Effect of evobrutinib, a Bruton's tyrosine kinase inhibitor, on patient-reported vitality and mental health in patients with relapsing multiple sclerosis in a Phase 2 trial

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CONCLUSIONS

- **Evobrutinib 75 mg BID significantly improved SF-36 mental component summary, vitality, and mental health scores from baseline to Week 48, compared to PBO/EVO low dose**
- **Evobrutinib 75 mg BID had a clear benefit over lower doses and QD dosing scheme on clinically meaningful changes to vitality and mental health scores**
- **Conversion to PROMIS Fatigue T-scores provides early evidence that evobrutinib may improve fatigue in people with RMS**

INTRODUCTION

- Evobrutinib is an oral, CNS-penetrant, and highly selective BTK inhibitor with promising efficacy and safety over 4.5 years in a Phase 2 and ongoing OLE study in RMS (NCT02975349)[1–4]
  - Evobrutinib is currently being assessed in two ongoing Phase 3 trials (NCT04338022 and NCT04338061) for RMS
- With MS severely impacting quality of life, and 80% of people with MS experiencing fatigue, we report the effects of evobrutinib on patient-reported outcomes comprising vitality and mental health during the 48-week DBP of the ongoing Phase 2 programme[5–6]

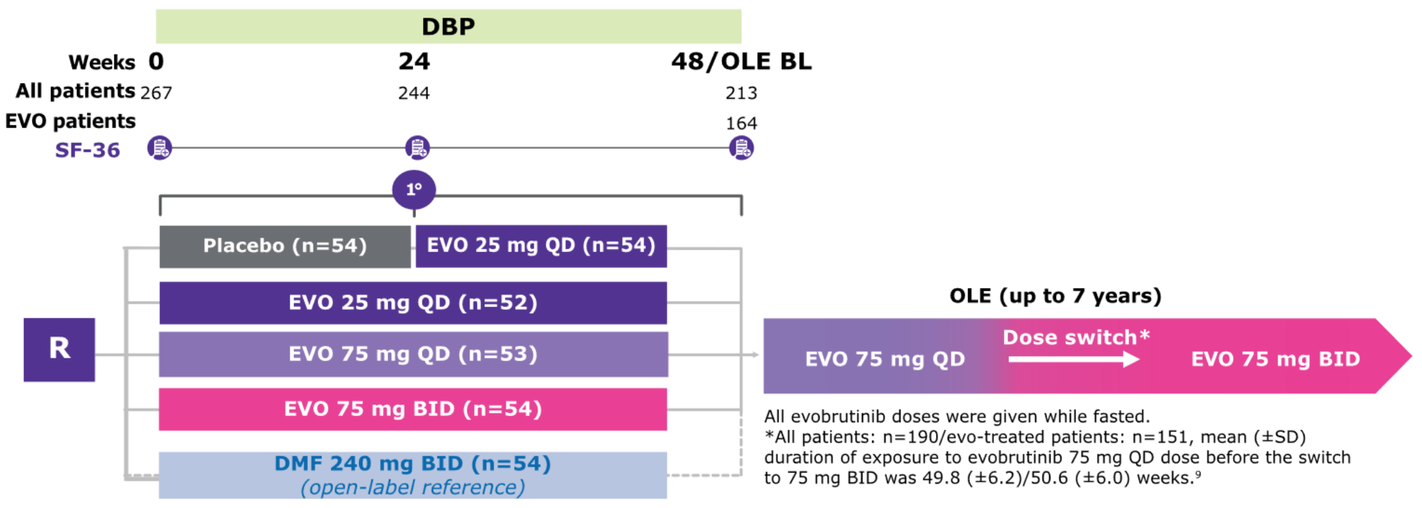
OBJECTIVES

- **To assess the effect of evobrutinib on SF-36 vitality and mental health scores during the 48-week DBP and ongoing OLE**
- **To evaluate the effect of evobrutinib on PROMIS Fatigue T-scores through conversion of SF-36 vitality scores**

