Pharmacodynamic interaction of remifentanil and dexmedetomidine on depth of sedation and tolerance of laryngoscopy

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Supplemental Digital Content 1 - *Supplementary tables and figures*

Table S1.1. Model performances evaluated by using Varvel criteria.[1] Sorted in ascending MDPE for session 1. Performance metrics are shown as mean and standard error of the mean (SE between parenthesis) across volunteers.

DEXMEDETOMIDINE				
	Dexmedetomidine only phase		Interaction phase	
Model	MDPE (%)	MDAPE (%)	MDPE (%)	MDAPE (%)
Hannivoort[2]	**27 (5.4)**	**34 (4.1)**	**5.7 (3.8)**	**20 (1.9)**
Talke[3]	39 (5.1)	41 (4.7)	17 (3.3)	22 (2.2)
Dyck[4]	48 (5.1)	56 (4.2)	30 (4.2)	33 (3.5)
Venn[5]	48 (5.6)	52 (4.9)	30 (3.9)	32 (3.3)
Lin[6]	50 (8.0)	56 (6.6)	24 (5.7)	32 (4.4)
Cortinez[7]	54 (8.1)	57 (7.5)	35 (5.7)	39 (5.0)

REMIFENTANIL				
	Remifentanil only phase		Interaction phase	
Model	MDPE (%)	MDAPE (%)	MDPE (%)	MDAPE (%)
Eleveld[8]	**3.6 (6.5)**	**32 (3.7)**	**35 (7.7)**	**45 (5.9)**
Minto[9]	-4.0 (5.8)	30 (3.2)	25 (7.0)	39 (4.7)

