

# SUPPLEMENT II

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# 1 Descriptive statistics for the pain composite scores

Descriptive statistics (mean and standard deviation, SD) of the pain composite scores (PCS) and sub-scores for pain intensity (PCS<sub>intensity</sub>), pain interference (PCS<sub>interference</sub>) and side effects (PCS<sub>side</sub>). Results are shown separately for the total cohort and women with regional anaesthesia (no general anaesthesia). In addition, the patient numbers (n) are shown.

Variable	Care group	Total cohort			Regional anaesthesia		
		Mean	SD	n	Mean	SD	n
<b>PCS<sub>total</sub></b>	Incomplete	3.82	1.74	3,071	3.92	1.77	2,509
	Intra-operative	3.52	1.66	186	3.55	1.65	167
	Post-operative	3.49	1.58	715	3.51	1.56	603
	Full care	3.25	1.54	1,010	3.19	1.52	934
<b>PCS<sub>intensity</sub></b>	Incomplete	5.02	2.05	3,071	5.19	2.09	2,509
	Intra-operative	4.39	2.04	186	4.37	2.04	167
	Post-operative	4.01	1.77	715	3.99	1.72	603
	Full care	3.98	1.94	1,010	3.88	1.88	934
<b>PCS<sub>interference</sub></b>	Incomplete	4.42	2.36	3,071	4.54	2.40	2,509
	Intra-operative	4.05	2.30	186	4.08	2.35	167
	Post-operative	4.25	2.09	715	4.27	2.05	603
	Full care	3.65	2.03	1,010	3.58	2.01	934
<b>PCS<sub>side</sub></b>	Incomplete	2.16	2.10	3,071	2.20	2.17	2,509
	Intra-operative	2.20	2.06	186	2.27	2.05	167
	Post-operative	2.14	1.98	715	2.21	2.02	603
	Full care	2.19	1.96	1,010	2.19	1.96	934

## 2 Model details: Total cohort

### 2.1 Pain Composite Score: total

Model parameter for the **total pain composite score** (PCS<sub>total</sub>, n = 4,982 patients). The PCS<sub>total</sub> was z-standardized before modelling. Significant regression coefficients are printed in bold (coefficient of determination:  $R^2_{\text{marginal}} = 0.025$ ,  $R^2_{\text{conditional}} = 0.216$ ).

Variable	[Reference/Unit]	$\beta$	95%CI		p
(Intercept)		-0.27	-0.59	0.06	0.114
<b>Perioperative treatment protocol:</b>					
Intra-operative	[vs. Incomplete]	-0.27	-0.42	-0.11	<b>&lt;0.001</b>
Post-operative	[vs. Incomplete]	-0.07	-0.19	0.04	0.216
Full care	[vs. Incomplete]	-0.36	-0.49	-0.23	<b>&lt;0.001</b>
<b>Group:</b>					
General anaesthesia (GA)	[vs. RA, regional anaesthesia]	0.16	0.04	0.28	<b>0.009</b>
Combined GA + RA	[vs. RA]	0.04	-0.14	0.22	0.659
Age	[years]	0.00	-0.01	0.00	0.138
Pre-existing chronic pain	[vs. no]	0.21	0.11	0.31	<b>&lt;0.001</b>
Ward: any opioid	[vs. none]	0.17	0.10	0.25	<b>&lt;0.001</b>
Income level: high	[vs. others]	0.32	-0.07	0.70	0.120

Estimated marginal means (covariate adjusted means) and 95% confidence intervals of the PCS<sub>total</sub> (n = 4,982 patients). Results are shown for the peri-operative treatment protocol groups. The PCS<sub>total</sub> was z-standardized before modelling.

