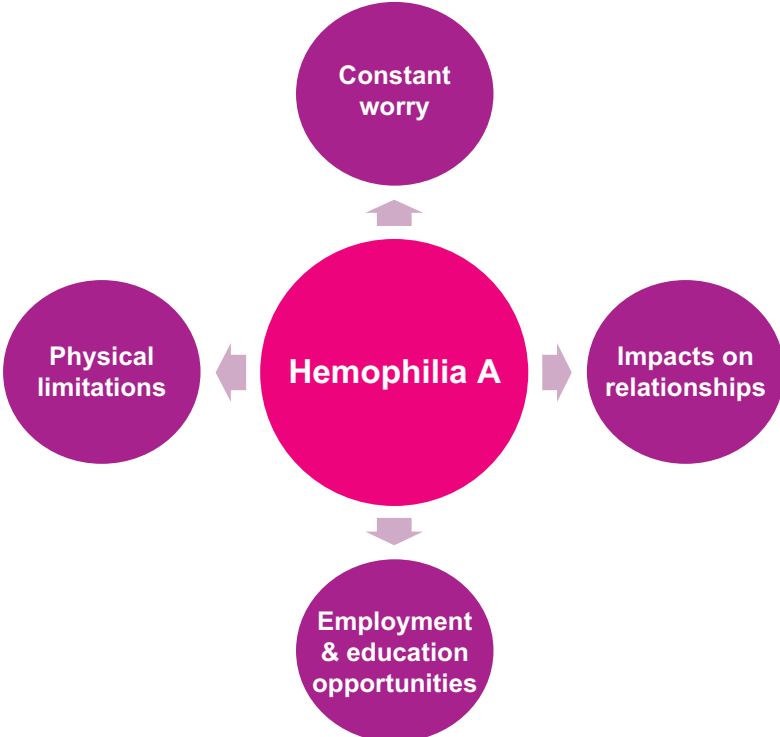
Hemophilia A

- People with hemophilia A lack the blood clotting protein factor VIII (FVIII) because the **gene that makes it is faulty**
- Low FVIII levels can result in **excessive bleeding** or bleeding with no apparent cause
- Current treatments are regular injections with clotting FVIII concentrate or non-factor therapies (emicizumab)
- Hemophilia A can **negatively affect mental health, relationships, employment, and overall well-being**^{1,2}

