Supplementary material to article by T. F. Kallman and E. Bäckryd."Prevalence of analgesic use in patients with chronic pain referred to a multidisciplinary pain centre and its correlation with patient-reported outcome measures: a cross-sectional, registry-based study"

Appendix S1. Descriptive data and inferential statistics for variables in the 4 groups and orthogonal projections to latent structures discriminant analysis (OPLS and OPLS-DA).

In order to better understand what the MVDA methods used in this paper are, one may imagine a room with *k* dimensions, where each variable constitutes a dimension. Each patient will be a point in the *k*-dimensional space. PCA, which structures data by defining only a few latent variables, is the first step in this MVDA workflow (1). These latent variables (also called principal components (PC)) are not correlated with each other, and simplify data by distinguishing relevant data from noise and allowing detection of relevant patterns in data. The optimal number of PCs is determined by cross-validation, which reliably tests the significance of the PCA model, which is a default procedure in SIMCA-P+. The R^2 value indicates how much of the original data is explained by the model (R^2=1.0 explains 100% of the data), and cross-validated Q^2 measures the predictive power of the model.

PCA can therefore be seen as a type of multivariate correlation analysis which simultaneously allows for the identification of outliers. Outliers may be identified by utilizing Hotelling's T2, which is a multivariate generalization of the 95% confidence interval (1). Each original variable relates to a PC by a loading (*p*), which has a value from −1 to +1. Without regard for the sign, variables with high loadings are considered to be important for the PC being considered. Furthermore, variables with high loadings (positive or negative sign) on the same PC are correlated. Two plots are generated from a PCA analysis: the score plot shows the relationship between the subjects using the PCs as axes in a 2-dimensional coordinate system and representing each subject by a dot. The loading plot is complementary to the score plot and represents the new values of the variables in the coordinate system, which in turn expounds the relationships between variables.

After overviewing data with PCA, a bottom-up HCA was applied to the PC score vectors, using the default Ward linkage criterion to identify relevant subgroups of patients (2,3). In the HCA dendrogram, 4 clusters were identified and, based on these groups, PLS-DA was performed using group belonging as outcome variable (Y-variable) and PROMs as independent variables (X-variables). The PLS-DA model was computed to identify associations between the independent variables and the subgroups.

Finally, the use of opioids was further investigated by OPLS-DA. OPLS-DA was performed using group belonging (on opioids vs not on opioids) as outcome variable and PROMs as predictors. The OPLS-DA was used to regress (predict) group membership, i.e. to identify which variables were responsible for group belonging (on opioids vs not on opioids). Therefore, the outcome variable (Y) was nominal (on opioids vs not on opioids), whereas predictor variables (X) were numerical (PROM scores). Variables with absolute values of *p*(corr)>0.5 may be considered "significant" (1). This p(corr) is not to be confused with a normal p-value. p(corr) are the new variable values visualized in the loading plot, scaled as a correlation coefficient (ranging from −1.0 to +1.0) between model and original data. An OPLS was also performed on the above-mentioned independent variables, but with OME as continuous outcome variable.

An OPLS-DA model was thus performed on the same 37 independent variables, with opioid treatment as dichotomous outcome variable. This model has 2 latent variables (R^2=0.19, Q^2=0.14, $p<0.001$ by CV-ANOVA). The p(corr)-values that predict opioid usage, i.e. $|p(corr)|>0.5$, are presented in Table SIII.

A second OPLS model was also performed on the above-mentioned independent variables, but with oral morphine equivalents (OME) as outcome variable, $n=126$. This model has 2 latent variables (R^2=0.31, Q^2=0.12, $p=0.007$ by CV-ANOVA). The variable *p*(corr)-values that are significantly associated with OME are summarized in Table SIV (in this case, $|p(corr)|>0.4$ was used).

