

Supplementary material: Tables and figures

Table S1: Questions included in the functional assessment of cancer therapy- breast (FACT-B) questionnaire, abbreviated label and information on reverse items

Subscale	FACT-B item	Abbreviated label	Reverse item?	Item number
Physical well-being	I have a lack of energy	Lack of energy	Yes	1
	I have nausea	Have nausea	Yes	2
	Because of my physical condition, I have trouble meeting the needs of my family	Meeting family needs	Yes	3
	I have pain	Have pain	Yes	4
	I am bothered by side effects of treatment	Bothered by side effects	Yes	5
	I feel ill	Feel ill	Yes	6
	I am forced to spend time in bed	Spend time in bed	Yes	7
Social/family well-being	I feel close to my friends	Close to friends	No	8
	I get emotional support from my family	Emotional support from family	No	9
	I get support from my friends	Support from friends	No	10
	My family has accepted my illness	Family accept illness	No	11
	I am satisfied with family communication about my illness	Family comm. about illness	No	12
	I feel close to my partner (or the person who is my main support)	Close to partner	No	13
	I am satisfied with my sex life	Sex life	No	14
Emotional well-being	I feel sad	Feel sad	Yes	15
	I am satisfied with how I am coping with my illness	Satisf. coping with illness	No	16
	I am losing hope in the fight against my illness	No hope with fight vs illness	Yes	17
	I feel nervous	Feel nervous	Yes	18
	I worry about dying	Worry about dying	Yes	19
	I worry that my condition will get worse	Condition get worse	Yes	20
Functional well-being	I am able to work (include work at home)	Able to work	No	21
	My work (include work at home) is fulfilling	Work fulfilling	No	22
	I am able to enjoy life	Enjoy life	No	23
	I have accepted my illness	Accept my illness	No	24
	I am sleeping well	Sleeping well	No	25
	I am enjoying the things I usually do for fun	Usually do for fun	No	26

Subscale	FACT-B item	Abbreviated label	Reverse item?	Item number
	I am content with the quality of my life right now	Quality of life	No	27
Breast cancer subscale	I have been short of breath	Short of breath	Yes	28
	I am self-conscious about the way I dress	Way I dress	Yes	29
	One or both of my arms are swollen or tender	Arms swollen or tender	Yes	30
	I feel sexually attractive	Sexually attractive	No	31
	I am bothered by hair loss	Bothered by hair loss	Yes	32
	I worry that other members of my family might someday get the same illness I have	Family mbr get same illness	Yes	33
	I worry about the effect of stress on my illness	Effect stress illness	Yes	34
	I am bothered by a change in weight	Bothered change weight	Yes	35
	I am able to feel like a woman	Feel like a woman	No	36
	I have certain parts of my body where I experience pain	Not included - Not currently scored		-

Table S2: Objective function values (OFV) obtained for each breast cancer subscale items when reassigning them to each of the other subscale.

Item	Subscale	OFV	Difference in OFV from best
Short of breath	Physical	5475	0
	Social/family	6001	526
	Emotional	5755	280
	Functional	5858	383
Self-conscious about way I dress	Physical	6038	77
	Social/family	6210	249
	Emotional	5961	0
	Functional	6139	178
Arms swollen or tender	Physical	6147	0
	Social/family	6373	226
	Emotional	6270	123
	Functional	6336	189
Feel sexually attractive	Physical	7325	473
	Social/family	7239	387
	Emotional	7366	514
	Functional	6852	0
Bothered by hair loss	Physical	6201	165
	Social/family	6284	248
	Emotional	6036	0
	Functional	6241	205
Worry that family members get the same illness	Physical	8209	377
	Social/family	8347	515
	Emotional	7832	0
	Functional	8299	467
Worry about effect of stress on illness	Physical	7603	583
	Social/family	7914	894
	Emotional	7020	0
	Functional	7801	781
Bothered by change in weight	Physical	7231	64
	Social/family	7381	214
	Emotional	7167	0
	Functional	7326	159
Feel like a woman	Physical	7418	626
	Social/family	7104	312
	Emotional	7427	635
	Functional	6792	0

Table S3: Item-specific parameter estimates from the final longitudinal item-response theory model.

Item	a	b ₁	δ ₂	δ ₃	δ ₄
Lack of energy	2.07	-2.32	0.973	1.02	1.27
Have nausea	1.47	-4.00	1.02	1.16	1.27
Meeting family needs	2.56	-2.25	0.689	0.876	0.977
Have pain	1.75	-2.71	1.04	0.964	1.23
Bothered by side effects	2.07	-2.70	0.879	0.991	1.21
Feel ill	3.15	-2.46	0.737	0.871	0.914
Spend time in bed	2.83	-2.63	0.765	0.709	0.913
Close to friends	3.04	-2.18	0.630	0.719	0.831
Emotional support from family	4.68	-2.10	0.478	0.593	0.735
Support from friends	3.54	-1.85	0.358	0.623	0.807
Family accept illness	2.45	-2.25	0.566	0.793	0.891
Family comm. about illness	3.13	-2.18	0.596	0.780	0.821
Close to partner	2.88	-2.01	0.350	0.640	0.698
Sex life	1.49	-1.42	0.465	0.979	1.04
Feel sad	2.19	-2.47	0.983	1.09	1.21
Satisf. coping with illness	0.830	-3.73	1.38	1.95	2.19
No hope with fight vs illness	2.06	-2.68	0.611	1.04	0.876
Feel nervous	2.04	-2.23	0.794	0.939	1.37
Worry about dying	2.18	-1.69	0.571	0.740	1.21
Condition get worse	2.43	-1.36	0.683	0.731	1.35
Able to work	2.03	-1.96	0.925	1.05	1.17
Work fulfilling	2.62	-1.65	0.648	0.952	1.04
Enjoy life	4.27	-1.94	0.735	0.864	0.893
Accept my illness	1.69	-2.34	0.763	1.04	1.20
Sleeping well	1.43	-2.56	1.06	1.46	1.23
Usually do for fun	3.76	-1.80	0.689	0.885	0.844
Quality of life	3.63	-1.74	0.684	0.996	0.953
Short of breath	1.19	-3.91	1.28	1.21	1.30
Way I dress	0.835	-4.13	1.18	1.62	1.40
Arms swollen or tender	0.765	-4.59	1.64	1.23	1.49
Sexually attractive	1.41	-1.22	0.776	1.44	1.23
Bothered by hair loss	0.840	-2.82	0.796	0.854	1.00
Family mbr get same illness	1.06	-1.33	1.08	0.766	1.40
Effect stress illness	1.51	-1.80	1.21	0.963	1.29
Bothered change weight	0.764	-3.28	1.32	1.31	1.38
Feel like a woman	1.52	-2.20	0.975	1.12	1.25

$b_2 = b_1 + \delta_2$; $b_3 = b_2 + \delta_3$; $b_4 = b_3 + \delta_4$. See also NONMEM code provided as Supplementary material.