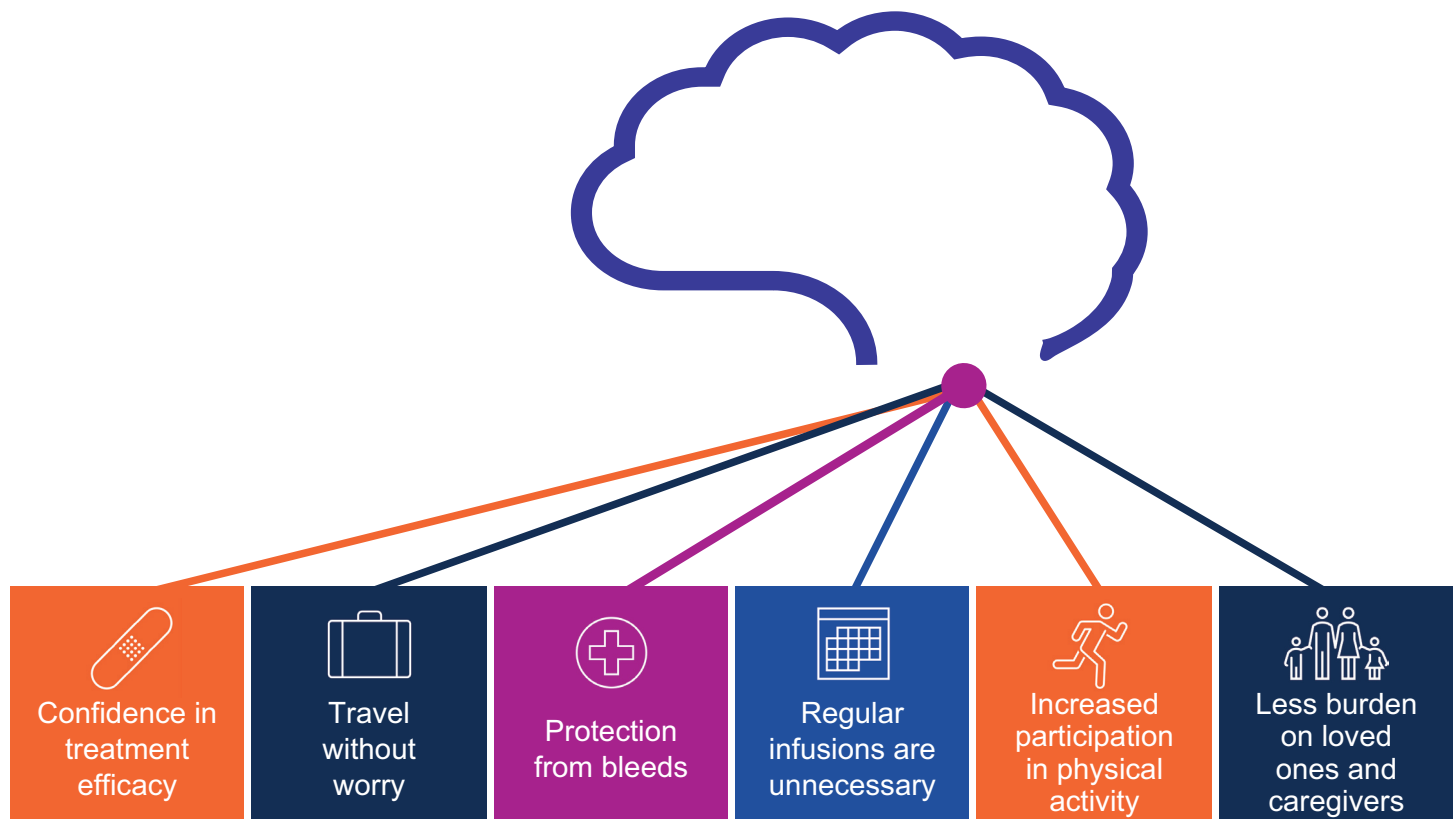
Valoctocogene roxaparvovec and HRQOL

- Valoctocogene roxaparvovec is a **gene therapy for severe hemophilia A** that delivers functional genetic instructions for producing FVIII
- Valoctocogene roxaparvovec provides **protection from bleeding with a single infusion**³, with the potential to reduce the burden and consequences of living with hemophilia A
- GENEr8-1 is a phase 3 trial to test how safe valoctocogene roxaparvovec treatment is and how well it protects against bleeding³⁻⁵

Hemophilia A negatively affects health-related quality of life (HRQOL)



Potential to reduce disease burden of hemophilia A⁶



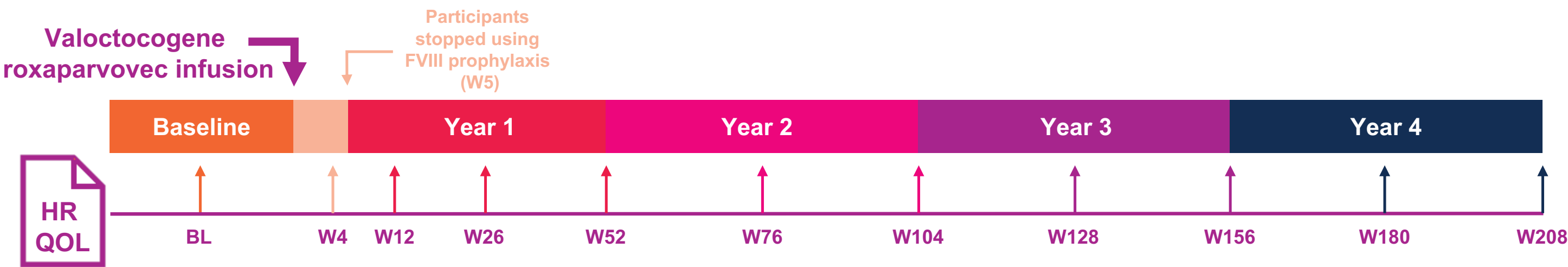
Methods

Study design

Eligibility	Endpoints*
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- Adult men with severe hemophilia A (FVIII ≤1 IU/dL, or 1% of healthy levels)
- Previously receiving FVIII prophylaxis
- No history of FVIII inhibitors or antibodies against the capsid
- No significant liver dysfunction
- Change from baseline – HRQOL