Table SI. Characteristics of the 4 groups. Statistics computed by Kruskal–Wallis except for sex and education, where Pearson-Chi was used

Variable	Group 1 (*n* = 123)	Group 2 (*n* = 104)	Group 3 (*n* = 67)	Group 4 (*n* = 140)	*p*-value
Age, years, mean (SD)	45 (16)	49 (17)	42 (16)	50 (14)	0.004*
Sex female, %	74	67	64	81	0.023*
Education (*n* = 436), %					0.081
Primary school	24	19	25	17	
High school	60	47	52	48	
University	13	27	19	28	
Other	3	7	3	7	
DaysNotWork, mean (SD)	2,075 (2,995)	3,100 (4,099)	1,647 (1,961)	2,181 (2,859)	0.549
NbDrVisits, mean (SD)	1.7 (0.5)	1.3 (0.7)	1.7 (0.6)	1.5 (0.7)	< 0.001*
PainDur (*n* = 398, days), mean (SD)	2,778 (2,969)	2,458 (3,314)	1,697 (2,929)	4,507 (4,624)	< 0.001*
PerPainDur (*n* = 330, days), mean (SD)	2,300 (2,697)	1,976 (2,180)	1,243 (2,123)	4,009 (4,765)	< 0.001*
NRS7d (*n* = 430, 0–10), mean (SD)	8.3 (1.2)	6.0 (1.8)	7.2 (1.5)	6.9 (1.6)	< 0.001*
NbPainReg2 (0–36), mean (SD)	16.3 (9.3)	9.5 (7.7)	9.8 (7.4)	15.7 (8.8)	< 0.001*
HAD-A, mean (SD)	11.8 (4.4)	4.2 (2.9)	9.2 (3.8)	6.6 (3.7)	< 0.001*
HAD-D, mean (SD)	11.9 (4.4)	3.3 (2.6)	7.9 (3.1)	8.1 (3.5)	< 0.001*
MPI-PainSev, mean (SD)	5.3 (0.6)	3.8 (0.8)	4.6 (0.8)	4.4 (0.9)	< 0.001*
MPI-Interf, mean (SD)	5.1 (0.7)	3.1 (1.1)	4.2 (0.8)	4.6 (0.8)	< 0.001*
MPI-Contr, mean (SD)	1.6 (1.0)	3.7 (1.0)	2.6 (1.0)	2.8 (1.0)	< 0.001*
MPI-AffDis, mean (SD)	4.4 (1.1)	2.1 (1.0)	3.7 (0.9)	3.0 (1.1)	< 0.001*
MPI-SocSup, mean (SD)	4.4 (1.5)	4.1 (1.3)	4.8 (1.0)	3.9 (1.5)	< 0.001*
MPI-Pun, mean (SD)	2.1 (1.6)	1.0 (0.8)	1.3 (1.1)	1.8 (1.2)	< 0.001*
MPI-Solic, mean (SD)	3.5 (1.6)	2.6 (1.3)	3.5 (1.5)	2.5 (1.4)	< 0.001*
MPI-Distra, mean (SD)	2.9 (1.3)	2.4 (1.2)	3.3 (1.1)	2.0 (1.2)	< 0.001*
MPI-GAI, mean (SD)	1.9 (0.9)	2.7 (0.8)	2.7 (0.8)	2.3 (0.8)	< 0.001*
EQ5D-Index, mean (SD)	−0.02 (0.18)	0.55 (0.26)	0.24 (0.25)	0.22 (0.26)	< 0.001*
EQ5D-VAS, mean (SD)	28 (19)	60 (17)	45 (17)	42 (17)	< 0.001*
SF36-PCS, mean (SD)	24.1 (6.7)	31.7 (9.6)	31.4 (5.4)	24.7 (8.5)	< 0.001*
SF36-MCS, mean (SD)	27.3 (9.6)	49.3 (10.9)	33.8 (8.9)	39.5 (10.8)	< 0.001*
CPAQ-AE, mean (SD)	16.7 (9.4)	38.2 (8.4)	28.4 (9.1)	28.9 (9.2)	< 0.001*
CPAQ-PW, mean (SD)	16.8 (7.2)	27.1 (8.4)	19.9 (7.6)	24.7 (7.5)	< 0.001*
TSK, mean (SD)	46.1 (9.0)	34.4 (7.8)	40.9 (8.4)	36.9 (7.9)	< 0.001*
PCS-Total, mean (SD)	34.9 (9.0)	16.4 (9.1)	28.9 (9.2)	20.4 (9.5)	< 0.001*
LiSat-Life, mean (SD)	2.4 (1.1)	4.7 (0.8)	4.2 (0.9)	3.5 (1.0)	< 0.001*
LiSat-Voc, mean (SD)	1.9 (1.2)	4.4 (1.3)	3.7 (1.6)	2.6 (1.5)	< 0.001*
LiSat-Eco, mean (SD)	2.7 (1.5)	4.6 (1.1)	4.1 (1.3)	3.3 (1.6)	< 0.001*
LiSat-Leis, mean (SD)	2.0 (1.1)	4.1 (1.1)	3.7 (1.0)	2.7 (1.1)	< 0.001*
LiSat-Soc, mean (SD)	2.7 (1.3)	4.9 (0.9)	4.5 (0.9)	3.6 (1.1)	< 0.001*
LiSat-Sex, mean (SD)	2.2 (1.4)	4.0 (1.5)	3.9 (1.5)	2.7 (1.4)	< 0.001*
LiSat-ADL, mean (SD)	3.6 (1.4)	5.0 (1.2)	5.0 (1.1)	4.1 (1.4)	< 0.001*
LiSat-Fam, mean (SD)	3.9 (1.4)	5.4 (0.7)	5.3 (1.0)	4.5 (1.3)	< 0.001*
LiSat-Part, mean (SD)	4.5 (1.5)	5.5 (0.8)	5.5 (0.8)	4.6 (1.3)	< 0.001*
LiSat-Phys, mean (SD)	1.4 (0.7)	3.3 (1.2)	2.8 (1.3)	2.0 (0.9)	< 0.001*
LiSat-Ment, mean (SD)	2.4 (1.2)	4.8 (1.1)	3.8 (1.1)	3.8 (1.2)	< 0.001*