METHODS

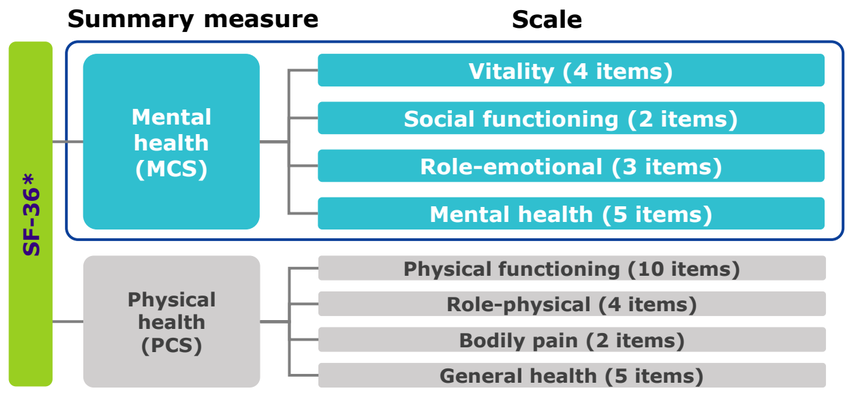
- SF-36 was evaluated at screening and all trial visits (**Figure 1**), with a focus on MCS for this analysis (**Figure 2**)[7]
- SF-36 vitality scores were converted into PROMIS Fatigue T-scores using the PROsetta stone method[8]
- Patients in the placebo/evobrutinib 25 mg QD and the evobrutinib 25 mg QD arms have been pooled into a "PBO/EVO low dose" group in this analysis
- Nominal p-values were generated from MMRM for comparing the treatment effect of evobrutinib 75 mg BID and QD groups versus PBO/EVO low dose

Figure 1: Phase 2 DBP and OLE study design



All evobrutinib doses were given while fasted.
*All patients: n=190/evo-treated patients: n=151, mean (±SD) duration of exposure to evobrutinib 75 mg QD dose before the switch to 75 mg BID was 49.8 (±6.2)/50.6 (±6.0) weeks.[9]

Figure 2: SF-36 components



*SF-36 consists of eight subscales and two component summary scores representing physical health (PCS) and mental health (MCS); each subscale ranges from 0 to 100, with higher scores indicating better health.

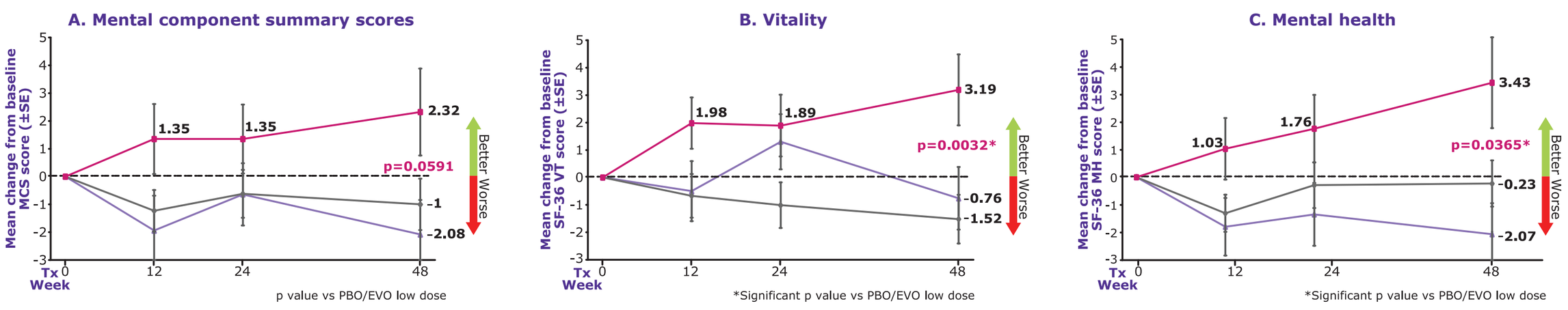
Please refer to supplementary data via the QR code for further information

RESULTS

Vitality and mental health: change from baseline to Week 48

- Patients receiving evobrutinib 75 mg BID in the DBP experienced notable improvements from baseline to Week 48 in MCS (p=0.0591; **Figure 3A**) and significant improvements compared to PBO/EVO low dose for vitality (p=0.0032; **Figure 3B**) and mental health (p=0.0365; **Figure 3C**)
- This treatment benefit of evobrutinib on vitality and mental health was maintained in the OLE period up to Week 240 (data not shown)