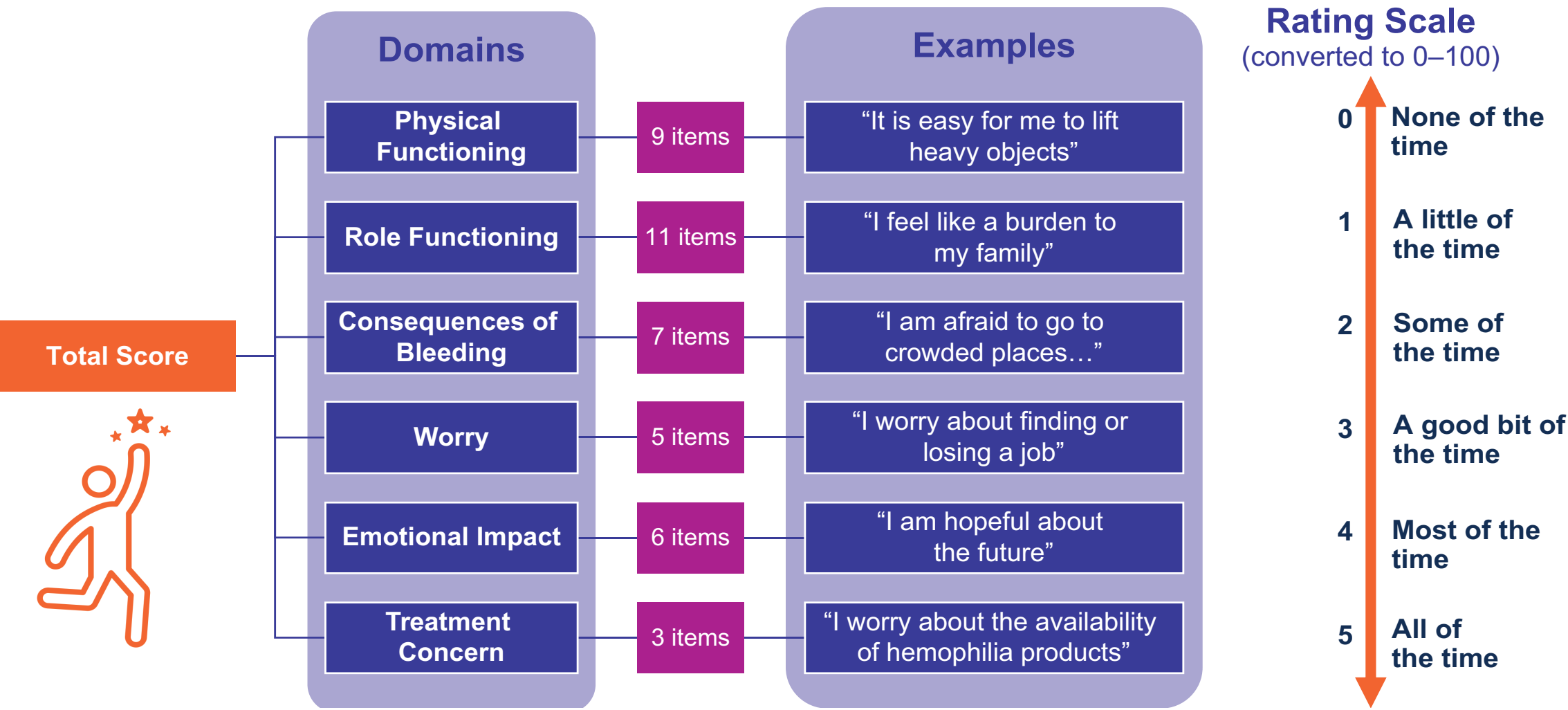
*FVIII activity levels, safety outcomes, and change from baseline in annualized bleeding rate and annualized FVIII infusion rate are reported in a separate poster.



BL, baseline; FVIII, factor VIII; HRQOL, health-related quality of life; W, week.

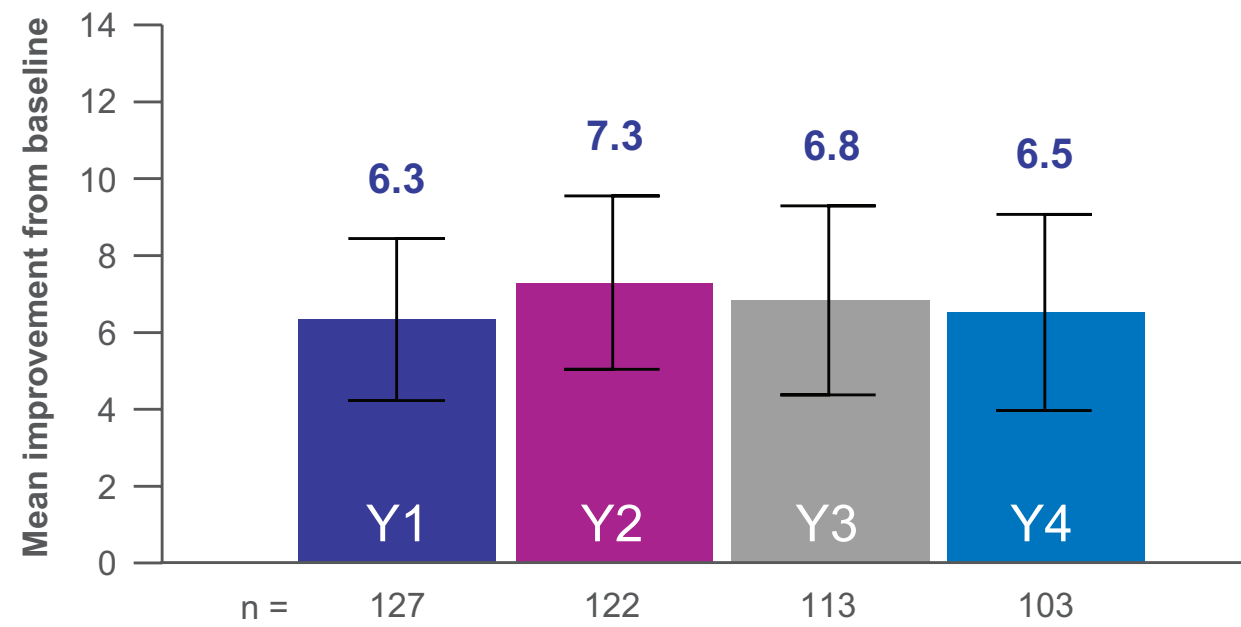
- 134 participants enrolled and received an infusion of valoctocogene roxaparvovec
- This analysis included the **132 participants** who were HIV-negative
- To ensure results are based only on the effects of valoctocogene roxaparvovec, **HRQOL data were analyzed by excluding data after participants restarted prophylaxis** with FVIII or emicizumab; results with those data included were similar
- HRQOL instruments included the Haemophilia-Specific Quality of Life Questionnaire for Adults (**Haemo-QOL-A**), the Haemophilia Activities List (**HAL**), and the Work Productivity and Impairment plus Classroom Impairment Questions: Hemophilia Specific (**WPAI+CIQ:HS**)