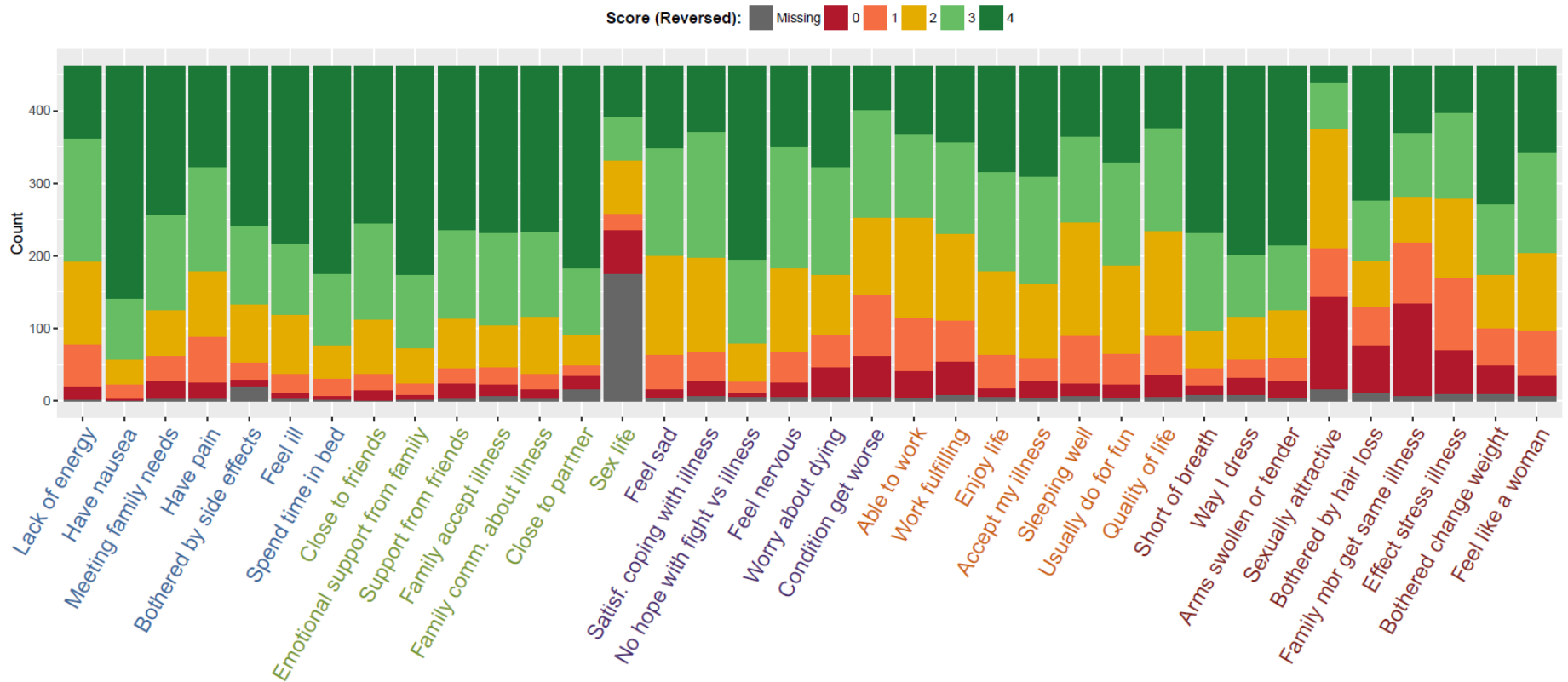


Figure S1: Distributions of observed FACT-B scores at baseline in T-DM1 arm. Label color corresponds to the item's subscale: blue for physical, green for social/family, purple for emotional, orange for functional and red for breast-cancer. Scores for reverse items have been reverse-scaled (i.e. higher score indicate better outcome)