Care group	mean	95% CI	
Incomplete	0.04	-0.17	0.25
Intra-operative	-0.23	-0.47	0.02
Post-operative	-0.03	-0.25	0.18
Full care	-0.32	-0.54	-0.09

Contrasts (differences of the estimated marginal means) and 95% confidence intervals for the **total pain composite score** (PCS<sub>total</sub>, n = 4,982 patients). Significant contrasts (p < 0.05) are printed in bold. The PCS<sub>total</sub> was z-standardized before modelling. Thus, differences can be interpreted as differences in standard deviations.

contrast		estimate	95% CI		p
Incomplete	vs. Intra-operative	-0.27	-0.42	-0.11	<b>0.002</b>
Incomplete	vs. Post-operative	-0.07	-0.19	0.04	0.432
Incomplete	vs. Full care	-0.36	-0.49	-0.23	<b>&lt;0.001</b>
Intra-operative	vs. Post-operative	0.19	0.03	0.36	0.064
Intra-operative	vs. Full care	-0.09	-0.25	0.06	0.432
Post-operative	vs. Full care	-0.28	-0.40	-0.17	<b>&lt;0.001</b>

## 2.2 Pain Composite Score: intensity sub-score

Model parameter for the **pain composite intensity sub-score** ( $PCS_{\text{intensity}}$ ,  $n = 4,982$  patients). The  $PCS_{\text{intensity}}$  was z-standardized before modelling. Significant regression coefficients are printed in bold (coefficient of determination:  $R^2_{\text{marginal}} = 0.025$ ,  $R^2_{\text{conditional}} = 0.249$ ).

Variable	[Reference/Unit]	$\beta$	95%CI		p
(Intercept)		-0.45	-0.78	-0.11	<b>0.013</b>
<b>Perioperative treatment protocol:</b>					
Intra-operative	[vs. Incomplete]	-0.20	-0.35	-0.06	<b>0.007</b>
Post-operative	[vs. Incomplete]	-0.05	-0.16	0.07	0.428
Full care	[vs. Incomplete]	-0.18	-0.30	-0.05	<b>0.006</b>
<b>Group:</b>					
General anaesthesia (GA)	[vs. RA, regional anaesthesia]	0.16	0.04	0.27	<b>0.007</b>
Combined GA + RA	[vs. RA]	0.09	-0.08	0.26	0.315
Age	[years]	0.00	0.00	0.01	0.206
Pre-existing chronic pain	[vs. no]	0.15	0.06	0.25	<b>0.002</b>
Ward: any opioid	[vs. none]	0.21	0.14	0.28	<b>&lt;0.001</b>
Income level: high	[vs. others]	-0.04	-0.45	0.36	0.843

Estimated marginal means (covariate adjusted means) and 95% confidence intervals of the **pain composite intensity sub-score** ( $PCS_{\text{intensity}}$ ,  $n = 4,982$  patients). Results are shown for the peri-operative treatment protocol groups. The  $PCS_{\text{intensity}}$  was z-standardized before modelling.

group	mean	95% CI	
Incomplete	-0.11	-0.33	0.11
Intra-operative	-0.31	-0.56	-0.06
Post-operative	-0.15	-0.38	0.07
Full care	-0.29	-0.52	-0.06

Contrasts (differences of the estimated marginal means) and 95% confidence intervals for the **pain composite intensity sub-score** ( $PCS_{\text{intensity}}$ ,  $n = 4,982$  patients). Significant contrasts ( $p < 0.05$ ) are printed in bold. The  $PCS_{\text{intensity}}$  was z-standardized before modelling. Thus, differences can be interpreted as differences in standard deviations.

contrast		estimate	95% CI		p
Incomplete	vs. Intra-operative	-0.20	-0.35	-0.06	<b>0.036</b>
Incomplete	vs. Post-operative	-0.05	-0.16	0.07	0.856
Incomplete	vs. Full care	-0.18	-0.30	-0.05	<b>0.036</b>
Intra-operative	vs. Post-operative	0.16	0.00	0.31	0.153
Intra-operative	vs. Full care	0.02	-0.13	0.17	0.856
Post-operative	vs. Full care	-0.13	-0.24	-0.02	0.076

## 2.3 Pain Composite Score: interference sub-score

Model parameter for the **pain composite interference sub-score** ( $PCS_{\text{interference}}$ ,  $n = 4,982$  patients). The  $PCS_{\text{interference}}$  was z-standardized before modelling. Significant regression coefficients are printed in bold (coefficient of determination:  $R^2_{\text{marginal}} = 0.025$ ,  $R^2_{\text{conditional}} = 0.225$ ).