Haemo-QOL-A measures HRQOL in people with hemophilia



Results

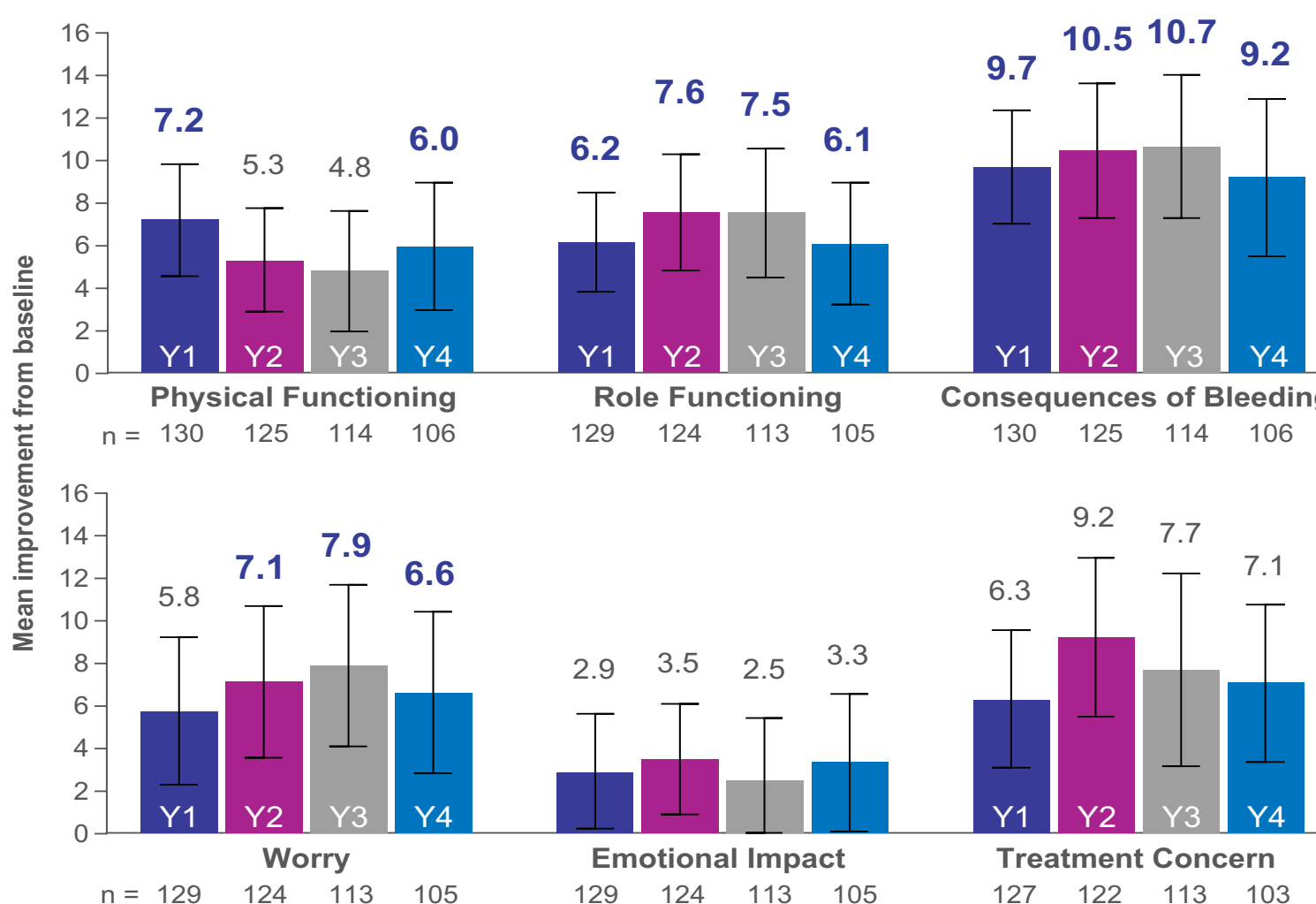
Valoctocogene roxaparvovec improved Haemo-QOL-A Total Score across 4 years



