

# Emicizumab ▼ prophylaxis improves long-term Physical Health scores in persons with haemophilia A (PwHA) with or without inhibitors: update from the HAVEN 3 and HAVEN 4 studies

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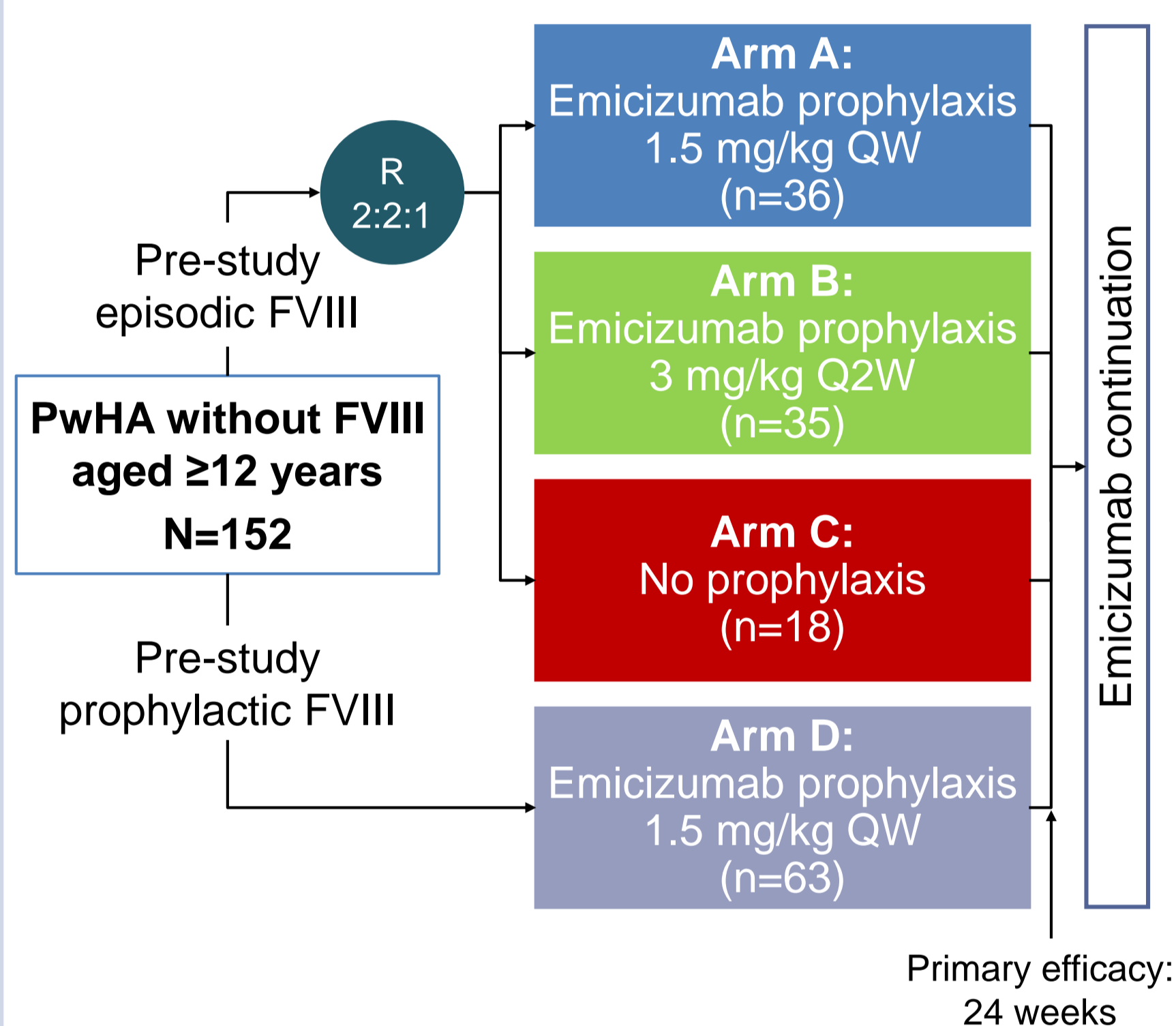
## BACKGROUND