Variable	[Reference/Unit]	$\beta$	95%CI		p
(Intercept)		-0.21	-0.54	0.12	0.226
<b>Perioperative treatment protocol:</b>					
Intra-operative	[vs. Incomplete]	-0.24	-0.39	-0.08	<b>0.002</b>
Post-operative	[vs. Incomplete]	-0.07	-0.19	0.05	0.240
Full care	[vs. Incomplete]	-0.35	-0.49	-0.22	<b>&lt;0.001</b>
<b>Group:</b>					
General anaesthesia (GA)	[vs. RA, regional anaesthesia]	0.19	0.07	0.31	<b>0.002</b>
Combined GA + RA	[vs. RA]	0.03	-0.15	0.21	0.722
Age	[years]	0.00	-0.01	0.00	0.152
Pre-existing chronic pain	[vs. no]	0.10	0.00	0.20	0.052
Ward: any opioid	[vs. none]	0.18	0.11	0.26	<b>&lt;0.001</b>
Income level: high	[vs. others]	0.38	-0.01	0.78	0.071

Estimated marginal means (covariate adjusted means) and 95% confidence intervals of the **pain composite interference sub-score** ( $PCS_{\text{interference}}$ ,  $n = 4,982$  patients). Results are shown for the peri-operative treatment protocol groups. The  $PCS_{\text{interference}}$  was z-standardized before modelling.

group	mean	95% CI	
Incomplete	0.09	-0.13	0.31
Intra-operative	-0.15	-0.40	0.10
Post-operative	0.02	-0.20	0.24
Full care	-0.27	-0.50	-0.04

Contrasts (differences of the estimated marginal means) and 95% confidence intervals for the **pain composite interference sub-score** ( $PCS_{\text{interference}}$ ,  $n = 4,982$  patients). Significant contrasts ( $p < 0.05$ ) are printed in bold. The  $PCS_{\text{interference}}$  was z-standardized before modelling. Thus, differences can be interpreted as differences in standard deviations.

contrast		estimate	95% CI		p
Incomplete	vs. Intra-operative	-0.24	-0.39	-0.08	<b>0.010</b>
Incomplete	vs. Post-operative	-0.07	-0.19	0.05	0.297
Incomplete	vs. Full care	-0.35	-0.49	-0.22	<b>&lt;0.001</b>
Intra-operative	vs. Post-operative	0.17	0.00	0.33	0.143
Intra-operative	vs. Full care	-0.12	-0.28	0.04	0.297
Post-operative	vs. Full care	-0.28	-0.40	-0.17	<b>&lt;0.001</b>

## 2.4 Pain Composite Score: side effects sub-score

Model parameter for the **pain composite side effects sub-score** (PCS<sub>side</sub>, n = 4,982 patients). The PCS<sub>side</sub> was z-standardized before modelling. Significant regression coefficients are printed in bold (coefficient of determination:  $R^2_{\text{marginal}} = 0.018$ ,  $R^2_{\text{conditional}} = 0.075$ ).