MDPE = Median Performance Error, MDAPE = Median Absolute Performance error

INFUSION SCHEMES

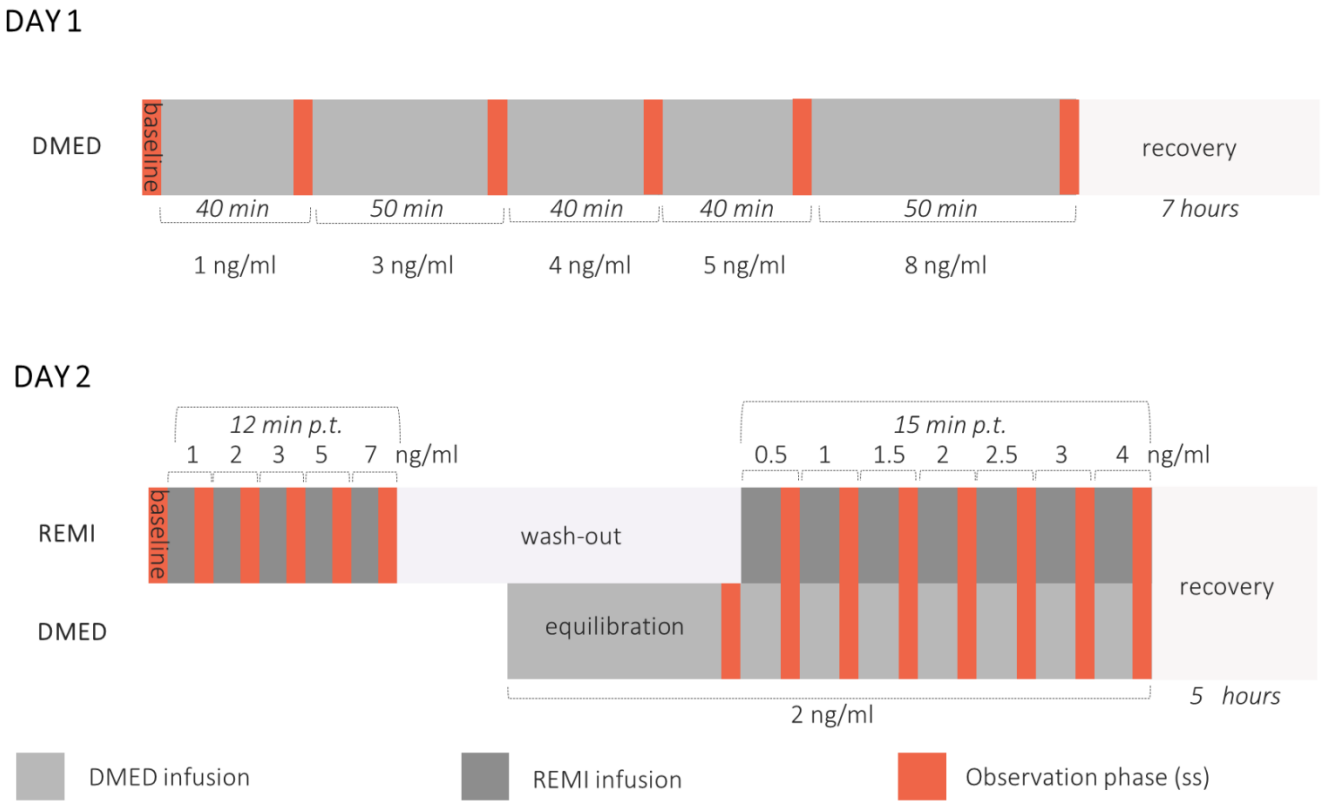

Fig. S1.1. Schematic overview of infusion regimens and observation phases. Concentrations are target controlled infusion target concentrations. DMED = dexmedetomidine, REMI = remifentanil, p.t. per target, ss=steady-state.

OBSERVATION PHASE (SS)

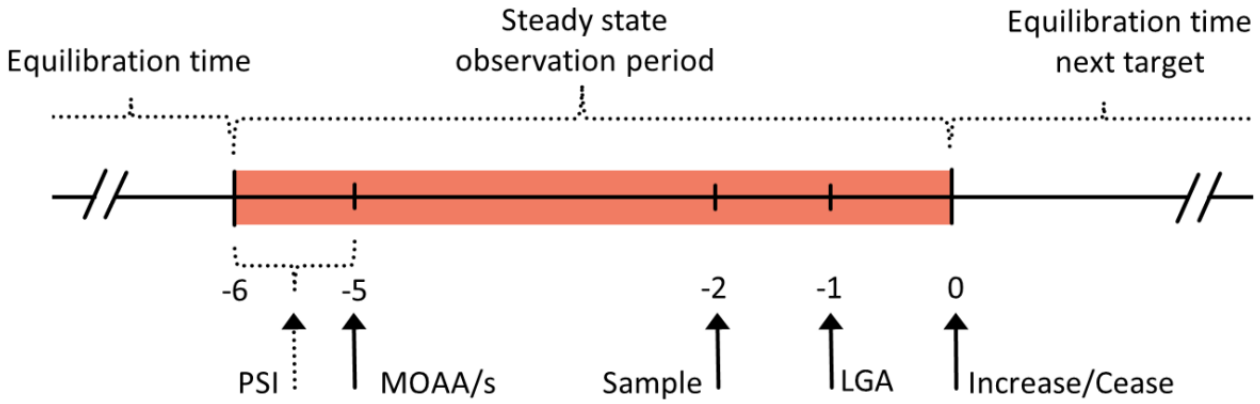

Fig. S1.2. Schematic overview of the timing of measurements during steady-state (SS) observation phases. Numbers indicate minutes before the end of the infusion step. PSI = Patient State Index, MOAA/S = Modified Observers Assessment of Alertness and Sedation scale[10], LGA = Laryngoscopy Attempt.