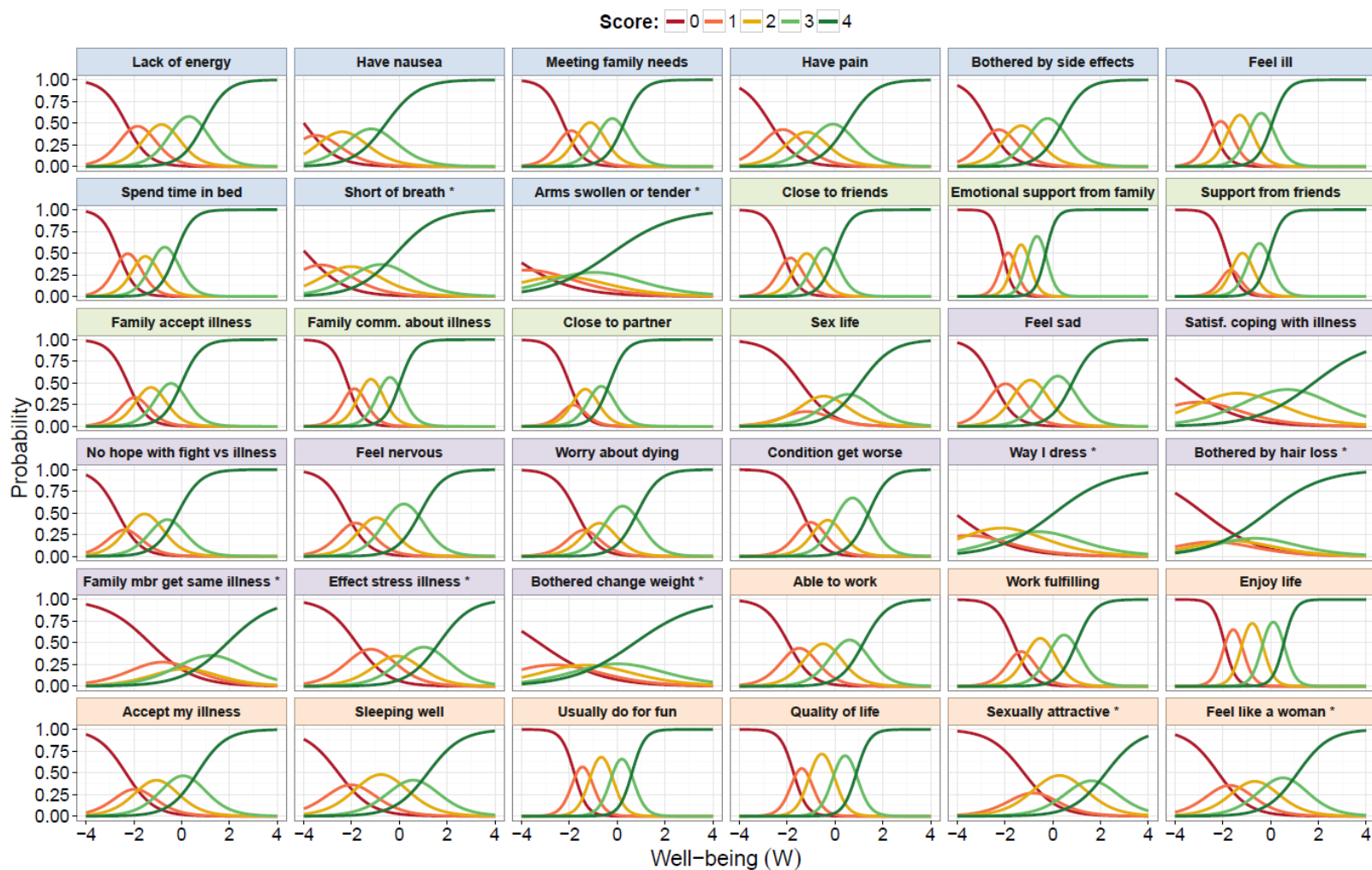


Figure S2: Item characteristic curves obtained from the final longitudinal item-response theory model. For each FACT-B item, the probability of each score is plotted against the latent well-being variable W . Panels' color correspond to the item subscale: blue for physical, green for social/family, purple for emotional and orange for functional. Scores for reverse items have been reverse-scaled (i.e. higher score indicate better outcome). * Items originally belonging to the breast-cancer subscale.