Variable	[Reference/Unit]	$\beta$	95%CI		p
(Intercept)		-0.03	-0.26	0.20	0.804
<b>Perioperative treatment protocol:</b>					
Intra-operative	[vs. Incomplete]	-0.17	-0.32	-0.01	<b>0.038</b>
Post-operative	[vs. Incomplete]	-0.04	-0.16	0.07	0.465
Full care	[vs. Incomplete]	-0.23	-0.37	-0.10	<b>&lt;0.001</b>
<b>Group:</b>					
General anaesthesia (GA)	[vs. RA, regional anaesthesia]	0.02	-0.11	0.14	0.787
Combined GA + RA	[vs. RA]	-0.01	-0.19	0.17	0.918
Age	[years]	-0.01	-0.01	0.00	<b>0.014</b>
Pre-existing chronic pain	[vs. no]	0.28	0.18	0.38	<b>&lt;0.001</b>
Ward: any opioid	[vs. none]	0.02	-0.06	0.09	0.621
Income level: high	[vs. others]	0.27	0.05	0.49	<b>0.026</b>

Estimated marginal means (covariate adjusted means) and 95% confidence intervals of the **pain composite side effects sub-score** (PCS<sub>side</sub>, n = 4,982 patients). Results are shown for the peri-operative treatment protocol groups. The PCS<sub>side</sub> was z-standardized before modelling.

group	mean	95% CI	
Incomplete	0.06	-0.08	0.20
Intra-operative	-0.10	-0.30	0.09
Post-operative	0.02	-0.13	0.17
Full care	-0.17	-0.33	-0.01

Contrasts (differences of the estimated marginal means) and 95% confidence intervals for the **pain composite side effects sub-score** (PCS<sub>side</sub>, n = 4,982 patients). Significant contrasts ( $p < 0.05$ ) are printed in bold. The PCS<sub>side</sub> was z-standardized before modelling. Thus, differences can be interpreted as differences in standard deviations.

contrast		estimate	95% CI		p
Incomplete	vs. Intra-operative	-0.17	-0.32	-0.01	0.152
Incomplete	vs. Post-operative	-0.04	-0.16	0.07	0.815
Incomplete	vs. Full care	-0.23	-0.37	-0.10	<b>0.003</b>
Intra-operative	vs. Post-operative	0.12	-0.05	0.29	0.466
Intra-operative	vs. Full care	-0.07	-0.23	0.09	0.815
Post-operative	vs. Full care	-0.19	-0.31	-0.07	<b>0.007</b>

### 3 Sensitivity analysis for the total Pain Composite Score

**Sensitivity analysis excluding one hospital with a high patient number.** Results of the multi-level regression models using the pain composite score (0-10) as dependent variable. Regression coefficients ( $\beta$ ) including 95% confidence intervals (95%CI) and p-values (p) are shown. In addition, results for the patient sample with regional anaesthesia are shown. Significant p-values are printed in bold.

variable	reference	total cohort [n = 3 041]				regional anaesthesia [n = 2 397]			
		$\beta$	95% CI		p	$\beta$	95% CI		p
(intercept)		-0.16	-0.55	0.22	0.419	-0.15	-0.62	0.31	0.527
<b>Peri-operative care group:</b>									
Intra-operative [only]	[vs. Incomplete]	-0.24	-0.43	-0.06	<b>0.009</b>	-0.22	-0.42	-0.02	<b>0.028</b>
Post-operative [only]	[vs. Incomplete]	-0.09	-0.20	0.03	0.154	-0.01	-0.14	0.13	0.917
Full care	[vs. Incomplete]	-0.38	-0.52	-0.25	<b>&lt; 0.001</b>	-0.39	-0.54	-0.24	<b>&lt; 0.001</b>
<b>group:</b>									
General anaesthesia	[vs. regional anaesthesia]	0.28	0.13	0.42	<b>&lt; 0.001</b>	<i>not modelled</i>			
Combined RA & GA	[vs. regional anaesthesia]	0.16	-0.08	0.39	0.196				
<b>Age</b>	[years]	-0.01	-0.01	0.00	<b>0.030</b>	-0.01	-0.02	0.00	<b>0.032</b>
<b>Pre-existing chronic pain: yes</b>	[vs. no]	0.27	0.15	0.39	<b>&lt; 0.001</b>	0.23	0.10	0.36	<b>&lt; 0.001</b>
<b>Intra-operative: neuraxial morphine</b>	[vs. others/none]	<i>not modelled</i>				-0.12	-0.23	-0.01	<b>0.032</b>
<b>Ward: opioid</b>	[vs. no]	0.18	0.10	0.26	<b>&lt; 0.001</b>	0.23	0.14	0.32	<b>&lt; 0.001</b>
<b>Income level: high</b>	[vs. others]	0.50	0.06	0.93	<b>0.037</b>	0.49	0.00	0.99	0.068