- Haemophilia A is a congenital bleeding disorder associated with a major impact on health-related quality of life (HRQoL) for those with or without factor VIII (FVIII) inhibitors.
- A greater understanding of the impact of haemophilia A disease- and treatment-related burdens on patients will provide valuable insights into patient needs.<sup>1</sup>
- Emicizumab, a bispecific, humanised, monoclonal antibody, binds activated FIX (FIXa) and FX to restore the function of missing FVIIIa in persons with haemophilia A (PwHA).<sup>2</sup>
- Emicizumab prophylaxis achieved highly efficacious bleed protection when administered once weekly (QW), once every 2 weeks (Q2W) or once every 4 weeks (Q4W) in PwHA with or without FVIII inhibitors.<sup>3-6</sup>
- Here we assess the impact of prophylactic emicizumab on long-term HRQoL of participants in the phase III HAVEN 3<sup>7</sup> (NCT02847637) and HAVEN 4<sup>8</sup> (NCT03020160) studies.

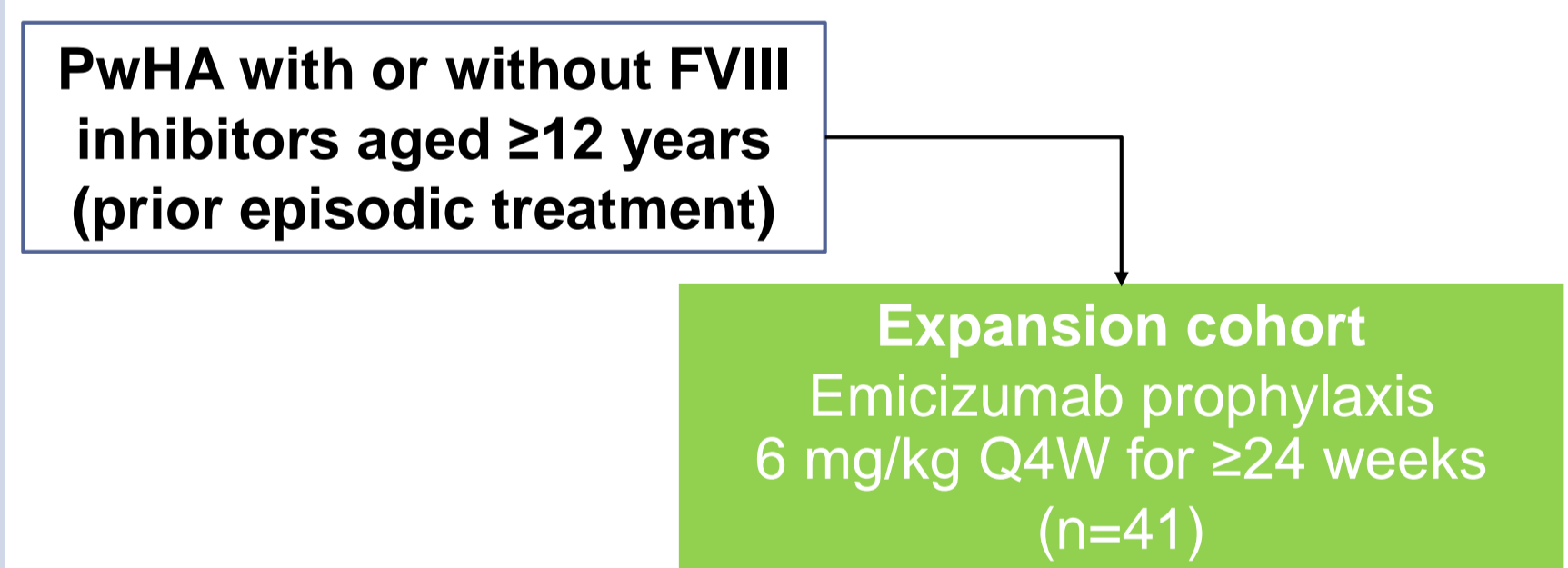
## METHODS

### Figure 1. HAVEN 3 and HAVEN 4 study designs

#### A. HAVEN 3 study of emicizumab prophylaxis in adults and adolescents ≥12 years old without FVIII inhibitors<sup>5</sup>



#### B. HAVEN 4\* study of Q4W emicizumab prophylaxis in adults and adolescents ≥12 years old with or without FVIII inhibitors<sup>6</sup>



R, randomised

All emicizumab regimens received a 3 mg/kg QW emicizumab loading dose for 4 weeks. Maintenance dosing as indicated started at Week 5. Data cut-offs: HAVEN 3, 4 October 2018; HAVEN 4, 11 October 2018. \*The run-in cohort in the study was not included in this analysis.