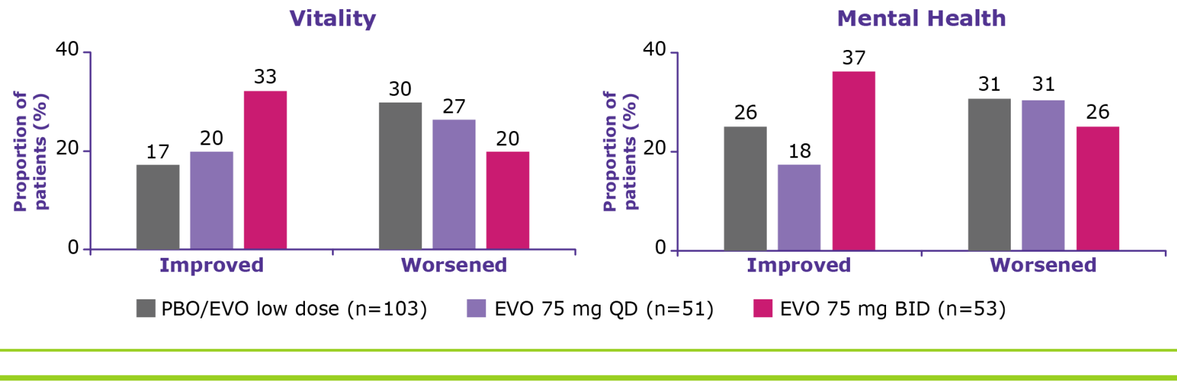
Figure 3. SF-36 scores up to Week 48



Vitality and mental health: clinically meaningful change to Week 48

- Numerically more patients experienced clinically meaningful improvements (≥5 points) from baseline in vitality and mental health, and fewer had clinically meaningful worsening, with evobrutinib 75 mg BID at Week 48 than with the lower doses[10] **(Figure 4)**

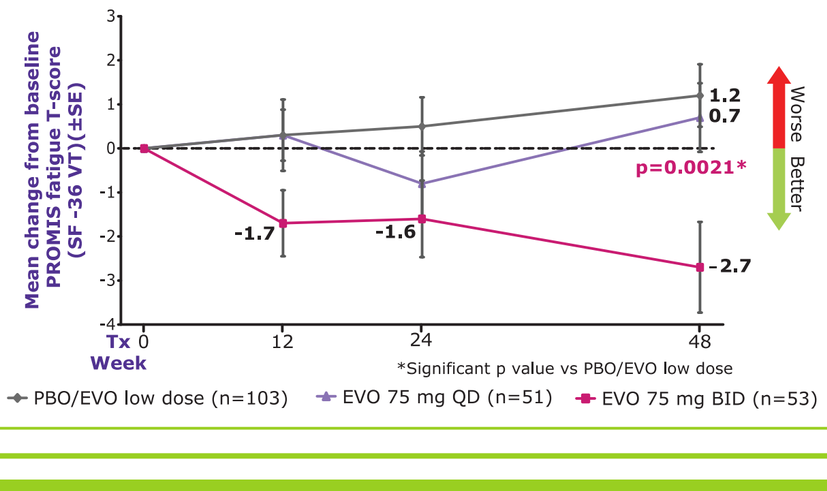
Figure 4: Clinically meaningful change from baseline to Week 48 (≥5 points)



PROMIS Fatigue T-score change to Week 48

- PROMIS Fatigue T-scores were significantly improved with evobrutinib 75 mg BID compared to PBO/EVO low dose **(Figure 5)**

Figure 5. PROMIS Fatigue T-score (SF-36 VT score) up to Week 48



Abbreviations: **BID**, twice daily; **BL**, baseline; **BTK**, Bruton's tyrosine kinase; **CNS**, central nervous system; **DBP**, double-blind period; **DMF**, dimethyl fumarate; **EVO**, evobrutinib; **MCS**, mental component summary; **MH**, mental health; **MMRM,** Mixed Models for Repeated Measures; **MS**, multiple sclerosis; **OLE**, open-label extension; **PBO**, placebo; **PCS**, physical component summary; **PROMIS**, Patient-Reported Outcome Measurement Information System; **QD**, once daily; **R**, randomisation; **RMS**, relapsing multiple sclerosis; **SD**, standard deviation; **SE**, standard error; **SF-36**, 36-Item Short Form; **VT**, vitality; **Tx**, treatment

References: 1. Haselmayer P, et al., *J Immunol.* 2019;202(10):2888–2906; 2. Caldwell RD, et al., *J Med Chem.* 2019;62(17):7643–7655; 3. Montalban X, et. al., *N Engl J Med.* 2019;380(25):2406–2417; 4. Biernacki T, et. al., *Brain Behav.* 2019;9(12):e01466; 5. Nordin Å, et. al., *BMC Med Res Methodol.* 2016;16:62; 6. Hobart J, et al., *J Neurol Neurosurg Psychiatry*. 2001;71(3):363–370; 7. Cella D, et. al., *Press release. A Rosetta stone for patient reported outcomes: PROMIS physical function and SF-36 physical function.* 2013; 8. Montalban X, et. al., Poster (P706) presented at ECTRIMS-ACTRIMS meeting 2023; 9. Papasouliotis O, et. al., *Clin Transl Sci.* 2022;15(12):2888–2898; 10. Goldman M, et al., *Neurology* 2019;93:e1921–e1931.