Estimated marginal means (EMM, z-scale) including 95% confidence intervals (CI) for the different multi-level models and models from sensitivity analysis. Pain composite scores served as dependent variables and covariates are listed at the end of the table.

<b>Model I: total sample [n = 4 982]</b>			
<b>Care group</b>	<b>EMM<sup>1</sup></b>	<b>95%CI</b>	
Incomplete	0.04	-0.17	0.25
intra-operative (only)	-0.23	-0.47	0.02
PACU/normal-ward (only)	-0.03	-0.25	0.18
Full Care	-0.32	-0.54	-0.09
<b>Model II: without one hospital [n = 3 041]</b>			
<b>Care group</b>	<b>EMM<sup>1</sup></b>	<b>95%CI</b>	
Incomplete	0.22	-0.03	0.46
intra-operative (only)	-0.03	-0.31	0.26
PACU/normal-ward (only)	0.13	-0.11	0.38
Full Care	-0.17	-0.42	0.09
<b>Model III: regional anaesthesia [n = 4 213]</b>			
<b>Care group</b>	<b>EMM<sup>2</sup></b>	<b>95%CI</b>	
Incomplete	-0.13	-0.35	0.10
intra-operative (only)	-0.36	-0.62	-0.11
PACU/normal-ward (only)	-0.14	-0.37	0.09
Full Care	-0.49	-0.73	-0.26
<b>Model IV: regional anaesthesia/without one hospital [n = 2 397]</b>			
<b>Care group</b>	<b>EMM<sup>2</sup></b>	<b>95%CI</b>	
Incomplete	-0.01	-0.29	0.27
intra-operative (only)	-0.23	-0.55	0.08
PACU/normal-ward (only)	-0.02	-0.30	0.26
Full Care	-0.40	-0.69	-0.12

<sup>1</sup> **adjusted for:** protocol of anaesthesia (regional anaesthesia vs. general anaesthesia vs. mixed protocols), chronic pre-existing pain (yes vs. no), age (years), opioid administration on the ward (yes vs. no), income level of the country (high vs. others), intra-operative use of dexamethasone (vs. no)

<sup>2</sup> **adjusted for:** chronic pre-existing pain (yes vs. no), age (years), opioid administration on the ward (yes vs. no), income level of the country (high vs. others), intra-operative use of neuraxial morphine (vs. no) and dexamethasone (vs. no)

Contrasts of the different multi-level models and multi-level models for sensitivity analysis for different sub-groups of peri-operative treatment protocol. Pain composite scores served as dependent variables. P-values were adjusted using the Bonferroni-Holm method. Significant p-values ( $p < 0.05$ ) are printed in bold.

		<b>Model</b>			
		<b>I</b>	<b>II</b>	<b>III</b>	<b>IV</b>
<b>contrast</b>		<b>p</b>	<b>p</b>	<b>p</b>	<b>p</b>
<b>Incomplete vs.</b>	<b>Intra-operative</b>	<b>0.002</b>	<b>0.037</b>	<b>0.021</b>	0.114
<b>Incomplete vs</b>	<b>Post-operative</b>	0.412	0.263	0.837	0.917
<b>Incomplete vs</b>	<b>Full care</b>	<b>&lt; 0.001</b>	<b>&lt; 0.001</b>	<b>&lt; 0.001</b>	<b>&lt; 0.001</b>
<b>Intra-operative vs.</b>	<b>Post-operative</b>	0.065	0.263	<b>0.045</b>	0.114
<b>Intra-operative vs.</b>	<b>Full care</b>	0.412	0.263	0.261	0.121
<b>Post-operative vs.</b>	<b>Full care</b>	<b>&lt; 0.001</b>	<b>&lt; 0.001</b>	<b>&lt; 0.001</b>	<b>&lt; 0.001</b>