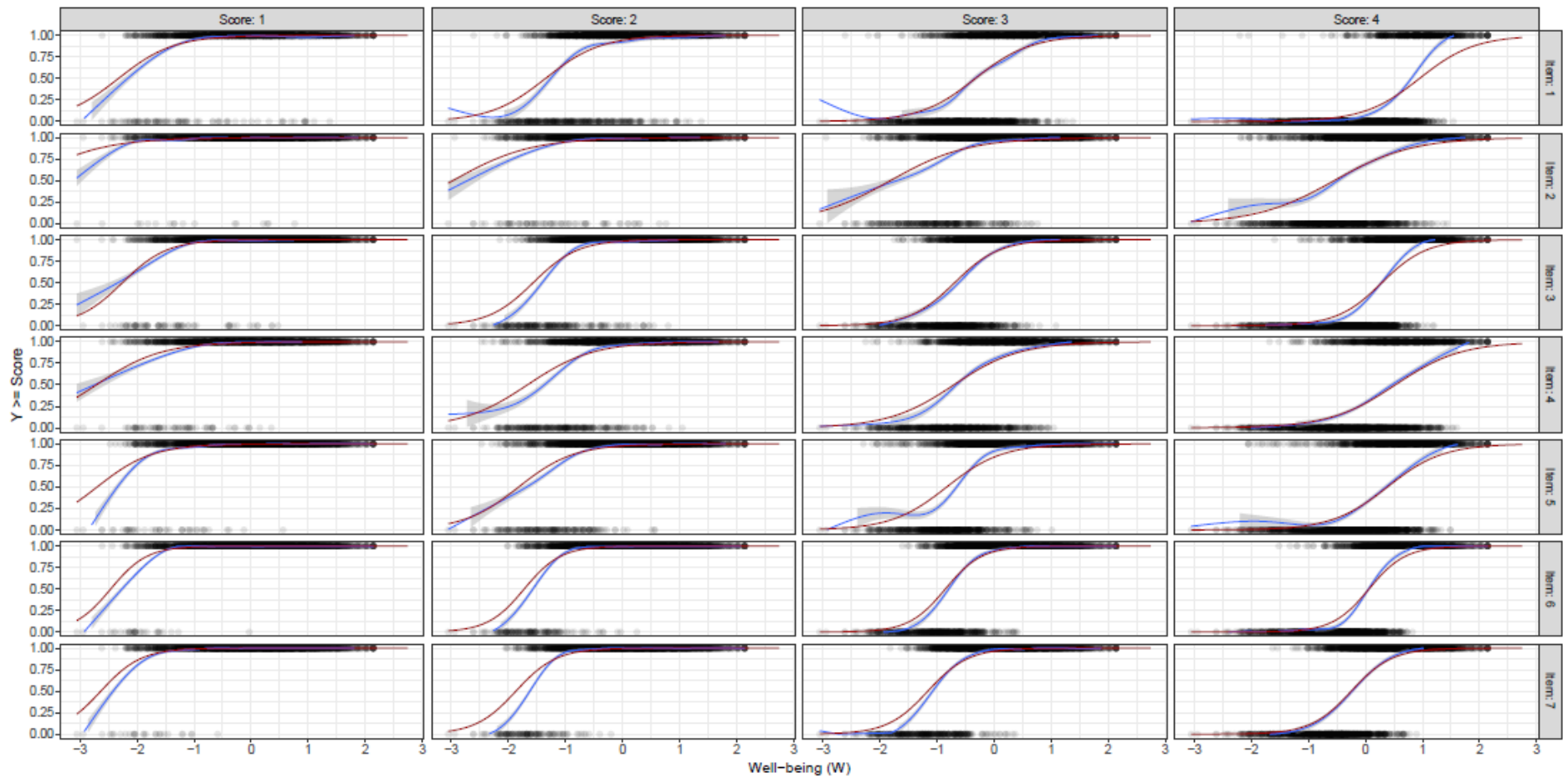


Figure S3: Diagnostic plots comparing the IRT model fit (red line) to the fit of generalized additive model (GAM) with cross-validated cubic spline as a smoothing function (blue line with 95% confidence interval in grey). Item numbers are as described in Table S1.

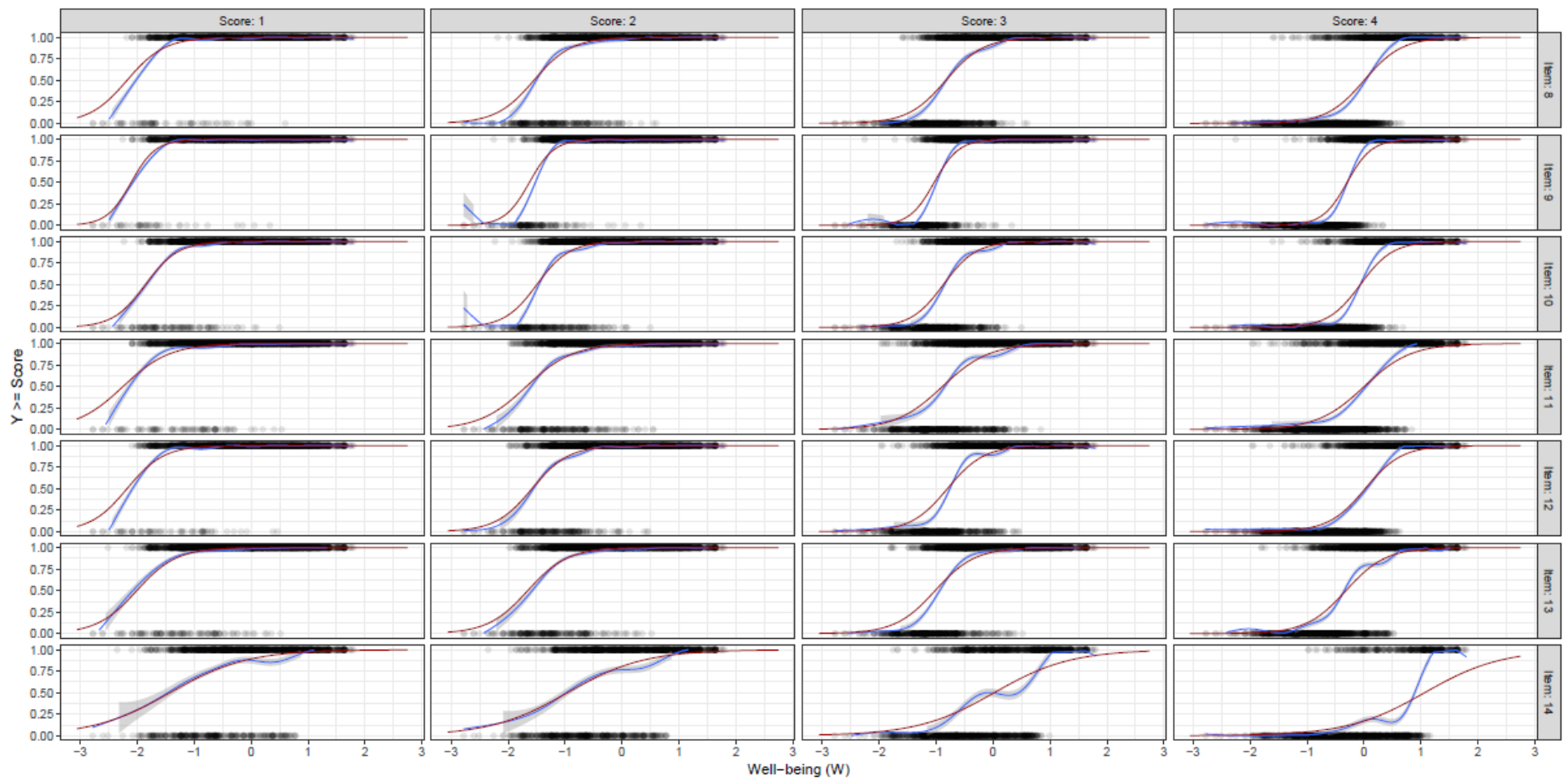


Figure S3 (continued): Diagnostic plots comparing the IRT model fit (red line) to the fit of generalized additive model (GAM) with cross-validated cubic spline as a smoothing function (blue line with 95% confidence interval in grey). Item numbers are as described in Table S1.