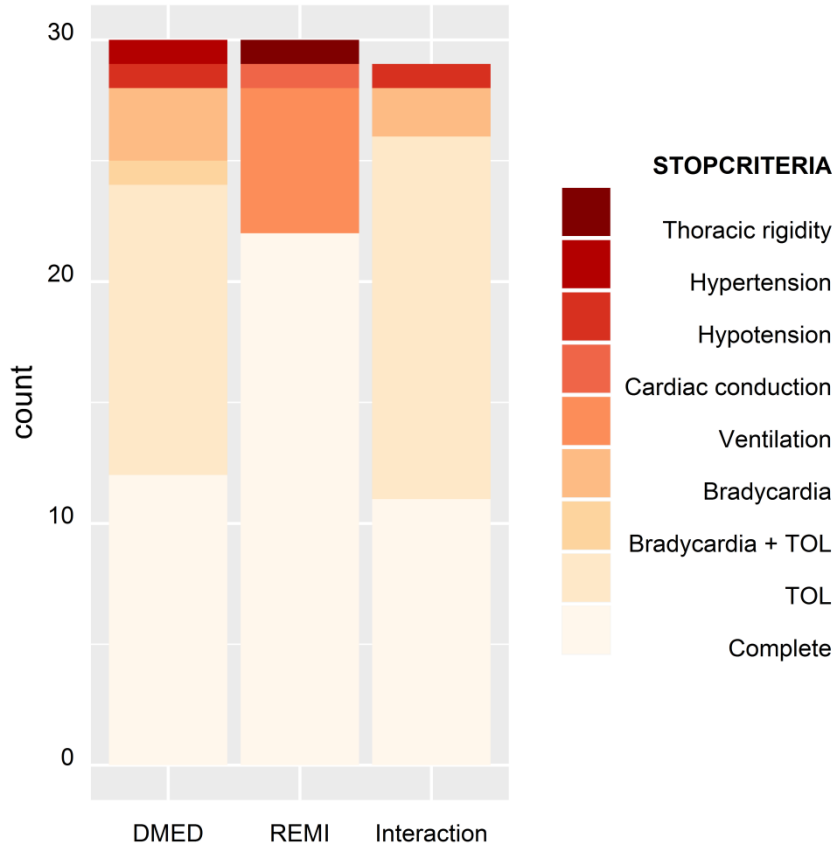

Fig. S1.3. Stop reasons of the dexmedetomidine (DMED), remifentanil (REMI) and DMED+REMI infusion phases. TOL = Tolerance of laryngoscopy.

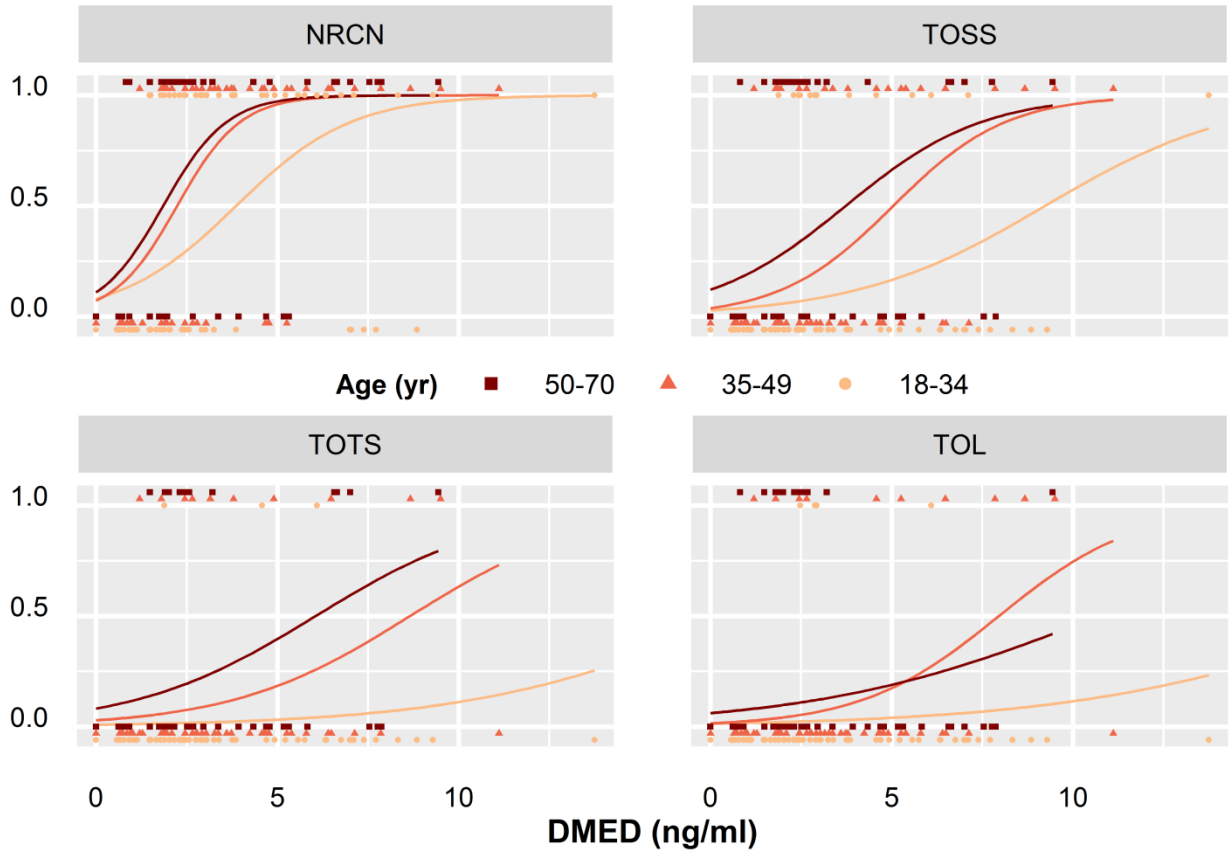

Fig. S1.4. Observations per age category, for no response to calling of name (NRCN), tolerance of shake and shout (TOSS), tolerance of trapezius squeeze (TOTS) and tolerance of laryngoscopy (TOL) versus dexmedetomidine concentrations (ng/ml).

