

QUALITY OF LIFE OF HEMOPHILIA PATIENTS WITH INHIBITORS – OPPORTUNITIES FOR IMPROVEMENT

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Conclusion

- + The MAA-201 subcutaneous prophylaxis trial using marzeptacog alfa (activated) (MarZAA), a modified FVIIa with 9-fold increased potency, has demonstrated a significant reduction in the Annualized Bleed Rate and proportion of days with bleeding
- + Subjects screened for MAA-201 had generally worse Quality of Life scores at baseline compared with reported scores for patients without inhibitors across the majority of domains
- + Quality of life scores uniformly trended toward improvement
- + Although this is a small sample, the trend toward improvement over such a short dosing period is very encouraging for subcutaneous prophylaxis using MarZAA

Introduction

- + Morbidity of hemophilia A and B increases with age
- + Patients who develop neutralizing antibodies (inhibitors) (HPWI) to replacement clotting factor typically receive bypassing agents for treatment of bleeds and are not provided prophylaxis
- + The very short half-life of available intravenous agents for HPWI means episodic treatment for bleeds that results in:
 - Subjectively poorer Quality of Life (QOL)
 - Significantly premature mortality
 - Worse musculoskeletal outcomes when compared with patients without inhibitors
- + QOL in hemophilia may be evaluated by Haem-A-QOL and impaired physical activity with Haemophilia Activities List (HAL)

Objectives

- + Document the baseline quality of life status of HPWI subjects entering the MAA-201 trial using two validated QOL tools
- + Compare the QOL of MAA-201 subjects with published values for a similar population without inhibitors
- + Compare before and after treatment Haem-A-QOL and HAL scores in the MAA-201 trial

Methods

- + MarZAA was administered in an open-label safety and efficacy trial (MAA-201) in HPWI (Minimum ABR 12 and documented inhibitor) and the efficacy results were presented at ISTH 2019
- + Baseline QOL for the 17 subjects screened for this trial were compared with published values for subjects with severe hemophilia using Haem-A-QOL and HAL
- + For Haem-A-QOL reference data were used from subjects without inhibitors recruited into a long term prophylaxis trial (The A-LONG trial)¹. For HAL we used the scores of van Genderen's HAL validation set²
- + Missing values were imputed or using last-value-carried-forward method
- + Evidence of interval change in QOL for subjects who completed the MAA-201 trial were assessed