## 4 Model details: Regional anaesthesia

### 4.1 Pain Composite Score: total

Model parameter for the **total pain composite score** (PCS<sub>total</sub>, n = 4,213 patients). The PCS<sub>total</sub> was z-standardized before modelling. Significant regression coefficients are printed in bold (coefficient of determination:  $R^2_{\text{marginal}} = 0.035$ ,  $R^2_{\text{conditional}} = 0.236$ ).

Variable	[Reference/Unit]	$\beta$	95%CI		p
(Intercept)		-0.30	-0.66	0.07	0.125
<b>Perioperative treatment protocol:</b>					
Intra-operative	[vs. Incomplete]	-0.24	-0.40	-0.07	<b>0.005</b>
Post-operative	[vs. Incomplete]	-0.01	-0.15	0.12	0.837
Full care	[vs. Incomplete]	-0.36	-0.51	-0.22	<b>&lt;0.001</b>
Age	[years]	0.00	-0.01	0.00	0.266
Pre-existing chronic pain	[vs. no]	0.17	0.07	0.28	<b>0.002</b>
Intra-operative neuraxial morphine: yes	[vs. no]	-0.16	-0.27	-0.05	<b>0.004</b>
Ward: any opioid	[vs. none]	0.20	0.12	0.28	<b>&lt;0.001</b>
Income level: high	[vs. others]	0.31	-0.11	0.73	0.162

Estimated marginal means (covariate adjusted means) and 95% confidence intervals of the **total pain composite score** (n = 4,213 patients). Results are shown for the peri-operative treatment protocol groups. The PCS<sub>total</sub> was z-standardized before modelling.

group	mean	95% CI	
Incomplete	-0.13	-0.35	0.10
Intra-operative	-0.36	-0.62	-0.11
Post-operative	-0.14	-0.37	0.09
Full care	-0.49	-0.73	-0.26

Contrasts (differences of the estimated marginal means) and 95% confidence intervals for the **total pain composite score** (PCS<sub>total</sub>, n = 4,213 patients). Significant contrasts (p < 0.05) are printed in bold. The PCS<sub>total</sub> was z-standardized before modelling. Thus, differences can be interpreted as differences in standard deviations.

contrast			estimate	95% CI		p
Incomplete	vs.	Intra-operative	-0.24	-0.40	-0.07	<b>0.021</b>
Incomplete	vs.	Post-operative	-0.01	-0.15	0.12	0.837
Incomplete	vs.	Full care	-0.36	-0.51	-0.22	<b>0.000</b>
Intra-operative	vs.	Post-operative	0.22	0.04	0.40	<b>0.045</b>
Intra-operative	vs.	Full care	-0.13	-0.29	0.04	0.261
Post-operative	vs.	Full care	-0.35	-0.47	-0.22	<b>0.000</b>

## 4.2 Pain Composite Score: intensity sub-score

Model parameter for the **pain composite intensity sub-score** (PCS<sub>intensity</sub>, n = 4,213 patients). The PCS<sub>intensity</sub> was z-standardized before modelling. Significant regression coefficients are printed in bold (coefficient of determination: R<sup>2</sup><sub>marginal</sub> = 0.057, R<sup>2</sup><sub>conditional</sub> = 0.295).