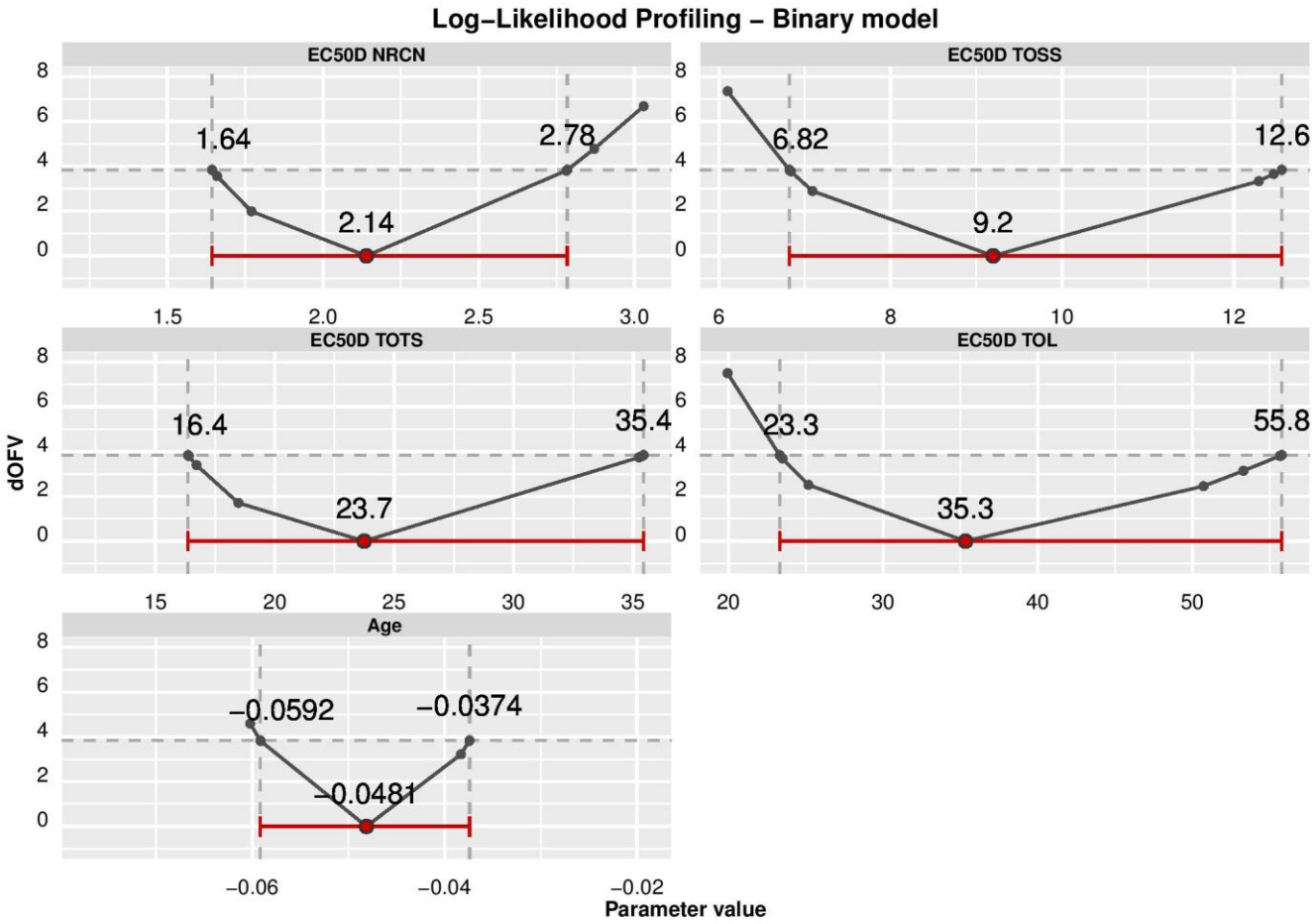

Fig. S1.5.Log-likelihood profiles for parameters estimates of the binary model, with 95% upper- and lower-confidence limits. dOFV= Δ objective function, EC50D = half maximal effective concentration dexmedetomidine (ng/ml) for no response to calling of name (NRCN), tolerance of shake and shout (TOSS), tolerance of trapezius squeeze (TOTS) and tolerance of laryngoscopy (TOL).