- Eligible participants (aged ≥18 years) completed the Haemophilia-Specific Quality of Life Questionnaire for Adults (Haem-A-QoL)<sup>7</sup> via an on-site electronic tablet.
  - The Haem-A-QoL is a self-reported, 10 domain questionnaire that assesses HRQoL in adults with haemophilia A.
  - Scores range from 0–100, with lower scores reflective of better functioning.
  - A 'Total' score is generated from all 10 domains.
- For this analysis, HRQoL data were pooled by study regardless of patient baseline characteristics or treatment.
- For the 'Physical Health' score subscale, a ≥10-point change from baseline is considered clinically meaningful.<sup>8</sup>
- Proportion of missed work days was also collected.
- The schedule of assessments for the Haem-A-QoL and the missed work day item for HAVEN 3 and HAVEN 4 (expansion cohort only) included: Weeks 1, 13, 25, 49, 61 (HAVEN 4 only), 73 (HAVEN 3 only), and study completion.

## ACKNOWLEDGEMENTS

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## RESULTS

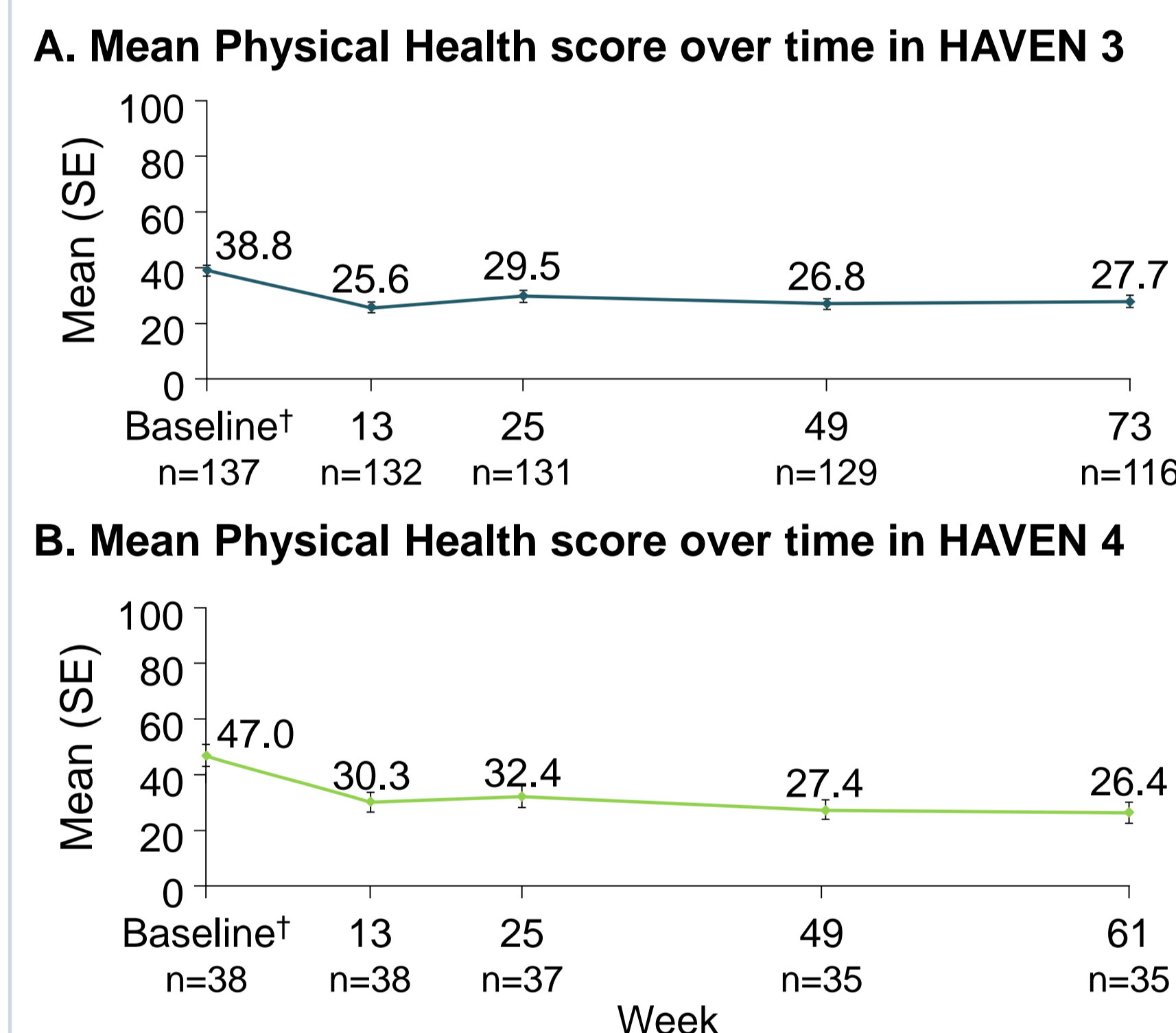
**Table 1. Baseline characteristics for all participants in HAVEN 3 and HAVEN 4 who were eligible to complete the Haem-A-QoL**