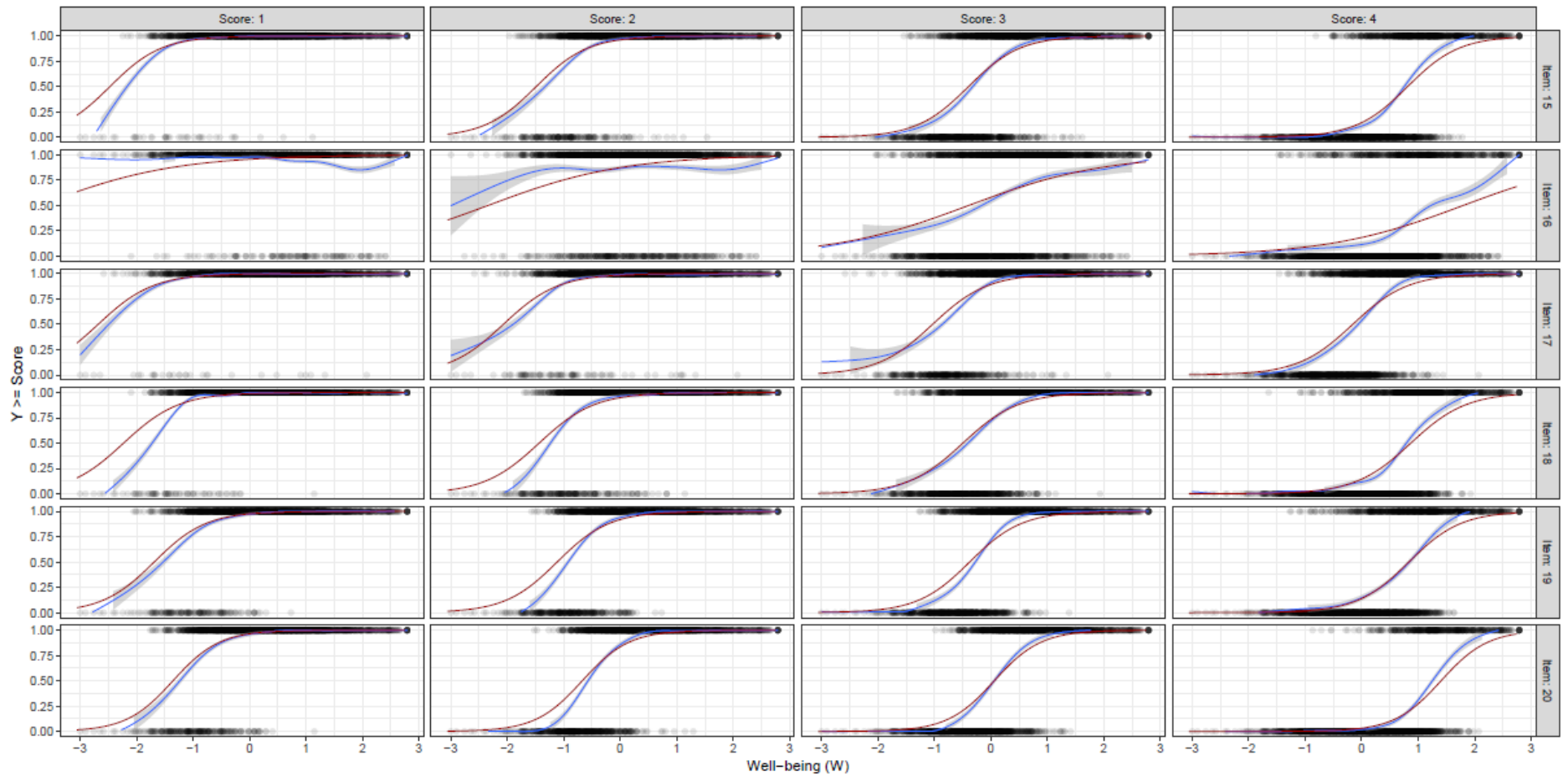


Figure S3 (continued): Diagnostic plots comparing the IRT model fit (red line) to the fit of generalized additive model (GAM) with cross-validated cubic spline as a smoothing function (blue line with 95% confidence interval in grey). Item numbers are as described in Table S1.