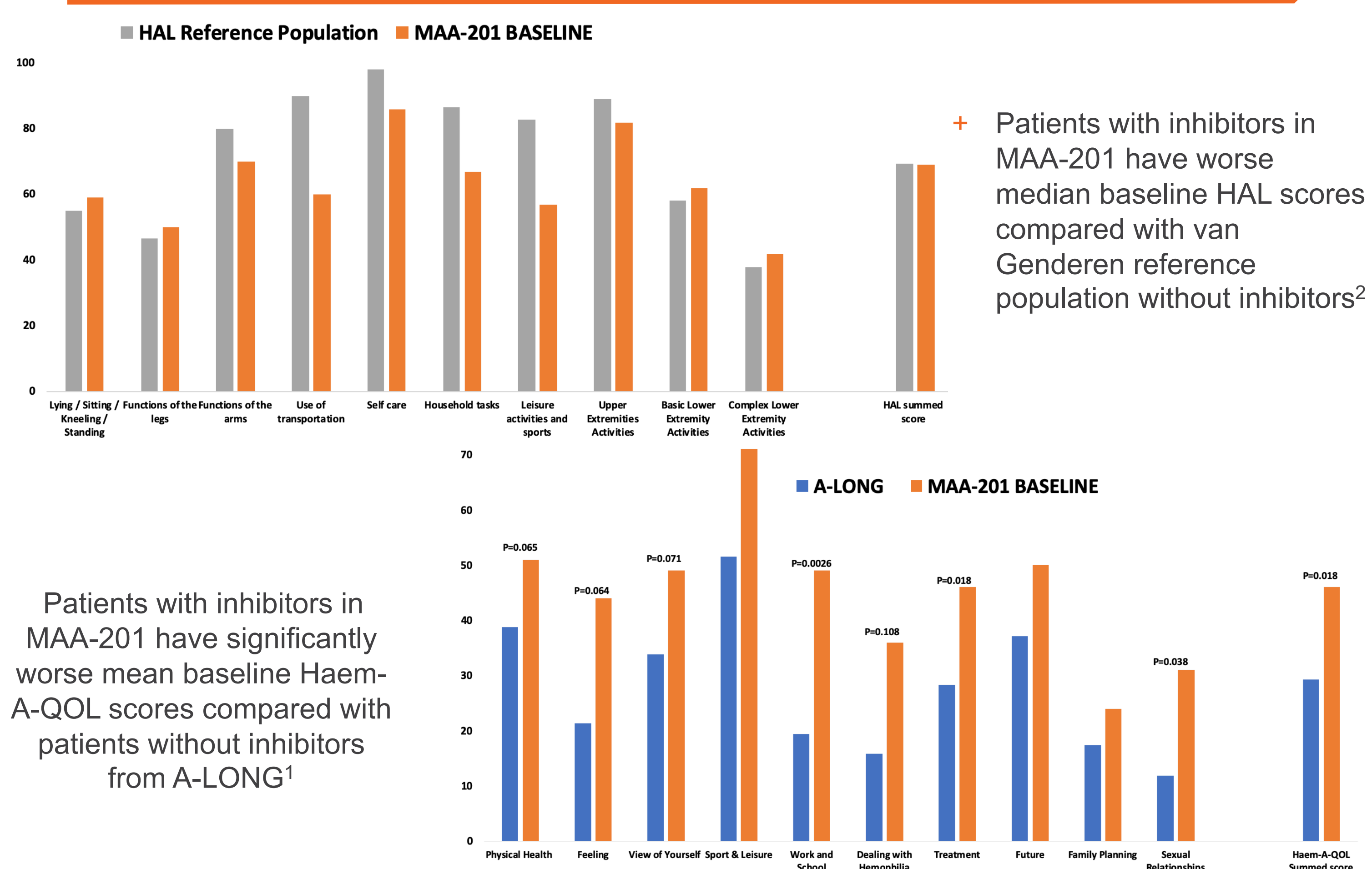
References

- 1 Su, J., Tsao, E., Feng, J., Myren, K.-J., & Glazebrook, D. (2017). Long-term quality-of-life outcomes with rFVIIIc prophylaxis in adult subjects with severe hemophilia A. In ISTH, Berlin, Germany, (p. 416, Vol. PB 1783)
 2 Van Genderen FR, Westers P, Heijnen L. Measuring patients' perceptions on their functional abilities: validation of the Haemophilia Activities List (HAL). Haemophilia. 2006; 12(1): 36-46