Baseline characteristic	HAVEN 3 N=143	HAVEN 4 N=38
Age (years), median (range)	39.0 (19–77)	42.0 (20–68)
Number of bleeds in the past 24 weeks, mean (SD)	13.5 (16.5)	9.6 (15.6)
Patients with target joints prior to study entry, n (%)	100 (70%)	25 (66%)
Prior episodic treatment, n (%)	87 (61%)	11 (29%)
Prior prophylactic treatment, n (%)	56 (39%)	27 (71%)

SD, standard deviation

- Haem-A-QoL questionnaire compliance rates were 94.3% in HAVEN 3 (up to Week 73) and 99.1% in HAVEN 4 (up to Week 61).
- Mean Physical Health scores improved after initiation of emicizumab prophylaxis; these improvements were maintained throughout the follow-up period (Figure 2). Scores improved by ≥10 points from baseline in over 44% and 65% of participants in HAVEN 3 and HAVEN 4 respectively (Figure 3).

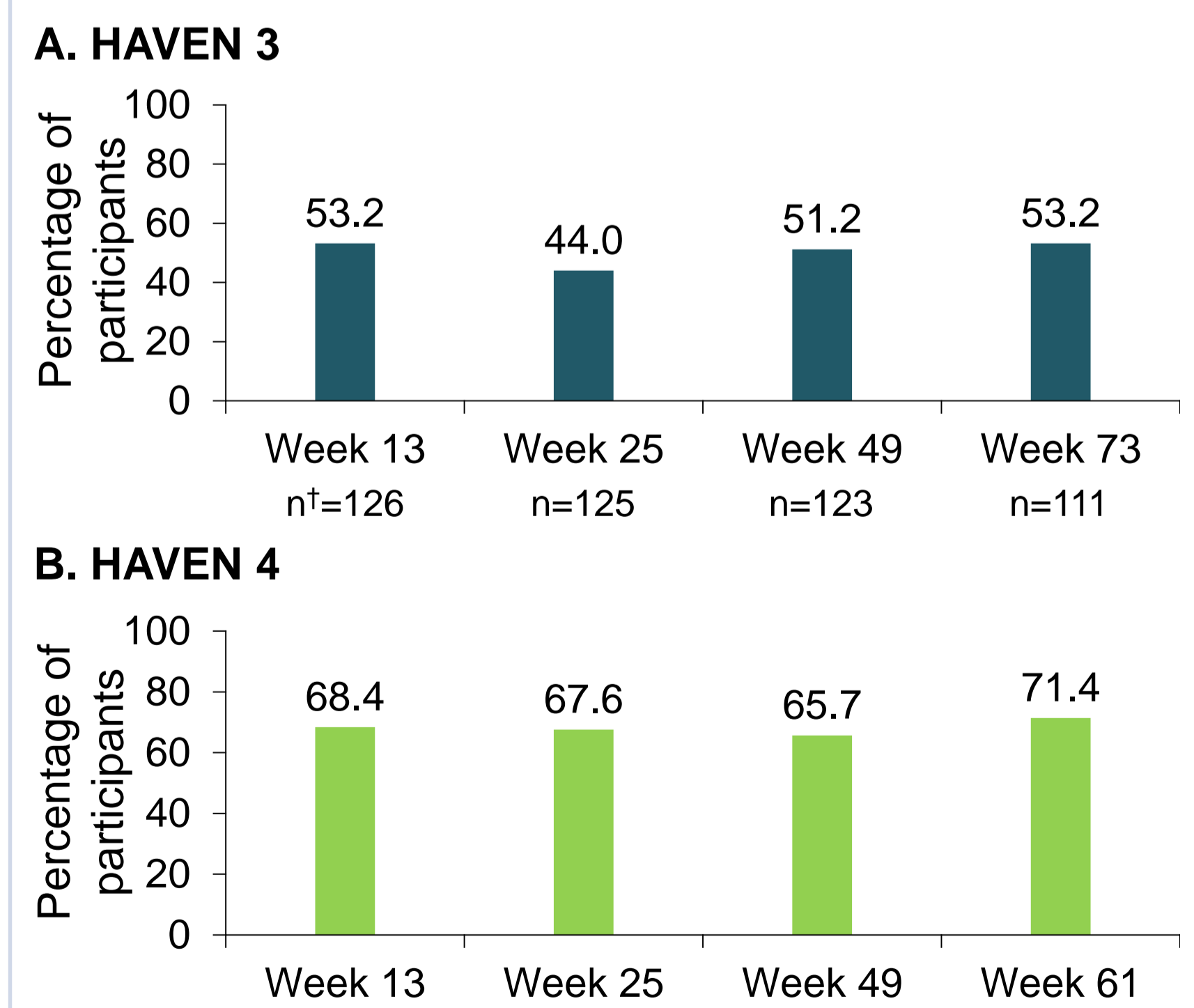
**Figure 2. Haem-A-QoL\* Physical Health score over time in eligible participants from HAVEN 3 and HAVEN 4**



SE, standard error

\*Lower scores reflect better functioning; Completed by participants aged ≥18 years only; †Baseline assessment is the last valid assessment on or before study day 1

**Figure 3. Percentage of participants with improvements in Haem-A-QoL\* Physical Health score greater than the responder threshold from baseline**



\*Completed by participants aged ≥18 years only; †Number of participants with available data to calculate change from baseline