The improvements at the end of each year were deemed clinically meaningful⁷

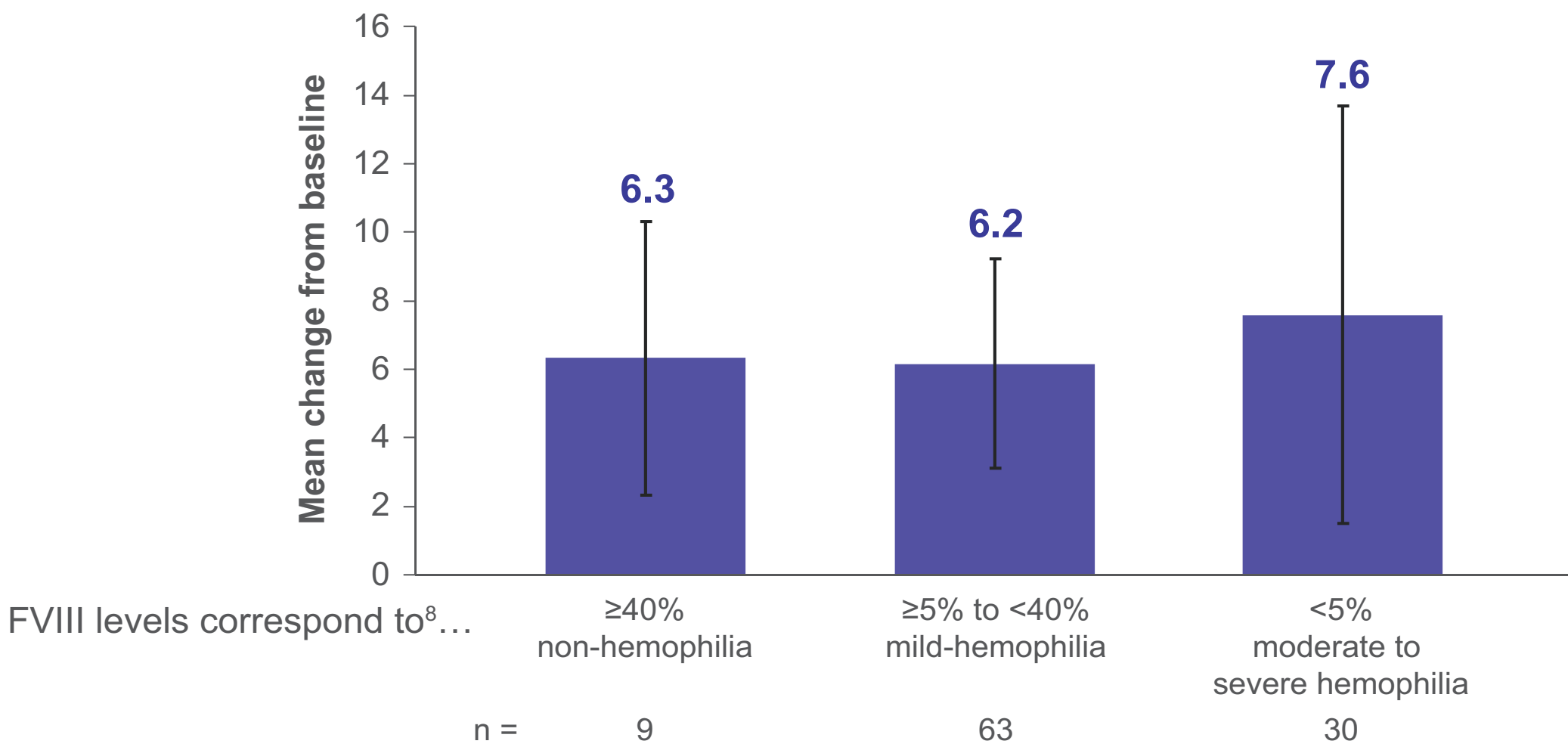
The clinically important difference (CID) for Total Score is 5.5 points. Change from baseline results are based on available data at each time point. Error bars represent 95% confidence intervals. Data after participants resumed prophylaxis were not included. Y, year.