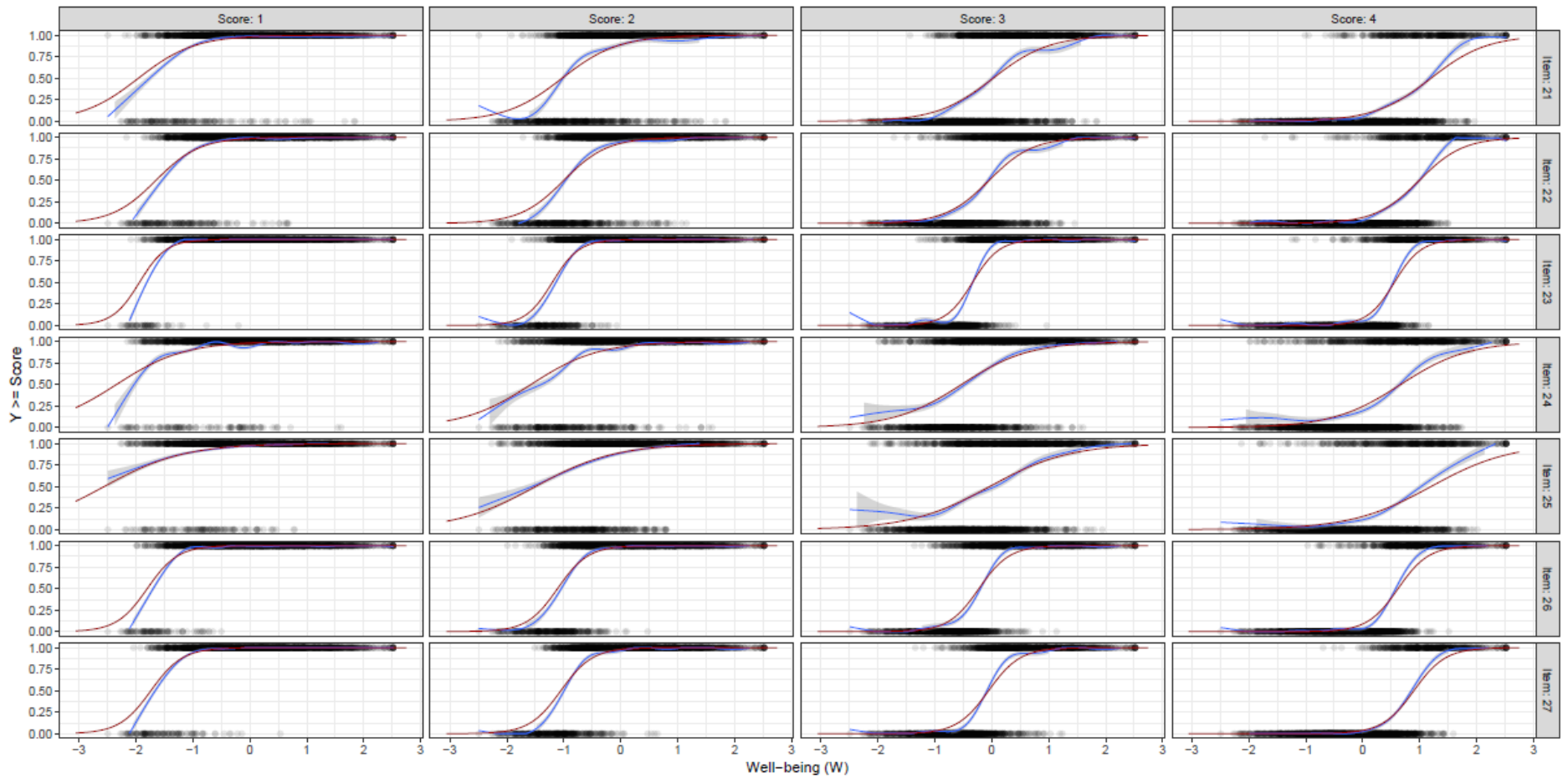


Figure S3 (continued): Diagnostic plots comparing the IRT model fit (red line) to the fit of generalized additive model (GAM) with cross-validated cubic spline as a smoothing function (blue line with 95% confidence interval in grey). Item numbers are as described in Table S1.

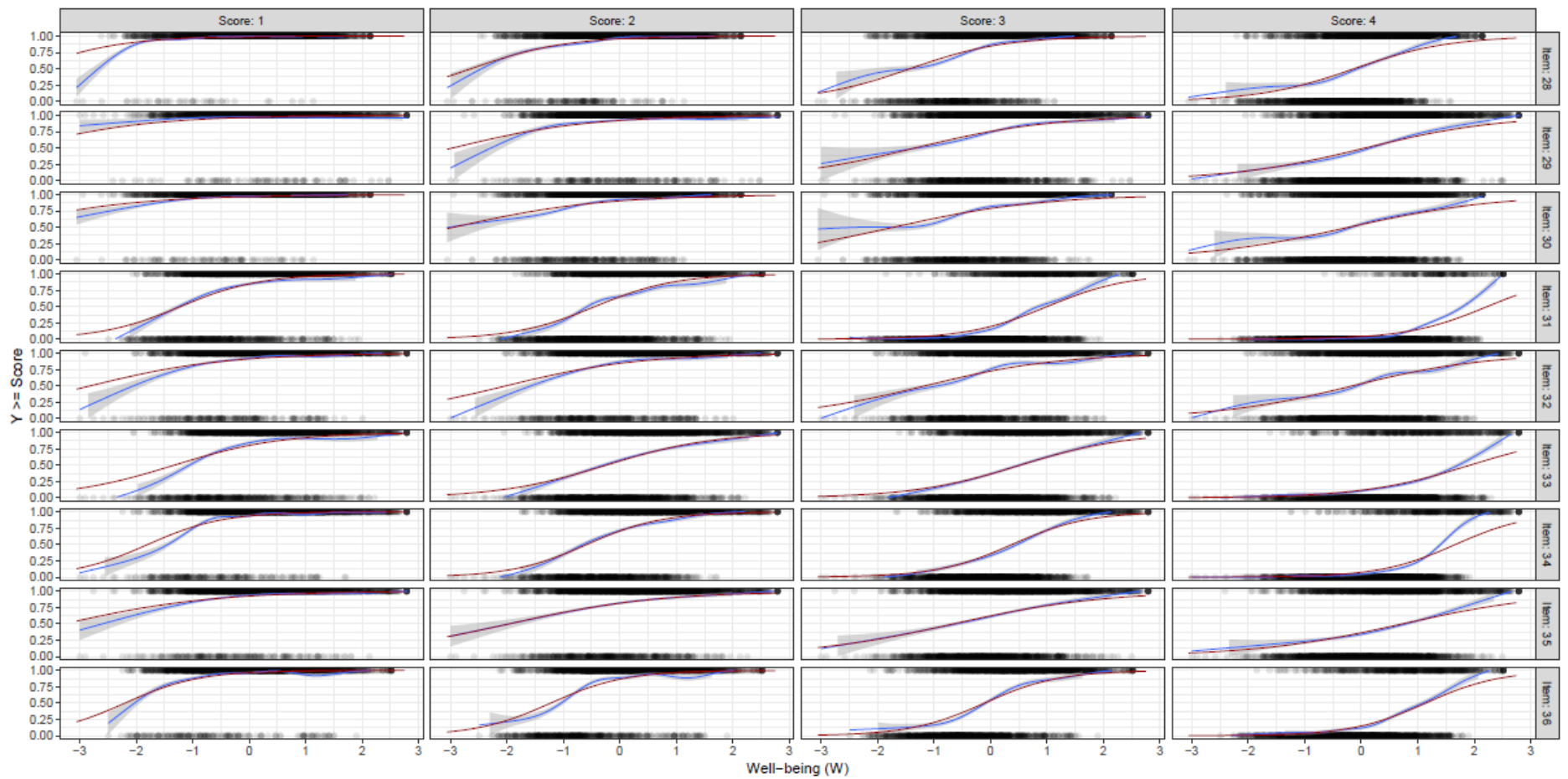


Figure S3 (continued): Diagnostic plots comparing the IRT model fit (red line) to the fit of generalized additive model (GAM) with cross-validated cubic spline as a smoothing function (blue line with 95% confidence interval in grey). Item numbers are as described in Table S1.