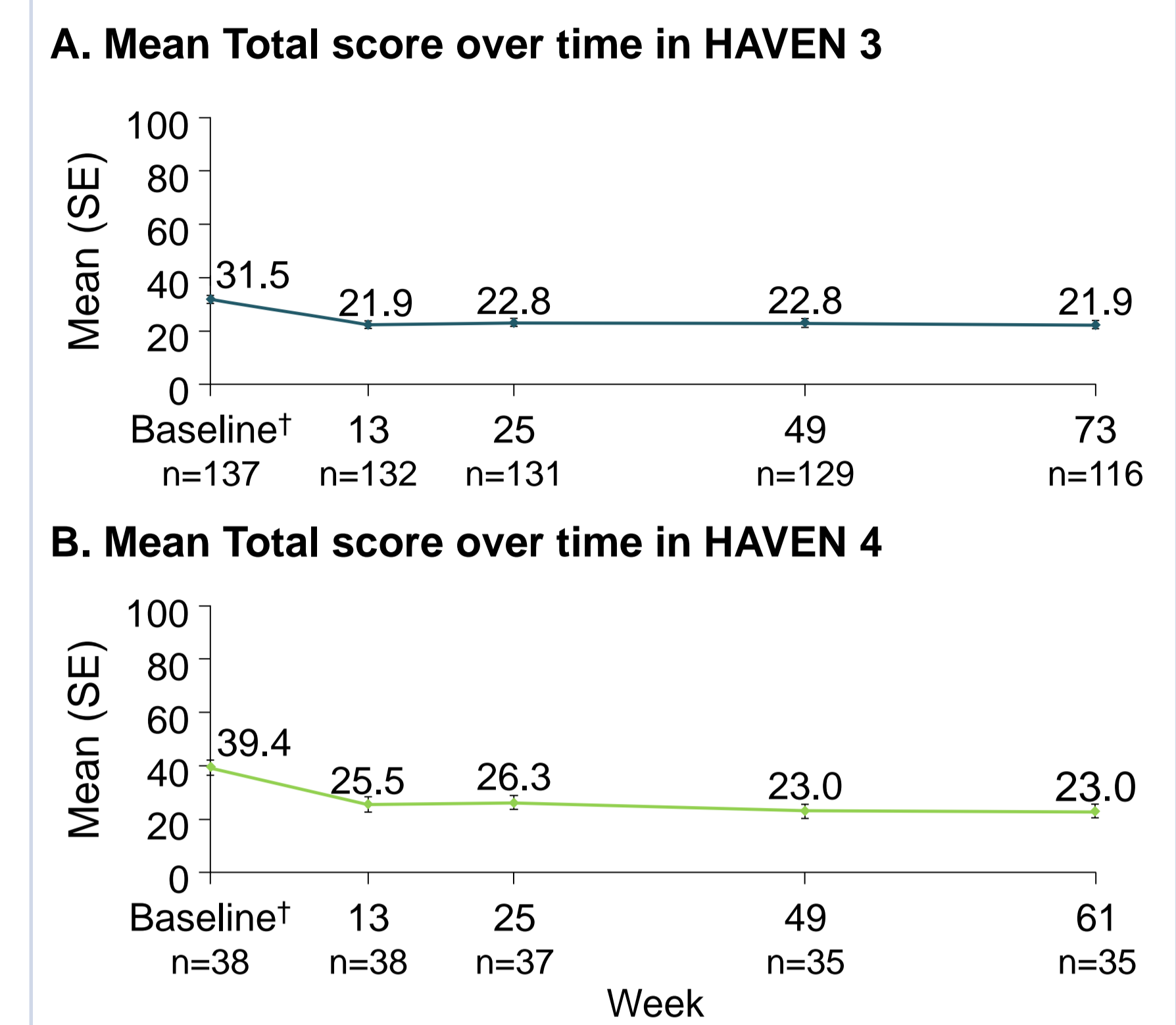
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- Mean Total score (SD) improved from 31.5 (15.0) and 39.4 (17.9) at baseline to 22.8 (15.1) and 26.3 (16.6) at Week 25 for HAVEN 3 and HAVEN 4, respectively. These improvements were maintained throughout the follow-up period (Figure 4).