Consistent improvements for Haemo-QOL-A domain scores



Improvements ≥6.0 points are considered clinically meaningful⁷

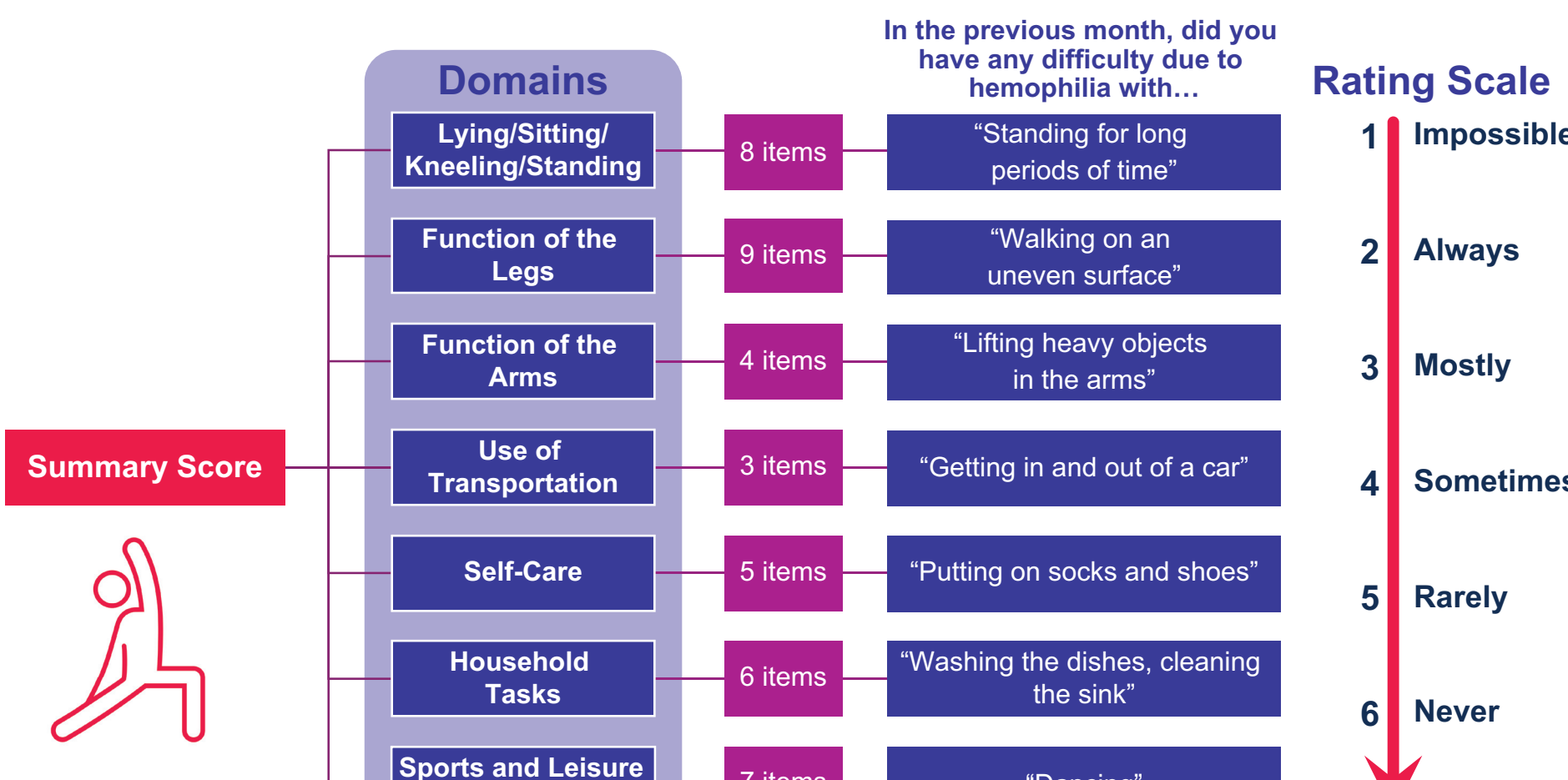
HRQOL improvements were partly independent of FVIII activity



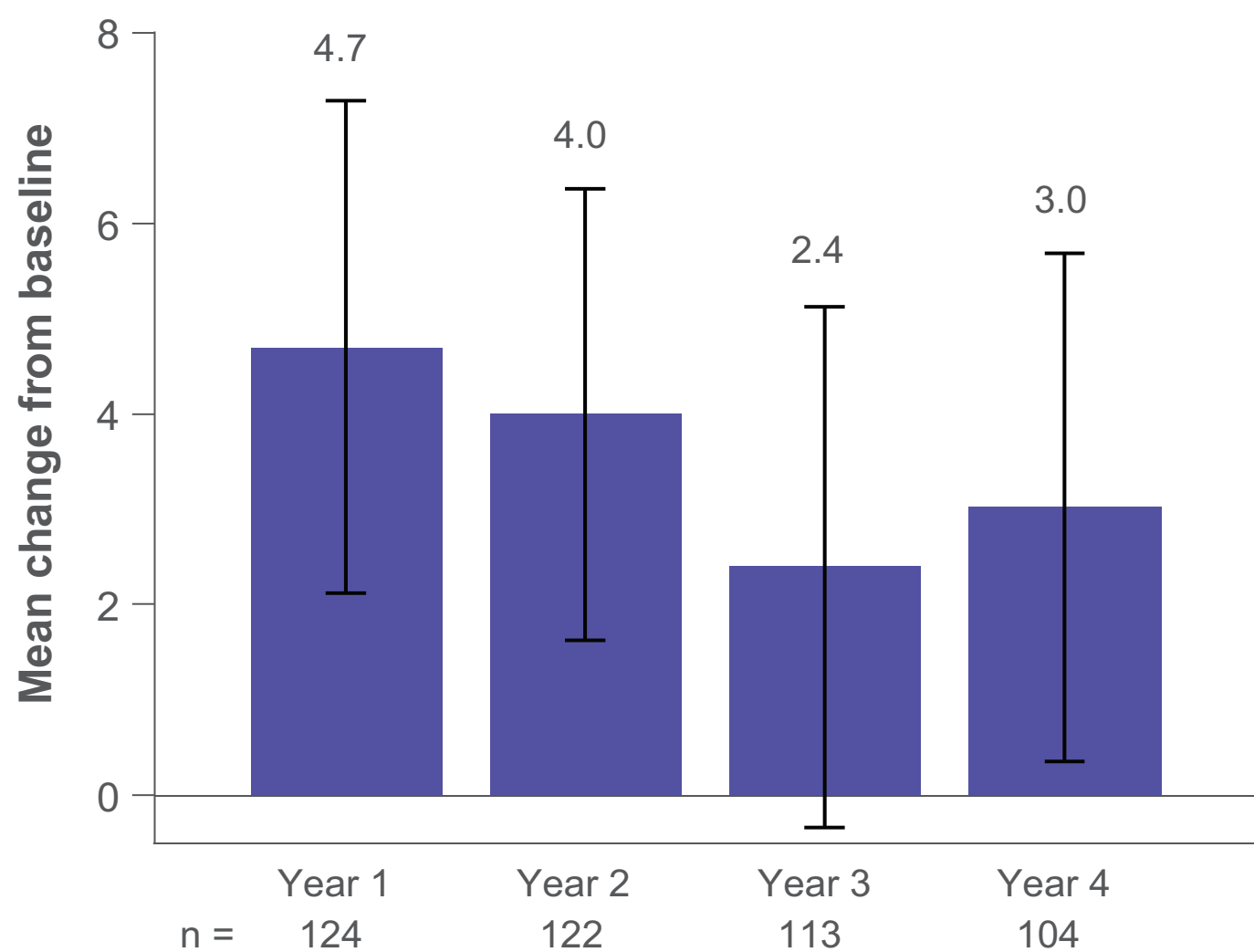
Improvement in Haemo-QOL-A Total Score at the end of year 4 was deemed clinically meaningful for participants with FVIII levels <5%⁷

