Short-term recovery trajectories of acute flares in knee pain: a UK-Netherlands multicenter prospective cohort analysis

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Supplementary Table 1 Goodness-of-fit statistics for quadratic and cubic models for pain trajectory, all participants (n=449)

Model	No of class	AIC	BIC	ABIC	Entropy	L	Sample size in each class, n (%)	Average posterior probability
Quadratic	1	-5853.85	-5862.70	-5860.01		-5850.85	449 (100)	1
	2	-5419.54	-5440.18	-5433.91	.8055834	-5412.54	160 (35.6), 289 (64.4)	0.91, 0.96
	3	-5317.45	-5349.89	-5340.04	.7762766	-5306.45	56 (12.5), 220 (49.0), 173 (38.5)	0.91, 0.88, 0.89
	4	-5300.87	-5345.11	-5331.67	.7777202	-5285.87	22 (4.9), 62 (13.8), 226 (50.3), 139 (31.0)	0.91, 0.83, 0.84, 0.90
	5	-5302.39	-5383.43	-5341.41	.9961464	-5283.39	2 (0.5), 23 (5.1), 60 (13.4), 226 (50.3), 138 (30.7)	0.91, 0.87, 0.84, 0.84, 0.90
	6	-5305.11	-5372.95	-5352.34	.7973556	-5282.11	151 (33.6), 207 (46.1), 22 (4.9), 60 (13.4), 3 (0.7), 6 (1.3)	0.82, 0.83, 0.91, 0.79, 0.71, 0.68
	7	-5309.00	-5388.63	-5364.44	.6773106	-5282.00	3 (0.7), 21 (4.7), 2 (0.5), 61 (13.6), 92 (20.5), 125 (27.8), 145 (32.3)	0.70, 0.92, 0.81, 0.75, 0.50, 0.60, 0.80
Cubic	1	-5726.36	-5743.91	-5739.43		-5724.36	449 (100)	1
	2	-5098.32	-5128.30	-5129.34	.8780987	-5098.80	244 (54.3), 205 (45.7)	0.97, 0.96
	3	-4809.48	-4853.72	-4840.28	.9210879	-4794.48	88 (19.6), 231 (51.5), 130 (29.0)	0.97, 0.97, 0.97
	4	-4716.28	-4745.20	-4757.28	.8697848	-4696.21	73 (16.3), 178 (39.6), 135 (30.1), 63 (14.0)	0.95, 0.92, 0.90, 0.94
	5	-4652.44	-4726.17	-4703.77	.9510735	-4627.44	28 (6.2), 83 (18.5), 194 (43.2), 114 (25.4), 30 (6.7)	0.96, 0.93, 0.91, 0.92, 0.92
	6	**-4591.59**	**-4680.07**	**-4653.19**	**.993965**	**-4561.59**	**38 (8.5), 98 (21.8), 41 (9.1), 143 (31.9), 104 (23.2), 25 (5.6)**	**0.99, 0.93, 0.88, 0.88, 0.89, 0.96**
	7	-4548.66	-4651.89	-4620.53	.9472097	-4513.66	75 (16.7), 26 (5.8), 120 (26.7), 58 (12.9), 55 (12.3), 94 (20.9), 21 (4.7)	0.86, 0.96, 0.85, 0.93, 0.83, 0.92, 0.95

AIC, Akaike Information Criteria; BIC, Bayesian Information Criteria; ABIC, Sample-size adjusted BIC; L, Log likelihood.

Supplementary Table 2 Model constraints applied to the 6-group cubic GMM model

Model	Constraint			Outcome
	Residual variances to be constrained to be equal across trajectory classes and time-points	Variance around the cubic term constrained to be equal to 0	Variance around the quadratic term constrained to be equal to 0	
GMM1	No	No	No	Best log likelihood not replicated
GMM2	Yes	No	No	Best log likelihood not replicated
GMM3	No	Yes	No	Best log likelihood not replicated
GMM4	Yes	Yes	No	Model could not be fully estimated under the model constraints listed
GMM5	No	Yes	Yes	Best log likelihood replicated

Footnote: The GMM models are fitted using Mplus version 8.1. GMM, Growth Mixture Model.