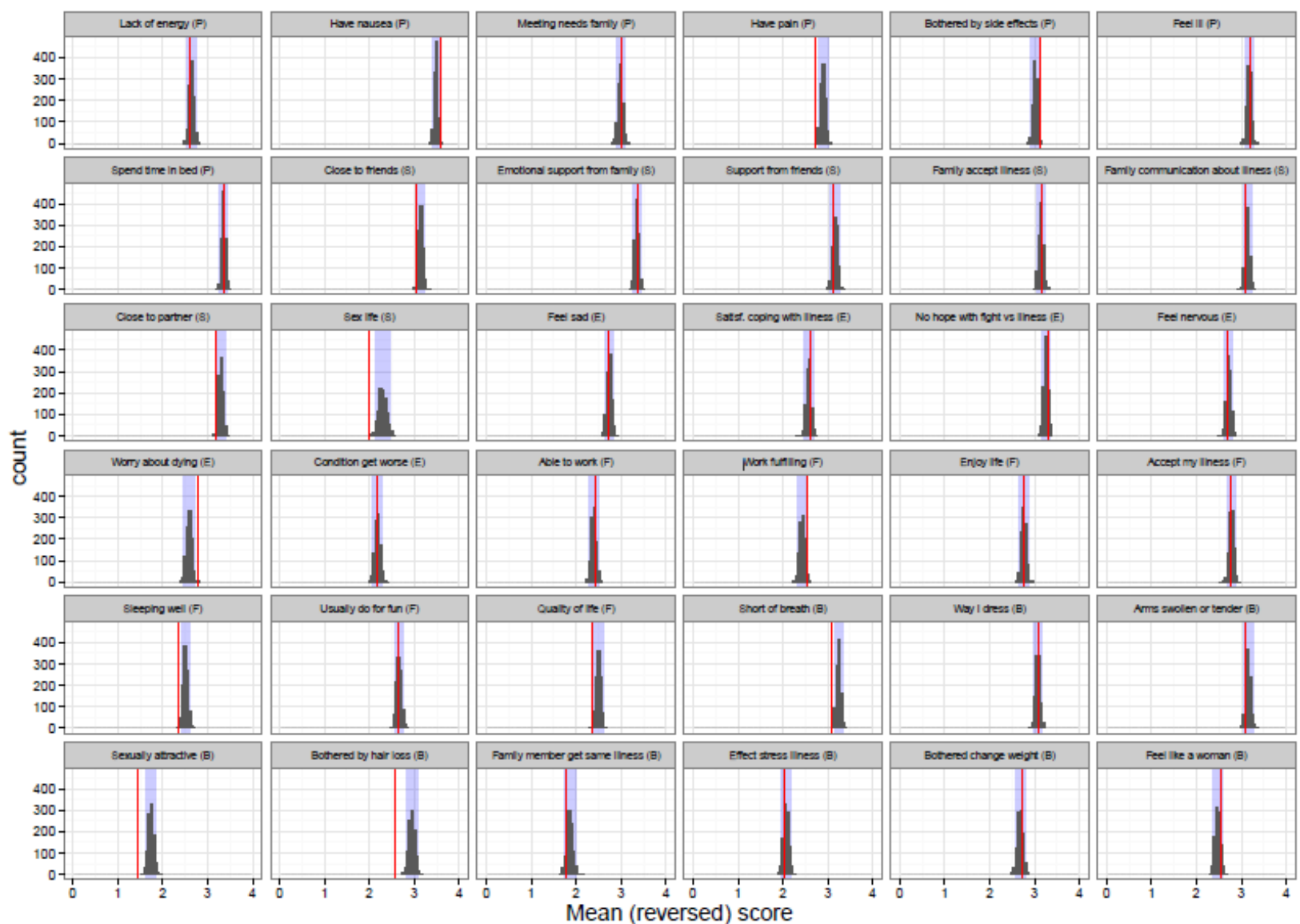


Figure S4: Mean scores for the original capecitabine-plus-lapatinib data set (red) compared to the mean score distribution in the simulated data sets obtained from the base IRT model (distribution in grey and 95% confidence interval in blue).