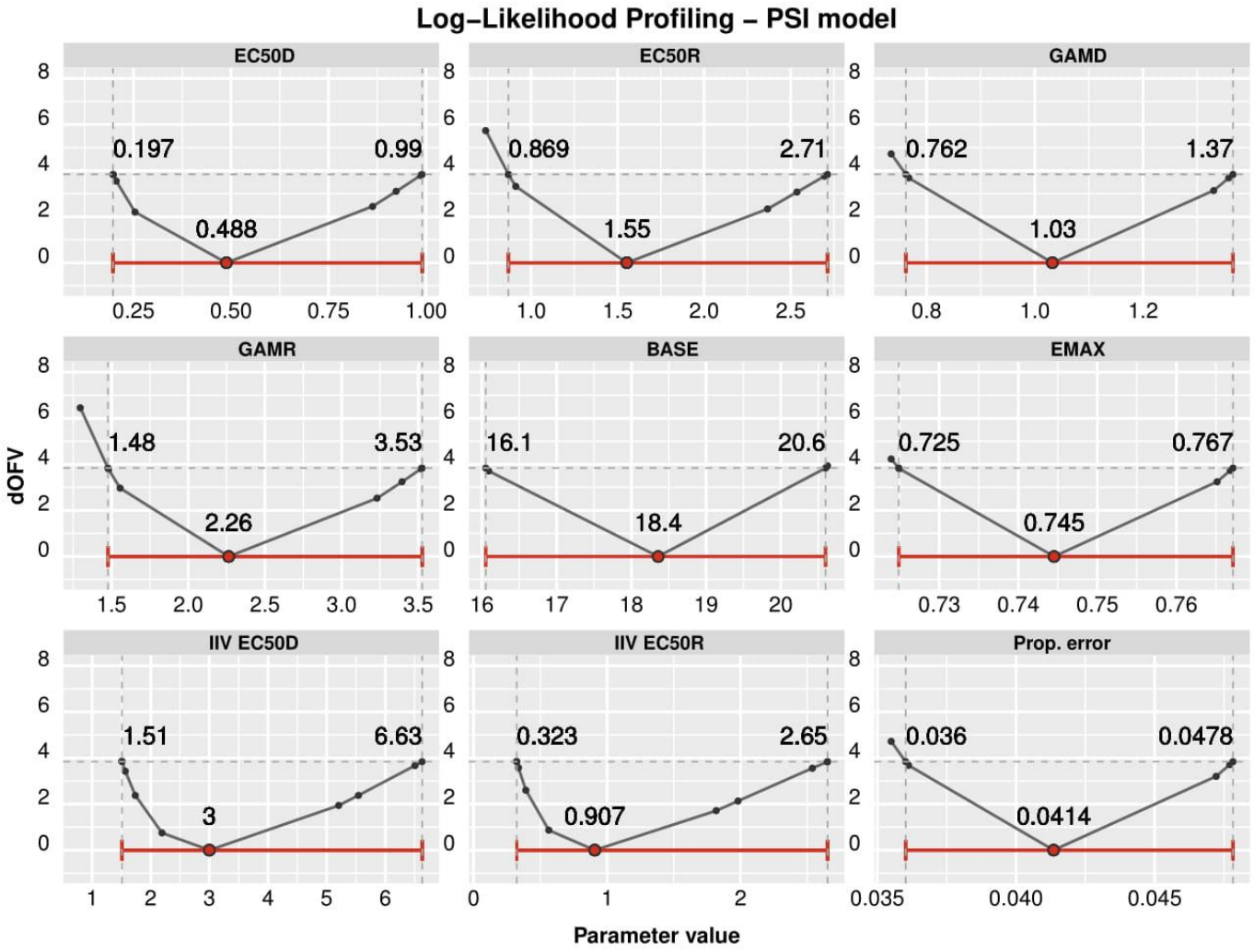

Fig. S1.6.Log-likelihood profiles for parameters estimates of the PSI model, with 95% upper- and lower-confidence limits. dOFV= Δ objective function, EC50D = half maximal effective concentration dexmedetomidine (ng/ml), EC50R = half maximal effective concentration remifentanil (ng/ml), GAMD= dexmedetomidine gamma, GAMR= remifentanil gamma, BASE= estimate for baseline PSI is 100-BASE. EMAX = Maximal effect, IIV= Inter Individual Variability, Prop. Error = proportional error.