*Statistically significant group differences. SD: standard deviation. For variable abbreviations, see the Methods section. A *p*-value of ≤ 0.05 was considered significant

Supplementary material to article by T. F. Kallman and E. Bäckryd."Prevalence of analgesic use in patients with chronic pain referred to a multidisciplinary pain centre and its correlation with patient-reported outcome measures: a cross-sectional, registry-based study"

Table SII. Posthoc *p*-values for patient-reported outcome measures (PROMs). Post-hoc statistics computed by Mann-Whitney *U*, except for sex and education, where Pearson-Chi or Fisher's exact test was used. For mean values, see Table SI. A *p*-value ≤0.05 was considered significant

Variable	Group 1 vs 2	Group 1 vs 3	Group 1 vs 4	Group 2 vs 3	Group 2 vs 4	Group 3 vs 4
Age	0.122	0.178	0.02[a]	0.013[a]	0.677	0.001[a]
Sex	0.306	0.184	0.18	0.741	0.016[a]	0.023[a]
Education	0.028[a]	0.664	0.008[a]	0.38	0.967	0.081
DaysNotWork	0.165	0.922	0.724	0.279	0.278	0.897
NbDrVisits	*	0.535	0.001[a]	0.001[a]	0.086	0.029[a]
PainDur	0.299	0.004[a]	0.001[a]	0.032[a]	*	*
PerPainDur	0.831	0.002[a]	0.001[a]	0.001[a]	*	*
NRS7d	*	*	*	0.001[a]	*	0.43
NbPainReg	*	*	0.683	0.499	*	*
HAD-A	*	*	*	*	*	*
HAD-D	*	*	*	*	*	0.980
MPI-PainSev	*	*	*	*	*	0.113
MPI-Interf	*	*	*	*	*	0.006[a]
MPI-Contr	*	*	*	*	*	0.24
MPI-AffDis	*	*	*	*	*	*
MPI-SocSup	0.029[a]	0.3	0.002[a]	0.001[a]	0.274	*
MPI-Pun	*	0.001[a]	0.376	0.15	*	0.003[a]
MPI-Solic	*	0.759	*	0.001[a]	0.321	*
MPI-Distra	0.016[a]	0.096	*	*	0.015[a]	*
MPI-GAI	*	*	*	0.658	*	0.001[a]
EQ5D-Index	*	*	*	*	*	0.322
EQ5D-VAS	*	*	*	*	*	0.239
SF36-PCS	*	*	0.776	0.774	*	*
SF36-MCS	*	*	*	*	*	*
CPAQ-AE	*	*	*	*	*	0.653
CPAQ-PW	*	0.007[a]	*	*	0.018[a]	*
TSK	*	*	*	*	0.016[a]	0.002[a]
PCS-Total	*	*	*	*	0.001[a]	*
LiSat-Life	*	*	*	*	*	*
LiSat-Voc	*	*	*	0.008[a]	*	*
LiSat-Eco	*	*	0.001[a]	0.01[a]	*	0.001[a]
LiSat-Leis	*	*	*	0.018[a]	*	*
LiSat-Soc	*	*	*	0.004[a]	*	*
LiSat-Sex	*	*	0.004[a]	0.482	*	*
LiSat-ADL	*	*	0.004[a]	0.346	*	*
LiSat-Fam	*	*	0.001[a]	0.797	*	*
LiSat-Part	*	*	0.812	0.784	*	*
LiSat-Phys	*	*	*	0.23[a]	*	*
LiSat-Ment	*	*	*	*	*	0.703