Variable	[Reference/Unit]	$\beta$	95%CI		p
(Intercept)		-0.47	-0.85	-0.09	<b>0.023</b>
<b>Perioperative treatment protocol:</b>					
Intra-operative	[vs. Incomplete]	-0.13	-0.28	0.03	0.109
Post-operative	[vs. Incomplete]	-0.01	-0.13	0.12	0.926
Full care	[vs. Incomplete]	-0.15	-0.29	-0.02	<b>0.029</b>
Age	[years]	0.01	0.00	0.01	<b>0.049</b>
Pre-existing chronic pain	[vs. no]	0.11	0.01	0.21	<b>0.029</b>
Intra-operative neuraxial morphine: yes	[vs. no]	-0.33	-0.43	-0.23	<b>&lt;0.001</b>
Ward: any opioid	[vs. none]	0.22	0.14	0.30	<b>&lt;0.001</b>
Income level: high	[vs. others]	-0.04	-0.49	0.40	0.847

Estimated marginal means (covariate adjusted means) and 95% confidence intervals of the **pain composite intensity sub-score** (PCS<sub>intensity</sub>, n = 4,213 patients). Results are shown for the peri-operative treatment protocol groups. The PCS<sub>intensity</sub> was z-standardized before modelling.

group	mean	95% CI	
Incomplete	-0.33	-0.56	-0.09
Intra-operative	-0.46	-0.72	-0.19
Post-operative	-0.33	-0.58	-0.09
Full care	-0.48	-0.73	-0.24

Contrasts (differences of the estimated marginal means) and 95% confidence intervals for the **pain composite intensity sub-score** (PCS<sub>intensity</sub>, n = 4,213 patients). Significant contrasts (p < 0.05) are printed in bold. The PCS<sub>intensity</sub> was z-standardized before modelling. Thus, differences can be interpreted as differences in standard deviations.

contrast		estimate	95% CI		p
Incomplete	vs. Intra-operative	-0.13	-0.28	0.03	0.435
Incomplete	vs. Post-operative	-0.01	-0.13	0.12	0.999
Incomplete	vs. Full care	-0.15	-0.29	-0.02	0.145
Intra-operative	vs. Post-operative	0.12	-0.05	0.29	0.473
Intra-operative	vs. Full care	-0.02	-0.18	0.13	0.999
Post-operative	vs. Full care	-0.15	-0.27	-0.03	0.094

### 4.3 Pain Composite Score: interference sub-score

Model parameter for the **pain composite interference sub-score** (PCS<sub>interference</sub>, n = 4,213 patients). The PCS<sub>interference</sub> was z-standardized before modelling. Significant regression coefficients are printed in bold (coefficient of determination: R<sup>2</sup><sub>marginal</sub> = 0.05, R<sup>2</sup><sub>conditional</sub> = 0.242).

Variable	[Reference/Unit]	$\beta$	95%CI		p
(Intercept)		-0.22	-0.58	0.15	0.254
<b>Perioperative treatment protocol:</b>					
Intra-operative	[vs. Incomplete]	-0.17	-0.34	-0.01	<b>0.042</b>
Post-operative	[vs. Incomplete]	-0.03	-0.17	0.10	0.647
Full care	[vs. Incomplete]	-0.34	-0.49	-0.20	<b>&lt;0.001</b>
Age	[years]	0.00	-0.01	0.00	0.456
Pre-existing chronic pain	[vs. no]	0.07	-0.04	0.17	0.215
Intra-operative neuraxial morphine: yes	[vs. no]	-0.37	-0.48	-0.26	<b>&lt;0.001</b>
Ward: any opioid	[vs. none]	0.18	0.10	0.26	<b>&lt;0.001</b>
Income level: high	[vs. others]	0.41	-0.01	0.83	0.068

Estimated marginal means (covariate adjusted means) and 95% confidence intervals of the **pain composite interference sub-score** (PCS<sub>interference</sub>, n = 4,213 patients). Results are shown for the peri-operative treatment protocol groups. The PCS<sub>interference</sub> was z-standardized before modelling.