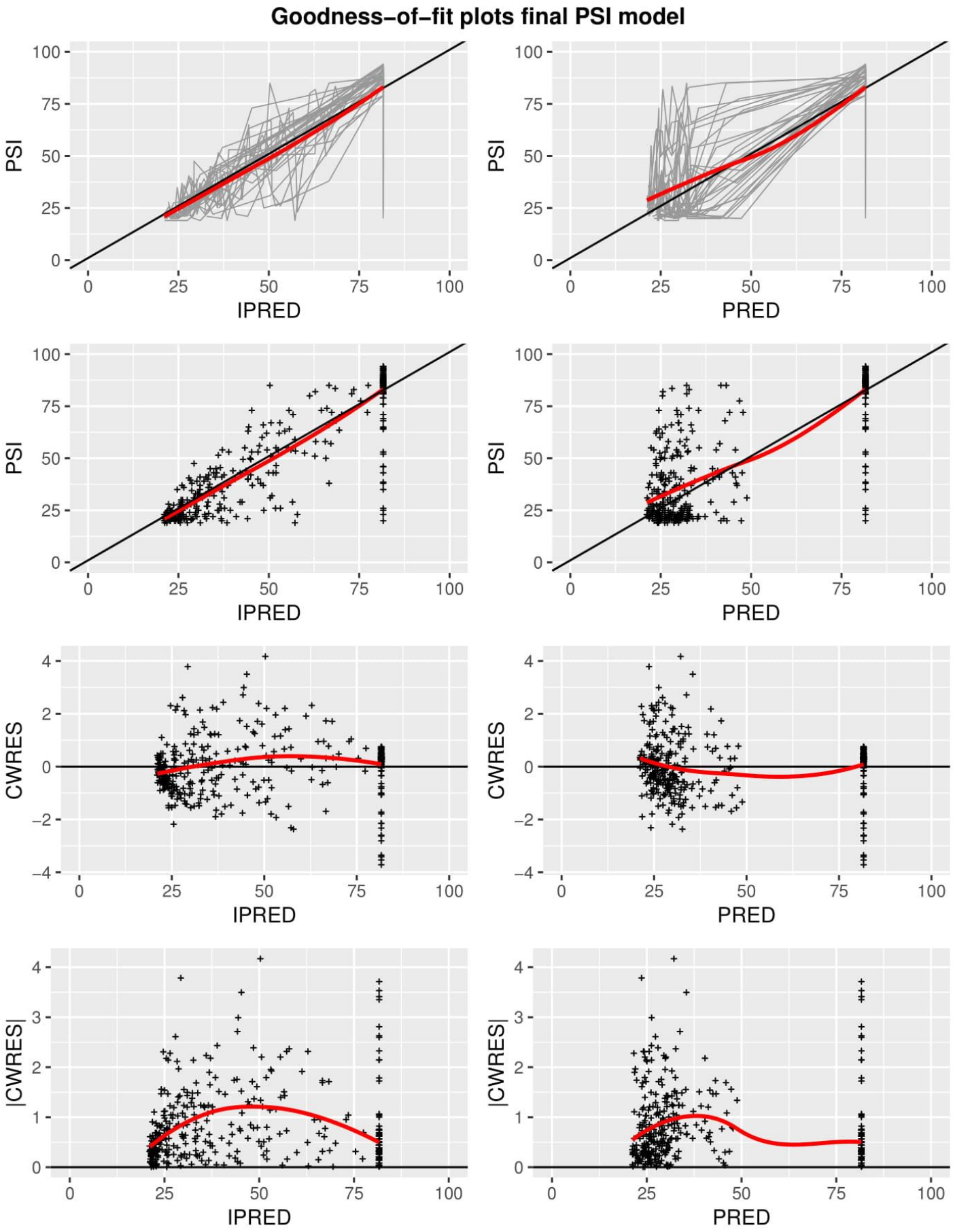

Fig. S1.7. PSI = patient state index, IPRED = Individual model predictions, PRED = population model predictions, CWRES = conditionally weighted residuals. Red lines are LOESS smoothers.

References:

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