Supplementary Table 3 Pain scale: goodness-of-fit statistics for a cubic GMM model with the variance of the cubic and quadratic term fixed at 0

No of groups	AIC	BIC	ABIC	Entropy	L	Sample size in each class, n (%)	Average posterior probability
1	9182	9235	9194		-4578	449 (100)	1.00
2	8853	8927	8870	0.80	-4409	131 (29), 318 (71)	0.91, 0.96
3	8830	8924	8851	0.81	-4392	299 (67), 130 (29), 20 (4)	0.94, 0.86, 0.83
4	8802	8917	8828	0.80	-4373	123 (27), 275 (61), 32 (7), 19 (4)	0.88, 0.90, 0.76, 0.87
5	8790	8926	8821	0.76	-4362	31 (7), 19 (4), 65 (14), 53 (12), 281 (63)	0.75, 0.82, 0.77, 0.75, 0.90
6	8776	8932	8811	0.67	-4350	172 (38), 60 (13), 33 (7), 56 (12), 17 (4), 111 (25)	0.76, 0.77, 0.75, 0.73, 0.81, 0.78
7	8771	8948	8811	0.71	-4343	15 (3), 2 (0), 97 (22), 51 (11), 65 (14), 181 (40), 38 (8)	0.83, 0.99, 0.77, 0.74, 0.78, 0.77, 0.74

Footnote: The GMM models are fitted using Mplus version 8.1. AIC, Akaike Information Criteria; BIC, Bayesian Information Criteria; ABIC, Sample-size adjusted BIC; L, Log likelihood.

Supplementary Table 4 Goodness-of-fit statistics for quadratic and cubic models for pain trajectory, diagnosed osteoarthritis only (n=187)

Model	No of class	AIC	BIC	ABIC	Entropy	L	Sample size in each class, n (%)	Average posterior probability
Quadratic	1	-2421.69	-2426.54	-2429.23		-2418.69	187 (100)	1
	2	-2251.89	-2263.20	-2269.47	0.8980591	-2244.89	85 (45.5), 102 (54.5)	0.92, 0.92
	3	-2203.10	-2220.87	-2230.72	0.9228409	-2192.10	24 (12.8), 113 (60.4), 50 (26.7)	0.92, 0.92, 0.92
	4	-2198.08	-2222.32	-2235.75	0.9313741	-2183.08	6 (3.2), 28 (15.0), 104 (55.6), 49 (26.2)	0.89, 0.83, 0.92, 0.90
	5	-2201.24	-2231.93	-2248.95	0.8749437	-2182.24	5 (2.7), 46 (24.6), 21 (11.2), 74 (39.6), 41 (21.9)	0.92, 0.65, 0.80, 0.70, 0.87
	6	-2204.50	-2241.66	-2262.26	0.8844616	-2181.50	5 (2.7), 47 (25.1), 21 (11.2), 25 (13.4), 87 (46.5), 2 (1.1)	0.92, 0.81, 0.79, 0.53, 0.73, 0.82
	7	-2208.50	-2252.12	-2276.31	0.8357559	-2181.50	2 (1.1), 21 (11.2), 68 (36.4), 5 (2.7), 0 (0.0), 42 (22.5), 49 (26.2)	0.82, 0.79, 0.43, 0.92, 0, 0.49, 0.79
Cubic	1	-2389.97	-2398.05	-2402.53		-2384.97	187 (100)	1
	2	-2114.27	-2130.43	-2139.38	0.9626631	-2104.27	131 (70.1), 56 (29.9)	0.97, 0.97
	3	-1964.48	-1988.71	-2002.15	0.9725973	-1949.48	38 (20.3), 101 (54.0), 48 (25.7)	0.96, 0.98, 0.97
	4	-1931.48	-1963.79	-1981.71	0.9976213	-1911.48	8 (4.3), 44 (23.5), 91 (48.7), 44 (23.5)	0.96, 0.93, 0.95, 0.97
	5	-1929.55	-1969.94	-1992.34	1	-1904.55	2 (1.1), 6 (3.2), 44 (23.5), 91 (48.7), 44(23.5)	0.998, 0.99, 0.93, 0.95, 0.97
	6	**-1868.99**	**-1917.45**	**-1944.33**	**1**	**-1838.99**	**3 (1.6), 50 (26.7), 27 (14.4), 59 (31.6), 37 (19.8), 11 (5.9)**	**0.99, 0.89, 0.96, 0.88, 0.95, 0.98**
	7	-1873.99	-1930.53	-1961.89	1	-1838.99	0 (0.0), 3 (1.6), 27 (14.4), 50 (26.7), 59 (31.6), 37 (19.8), 11 (5.9)	0, 0.99, 0.96, 0.89, 0.88, 0.95, 0.98

AIC, Akaike Information Criteria; BIC, Bayesian Information Criteria; ABIC, Sample-size adjusted BIC; L, Log likelihood.