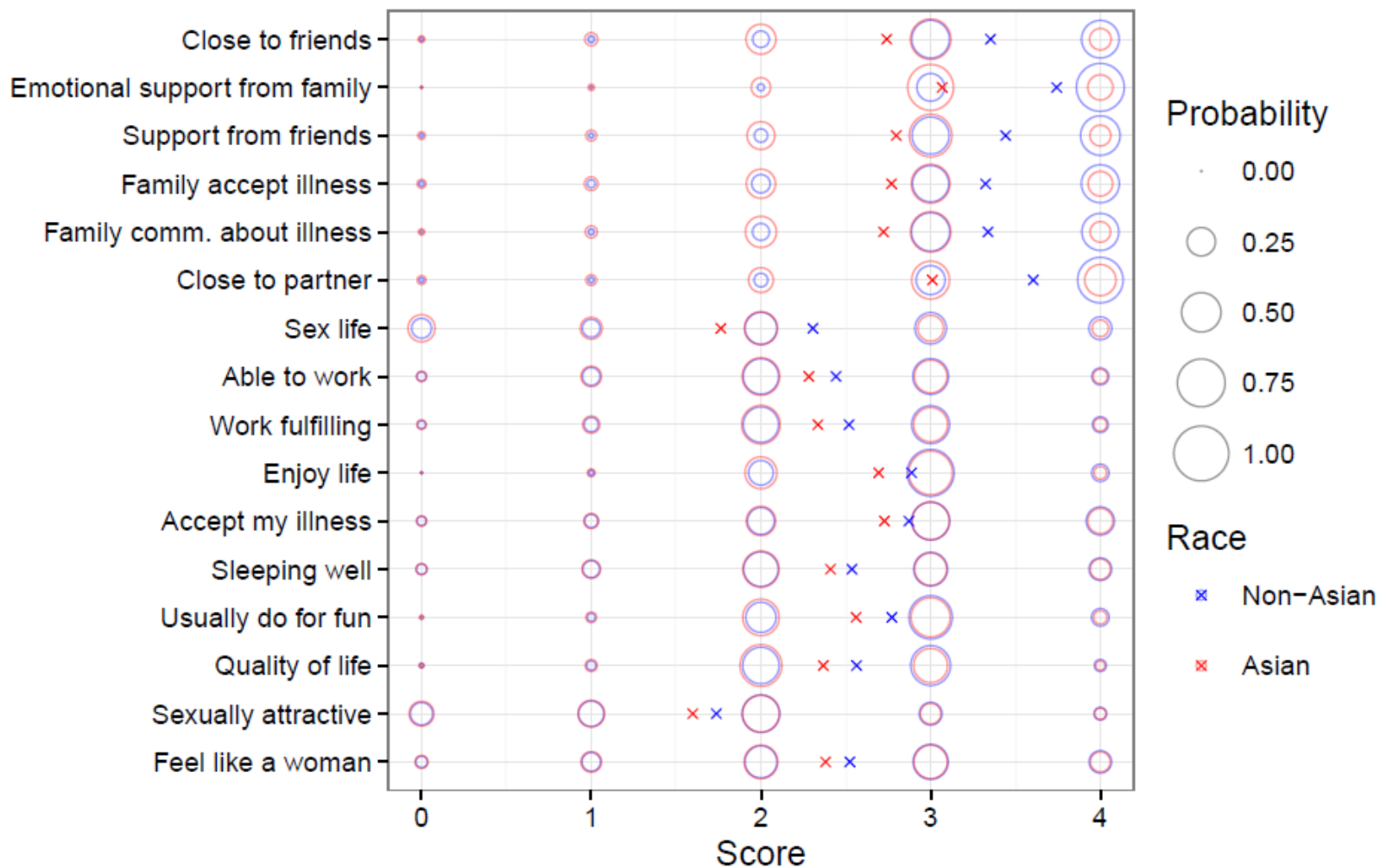


Figure S5: Schematic representation of the item score probabilities and expected score at baseline for a typical patient with baseline ECOG of 0, as predicted by the final longitudinal item-response theory model and differentiated by race. Circle surface areas are proportional to the score probability. Cross symbols represent expected scores, calculated as $\sum_{k=0}^4 P(Y = k) \cdot k$. Scores for reverse items have been reverse-scaled (i.e. higher score indicate better outcome).

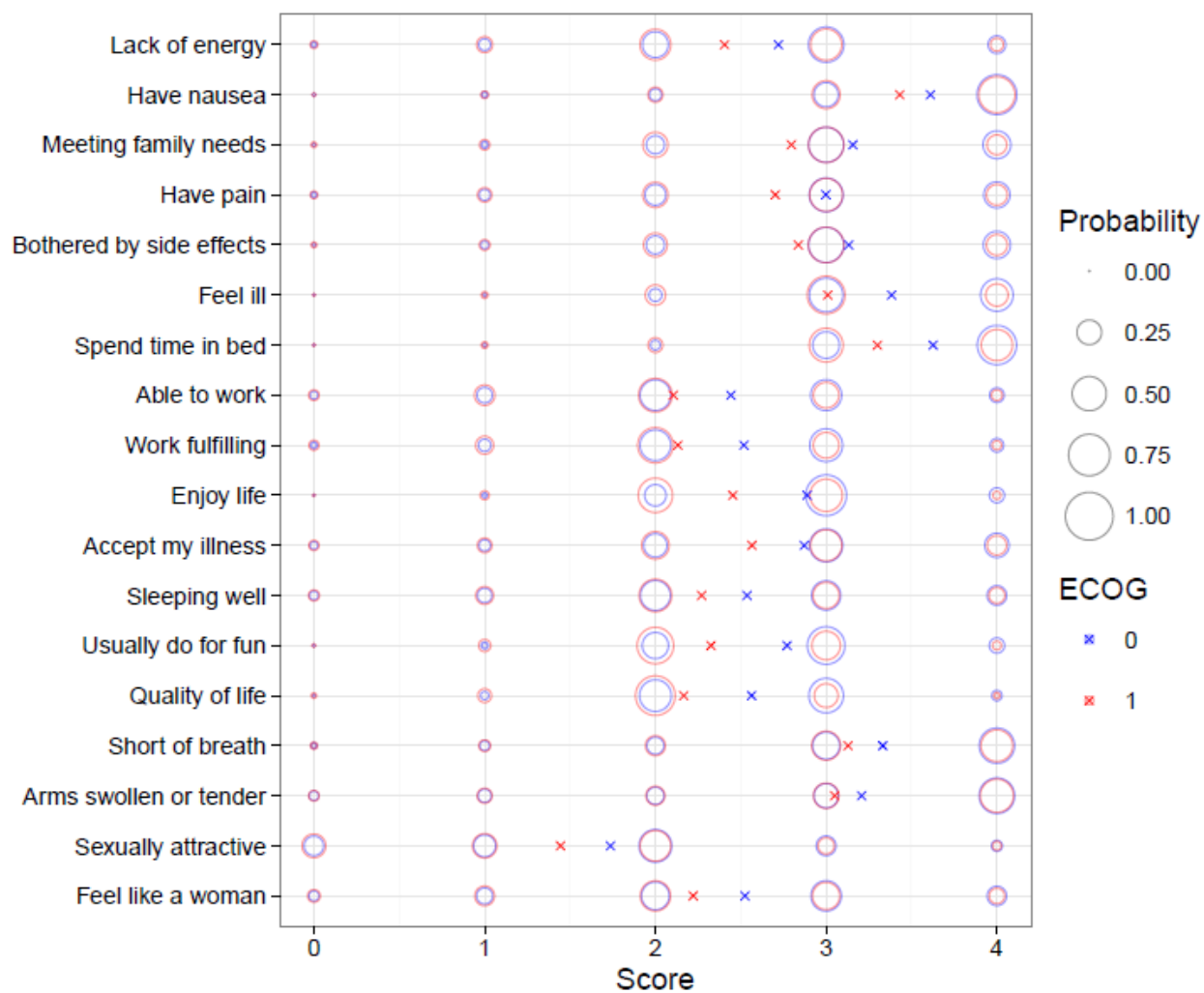


Figure S6: Schematic representation of the item score probabilities and expected score at baseline for a typical non-Asian patient, as predicted by the final longitudinal item-response theory model and differentiated by baseline ECOG. Circle surface areas are proportional to the score probability. Cross symbols represent expected scores, calculated as $\sum_{k=0}^4 P(Y = k) \cdot k$. Scores for reverse items have been reverse-scaled (i.e. higher score indicate better outcome).