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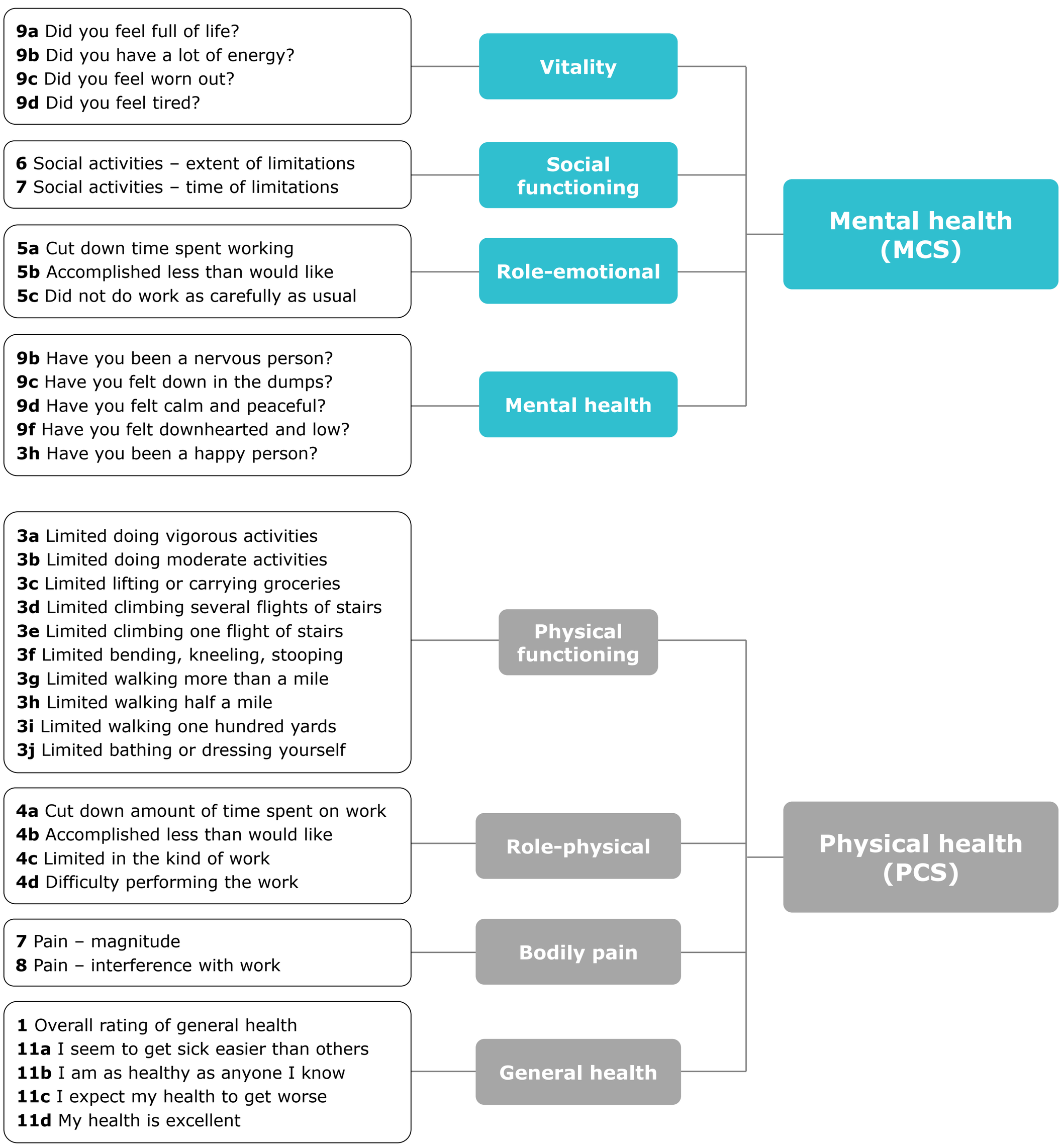
Supplementary information

The 36-item short form health survey questionnaire[1–3]



Abbreviations: MCS, mental component summary; **PCS**, physical component summary

References: 1. Ware JE Jr, et. al., *User's manual for the SF-36 v2 Health Survey (2nd edition)*. Lincoln, RI: Quality Metric Incorporated, 2007; 2. Hobart J, et al., *J Neurol Neurosurg Psychiatry*. 2001;71(3):363–370; 3. Montalban X, et. al., Poster (P706) presented at ECTRIMS-ACTRIMS meeting 2023.

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