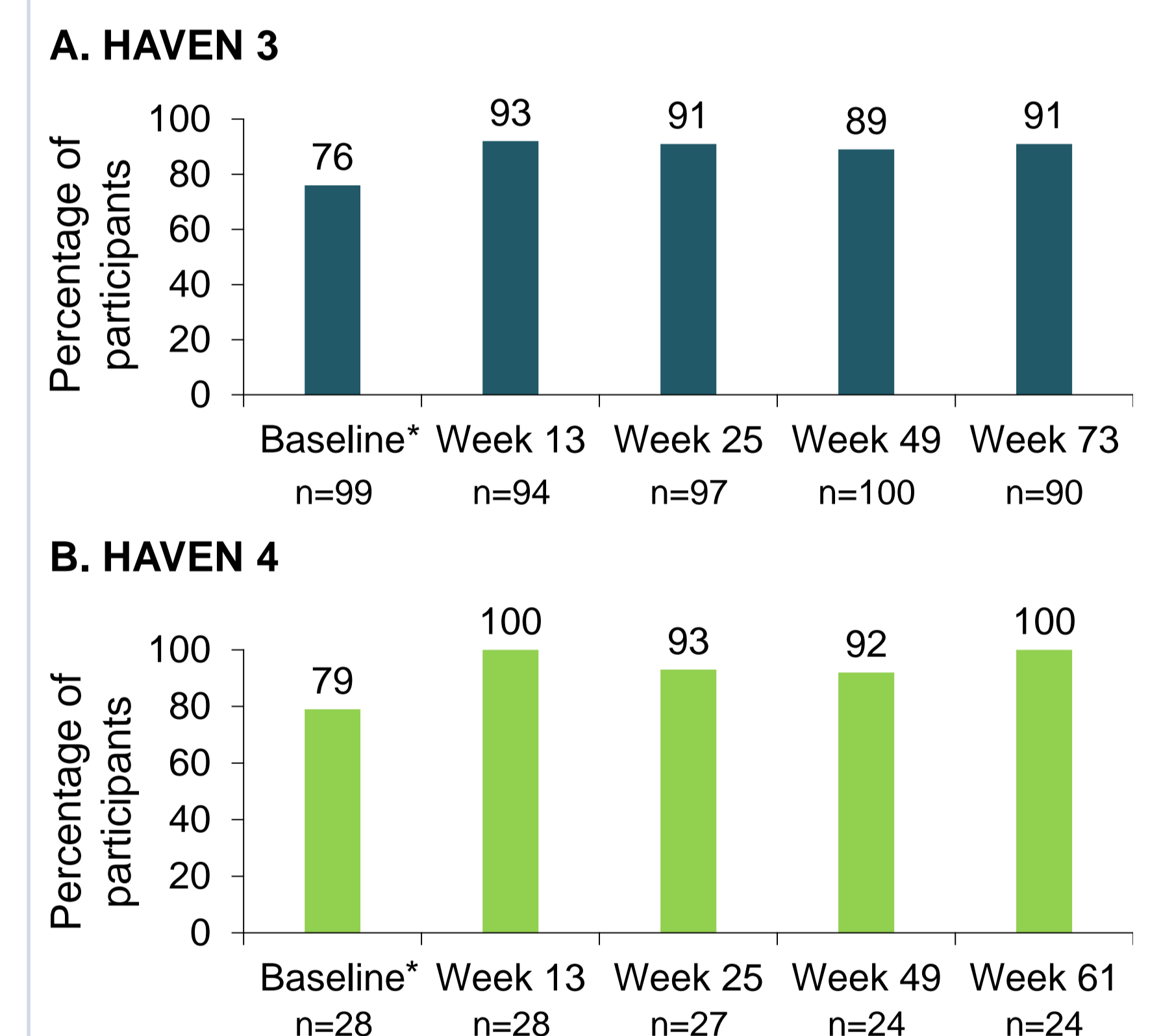
**Figure 4. Mean Haem-A-QoL\* Total score over time in eligible participants from HAVEN 3 and HAVEN 4**



\*Lower scores are indicative of better functioning. Completed by participants aged ≥18 years only; †Baseline assessment is the last valid assessment on or before study day 1

- Following administration of emicizumab, fewer employed participants missed days of work than in the 28 days prior to study enrolment (Figure 5).

**Figure 5. Percentage of employed participants with no missed days of work in the previous 28 days**



n is the number of participants enrolled in work at each time point  
\*Reflects the work period 28 days prior to enrolment

## CONCLUSIONS

- Clinically meaningful improvements were observed in Haem-A-QoL Physical Health scores with emicizumab prophylaxis in ≥44% and ≥65% of participants in HAVEN 3 and HAVEN 4, respectively.
  - These improvements are consistent with the demonstrated efficacy of emicizumab.<sup>5,6</sup>
  - Participants in HAVEN 3 and HAVEN 4 achieved similar Physical Health and Total scores from Week 13 onwards, regardless of baseline QoL scores.
- The proportion of participants with no missed work days increased to ≥90% with emicizumab prophylaxis in both HAVEN 3 and HAVEN 4.
- The HRQoL results seen here are consistent with those seen in the HAVEN 1 study,<sup>3</sup> indicating that emicizumab improves aspects of HRQoL regardless of inhibitor status.

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