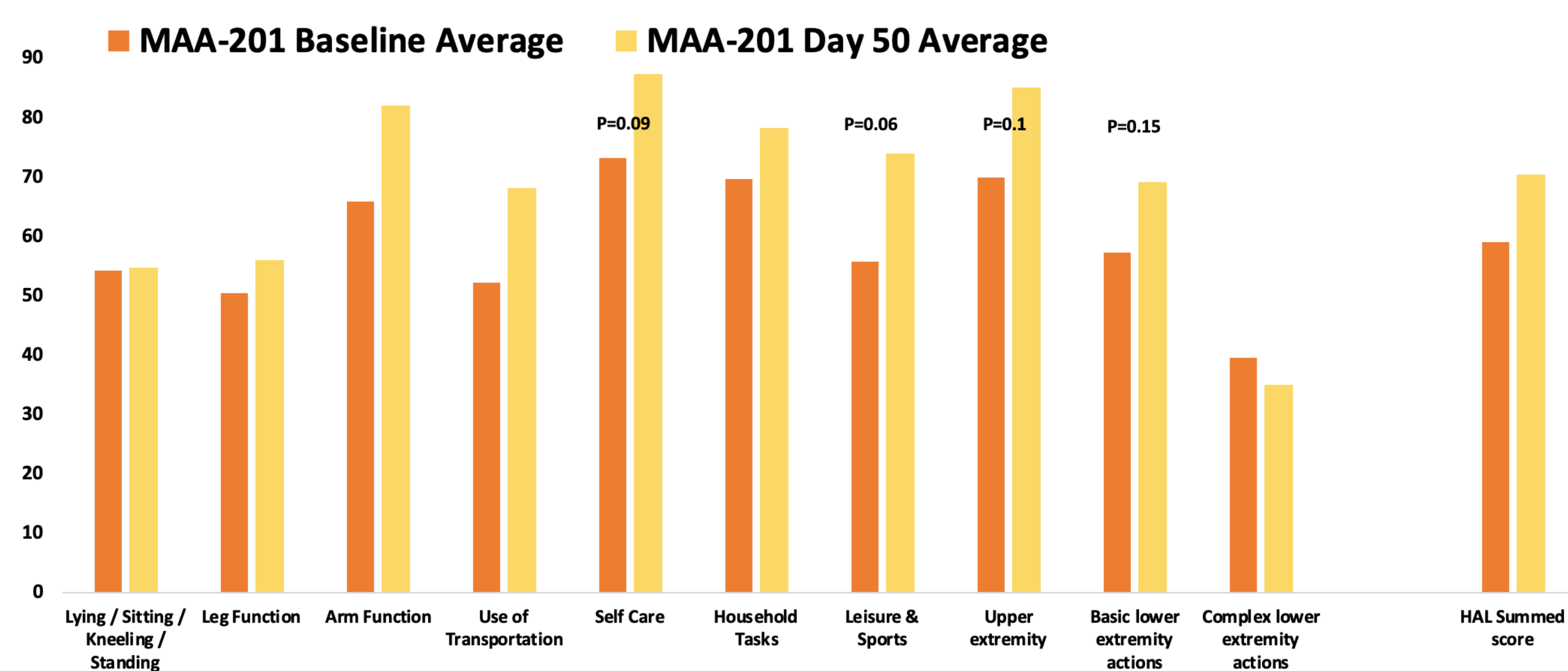
Results

- + Seventeen subjects were screened; 6 were screen failures; 1 subject withdrew consent after a single SQ dose of MarZAA; 1 subject died from an unrelated SAE 12 days into the study
- + Baseline QOL data was available (Haem-A-QOL and HAL) for 16 screened subjects
- + Baseline QOL scores in MAA-201 were worse across the majority of domains compared with the published reference groups
- + Eight subjects had interval reassessment of QOL (6 subjects 50 days; 1 subject 42 days and 1 subject 28 days)
- + There were 8 QOL interval pairs for Haem-A-QOL and 7 pairs for HAL

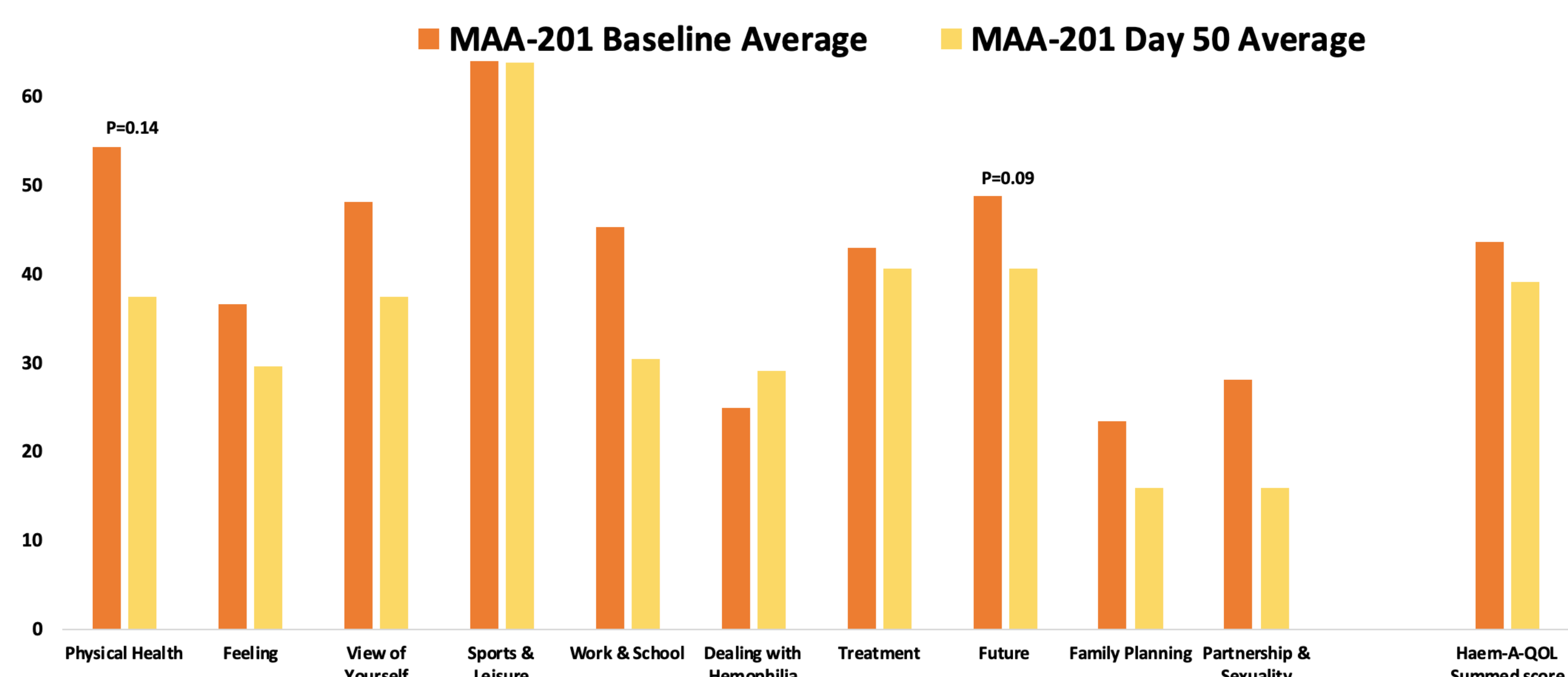
Baseline comparisons of screened subjects with published scores



Trend toward improvement in HAL Scores in almost all domains



Consistent trend toward improvement in Mean Haem-A-QOL Scores in treated subjects



Normal function for HAL is 100, thus an increase from baseline is an improvement. Normal function for Haem-A-QOL is zero, thus a decrease from baseline represents an improvement

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