Due to the high number of highly significant comparisons, for the sake of clarity and readability, *$p < 0.001$ is denoted. [a]All other significant comparisons. For variable abbreviations, see Methods.

Table SIII. *p*(corr)-values of orthogonal projections to latent structures discriminant analysis (OPLS-DA) model with daily opioid treatment as dichotomous outcome variable. *p*(corr)-values are not to be confused with a normal *p*-value. *p*(corr) are the new variable values visualized in the loading plot, scaled as a correlation coefficient (ranging from −1.0 to +1.0) between model and original data. $|p(corr)| > 0.5$ was considered "significant". In this model, a positive p(corr) for a given variable indicates that daily opioid treatment is associated with higher scores of that variable, e.g. daily opioid treatment is associated with high MPI-PainSev scores (high pain severity). Likewise, a negative *p*(corr) indicates that daily opioid treatment is associated with a lower score of that variable, e.g. daily opioid treatment is associated with low Short Form Health Survey Physical Component Score (SF36-PCS) scores (i.e. low physical activity)

Variable	*p*(corr)
SF36-PCS	−0.72
EQ5D-Index	−0.60
LiSat-ADL	−0.59
EQ5D-VAS	−0.53
NRS7d	0.54
MPI-Interf	0.61
MPI-PainSev	0.64

For variable abbreviations, see Methods .

Table SIV. *p*(corr) values of orthogonal projections to latent structures discriminant analysis (OPLS-DA) model with oral morphine equivalents (OME) as outcome variable. *p*(corr)-values are not to be confused with a normal *p*-value. *p*(corr) are the new variable values visualized in the loading plot, scaled as a correlation coefficient (ranging from −1.0 to +1.0) between model and original data. In this model, a negative *p*(corr) indicates a negative correlation with OME, e.g. there is a negative correlation between OME and Short Form Health Survey Physical Component Score (SF36-PCS) scores. A positive *p*(corr) indicates a positive correlation with OME, e.g. there is a positive correlation between OME and MPI-Interf

Variable	*p*(corr)
SF36-PCS	−0.82
LiSat-ADL	−0.69
MPI-GAI	−0.54
EQ5D-Index	−0.44
MPI-Interf	0.40

For variable abbreviations, please see the Methods.

SUPPLEMENTARY REFERENCES

1. Wheelock ÅM, Wheelock CE. Trials and tribulations of 'omics data analysis: assessing quality of SIMCA-based multivariate models using examples from pulmonary medicine. Mol Biosyst 2013; 9: 2589–2596.
2. Bäckryd E, Persson EB, Larsson AI, Fischer MR, Gerdle B. Chronic pain patients can be classified into 4 groups: clustering-based discriminant analysis of psychometric data from 4665 patients referred to a multidisciplinary pain centre (a SQRP study). PLoS One 2018; 13: e0192623.
3. Eriksson L, Byrne T, Johansson E, Trygg J, and Vikström C. Multi- and megavariate data analysis basic principles and applications volume 1. 3rd edn. Malmö: MKS Umetrics; 2013.