group	mean	95% CI	
Incomplete	-0.14	-0.36	0.09
Intra-operative	-0.31	-0.57	-0.05
Post-operative	-0.17	-0.40	0.06
Full care	-0.48	-0.71	-0.25

Contrasts (differences of the estimated marginal means) and 95% confidence intervals for the **pain composite interference sub-score** (PCS<sub>interference</sub>, n = 4,213 patients). Significant contrasts (p < 0.05) are printed in bold. The PCS<sub>interference</sub> was z-standardized before modelling. Thus, differences can be interpreted as differences in standard deviations.

contrast		estimate	95% CI		p
Incomplete	vs. Intra-operative	-0.17	-0.34	-0.01	0.166
Incomplete	vs. Post-operative	-0.03	-0.17	0.10	0.647
Incomplete	vs. Full care	-0.34	-0.49	-0.20	<b>&lt;0.001</b>
Intra-operative	vs. Post-operative	0.14	-0.04	0.32	0.247
Intra-operative	vs. Full care	-0.17	-0.34	0.00	0.166
Post-operative	vs. Full care	-0.31	-0.44	-0.19	<b>&lt;0.001</b>

#### 4.4 Pain Composite Score: side effects sub-score

Model parameter for the **pain composite side effects sub-score** (PCS<sub>side</sub>, n = 4,213 patients). The PCS<sub>side</sub> was z-standardized before modelling. Significant regression coefficients are printed in bold (coefficient of determination:  $R^2_{\text{marginal}} = 0.035$ ,  $R^2_{\text{conditional}} = 0.083$ ).

Variable	[Reference/Unit]	$\beta$	95%CI		p
(Intercept)		-0.06	-0.30	0.19	0.643
<b>Perioperative treatment protocol:</b>					
Intra-operative	[vs. Incomplete]	-0.23	-0.40	-0.06	<b>0.008</b>
Post-operative	[vs. Incomplete]	0.02	-0.11	0.15	0.771
Full care	[vs. Incomplete]	-0.27	-0.41	-0.13	<b>&lt;0.001</b>
Age	[years]	-0.01	-0.01	0.00	<b>0.003</b>
Pre-existing chronic pain	[vs. no]	0.25	0.14	0.36	<b>&lt;0.001</b>
Intra-operative neuraxial morphine: yes	[vs. no]	0.36	0.26	0.47	<b>&lt;0.001</b>
Ward: any opioid	[vs. none]	0.07	-0.01	0.16	0.084
Income level: high	[vs. others]	0.20	-0.01	0.42	0.081

Estimated marginal means (covariate adjusted means) and 95% confidence intervals of the **pain composite side effects sub-score** (PCS<sub>side</sub>, n = 4,213 patients). Results are shown for the peri-operative treatment protocol groups. The PCS<sub>side</sub> was z-standardized before modelling.

group	mean	95% CI	
Incomplete	0.12	-0.01	0.26
Intra-operative	-0.10	-0.29	0.08
Post-operative	0.14	0.00	0.29
Full care	-0.15	-0.30	0.00

Contrasts (differences of the estimated marginal means) and 95% confidence intervals for the **pain composite side effects sub-score** (PCS<sub>side</sub>, n = 4,213 patients). Significant contrasts ( $p < 0.05$ ) are printed in bold. The PCS<sub>side</sub> was z-standardized before modelling. Thus, differences can be interpreted as differences in standard deviations.

contrast		estimate	95% CI		p
Incomplete	vs. Intra-operative	-0.23	-0.40	-0.06	<b>0.031</b>
Incomplete	vs. Post-operative	0.02	-0.11	0.15	0.999
Incomplete	vs. Full care	-0.27	-0.41	-0.13	<b>&lt;0.001</b>
Intra-operative	vs. Post-operative	0.25	0.06	0.43	<b>0.031</b>
Intra-operative	vs. Full care	-0.04	-0.21	0.12	0.999
Post-operative	vs. Full care	-0.29	-0.42	-0.17	<b>&lt;0.001</b>