Results are based on available data at each time point. Error bars represent 95% confidence intervals. Participants who resumed prophylaxis were excluded.

HAL measures self-reported functional ability for people with hemophilia

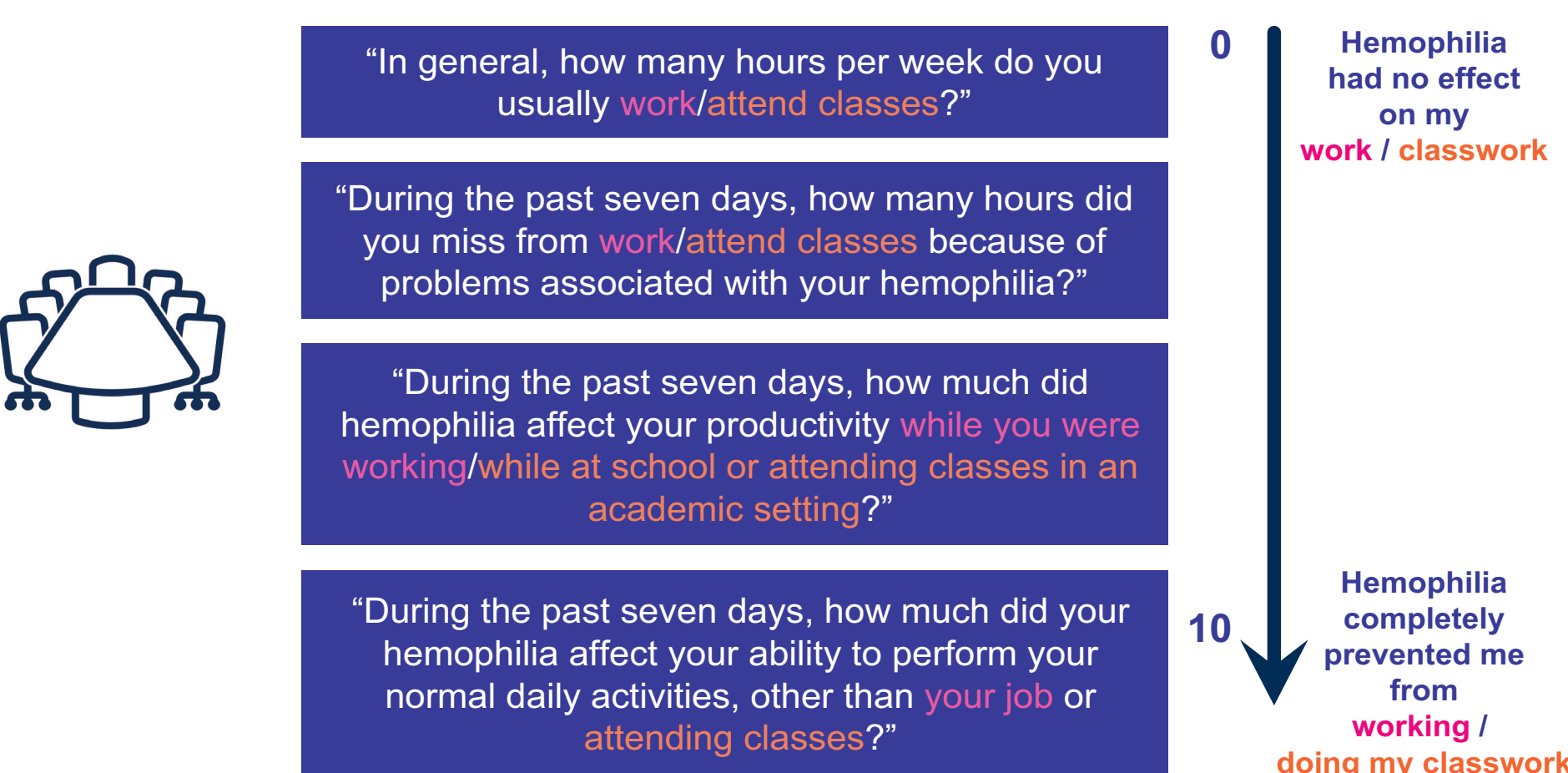


HAL Summary Score improved over 4 years

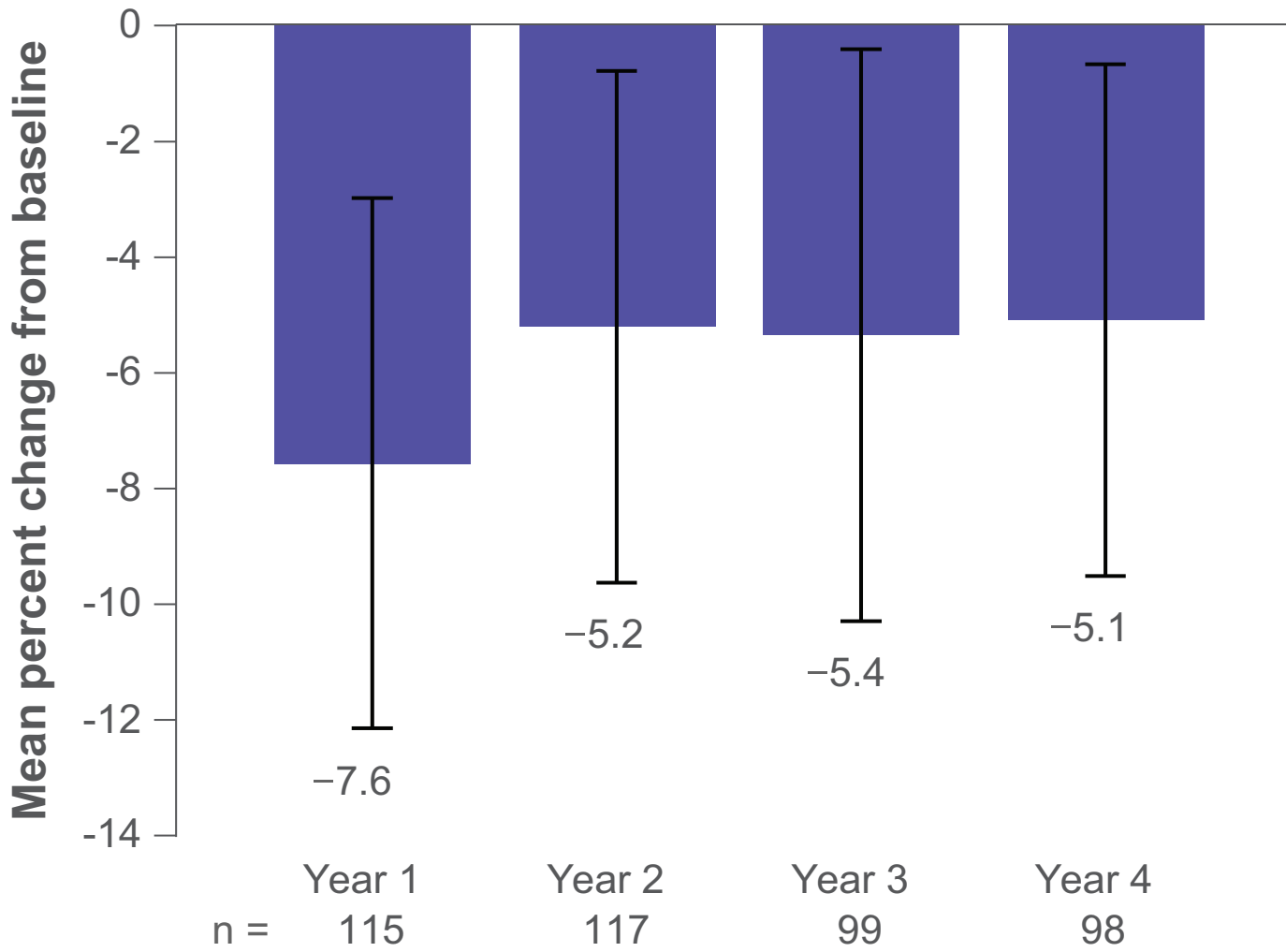


Results are based on available data at each time point. Error bars represent 95% confidence intervals. Data after participants resumed prophylaxis were not included.

The WPAI+CIQ:HS measures impairment at work and school due to hemophilia



WPAI+CIQ:HS activity impairment was reduced over 4 years



Results are based on available data at each time point. Error bars represent 95% confidence intervals. Data after participants resumed prophylaxis were not included.

Conclusions



Haemo-QOL-A

- Valoctocogene roxaparvovec provides **clinically meaningful HRQOL improvements** over 4 years
- The meaningful improvements also apply to **participants with FVIII activity <5% at year 4**



HAL

- Participants reported **improved ability to perform daily activities** over 4 years



WPAI+CIQ:HS

- Work and school **activity impairment scores were reduced** over 4 years



- In general, HRQOL questionnaires try to capture the **highly individual experiences of each person** — as with any study, average values do not necessarily reflect the results of all participants

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