Supplementary Table 5 Differences in baseline characteristics by pain trajectory group, expressed as relative risk ratios from multinomial logistic regression, all participants

		Group 1 □	Group 2 ○	Group 3 ◇	Group 4 ●	Group 5 ◆	Group 6 ■	
N		41	38	98	143	104	25	**Likelihood ratio test**
Age		0.99 (0.96, 1.02)	1.01 (0.98, 1.04)	1.01 (0.99, 1.04)	Reference	0.98 (0.96, 1.00)	0.99 (0.96, 1.02)	χ^2=10.16, p=0.07
Female gender		1.23 (0.61, 2.47)	1.04 (0.50, 2.14)	0.76 (0.44, 1.29)	Reference	1.09 (0.65, 1.81)	1.31 (0.56, 3.08)	χ^2=2.85, p=0.72
Osteoarthritis		0.79 (0.39, 1.60)	0.90 (0.44, 1.85)	0.89 (0.53, 1.49)	Reference	0.71 (0.42, 1.19)	1.14 (0.49, 2.67)	χ^2=2.23, p=0.82
Body Mass Index (kg/m²)	<25.0	1	1	1	Reference	1	1	
	25.0-29.9	0.57 (0.25, 1.31)	1.52 (0.54, 4.25)	1.62 (0.82, 3.18)	Reference	1.06 (0.55, 2.06)	0.57 (0.17, 1.91)	χ^2=16.68, p=0.08
	30.0-39.0	0.47 (0.19, 1.14)	1.69 (0.60, 4.76)	0.84 (0.40, 1.75)	Reference	1.05 (0.53, 2.06)	1.38 (0.48, 3.97)	
Baseline severe pain		0.95 (0.47, 1.91)	6.32 (2.13, 18.76)	0.36 (0.21, 0.62)	Reference	3.12 (1.73, 5.63)	17.9 (2.35, 135.6)	χ^2=84.74, p=<0.001
Baseline WOMAC pain score (0-50)		0.93 (0.88, 0.97)	1.06 (1.01, 1.12)	0.93 (0.89, 0.96)	Reference	1.08 (1.05, 1.13)	1.24 (1.15, 1.34)	χ^2=120.70, p=<0.001
Baseline WOMAC stiffness score (0-20)		0.88 (0.81, 0.96)	1.04 (0.94, 1.14)	0.95 (0.89, 1.02)	Reference	1.07 (1.00, 1.15)	1.40 (1.19, 1.64)	χ^2=44.21, p=<0.001
Baseline WOMAC function score (0-170)		0.97 (0.96, 0.98)	1.01 (1.00, 1.02)	0.97 (0.96, 0.98)	Reference	1.01 (1.00, 1.02)	1.05 (1.03, 1.07)	χ^2=110.33, p=<0.001
Days since flare started:	0 day	1	1	1	Reference	1	1	
	1 day	0.77 (0.37, 1.63)	1.02 (0.46, 2.26)	1.05 (0.59, 1.87)	Reference	1.19 (0.66, 2.12)	1.33 (0.46, 3.89)	χ^2=12.34, p=0.65
	2 days	0.71 (0.07, 6.94)	-	0.74 (0.13, 4.33)	Reference	1.15 (0.24, 5.58)	4.00 (0.58, 27.7)	
	≥ 3 days	-	-	0.49 (0.05, 5.00)	Reference	0.51 (0.05, 5.20)	5.34 (0.71, 40.1)	
NSAID regime:	Lipid 1200	1	1	1	Reference	1	1	
	Soft gel 1200	0.99 (0.42, 2.34)	0.60 (0.24, 1.50)	1.41 (0.73, 2.74)	Reference	1.52 (0.82, 2.81)	1.19 (0.44, 3.19)	χ^2=10.42, p=0.40
	Soft gel 2400	0.90 (0.39, 2.09)	0.73 (0.32, 1.69)	1.45 (0.77, 2.73)	Reference	0.85 (0.45, 1.61)	0.60 (0.20, 1.82)	

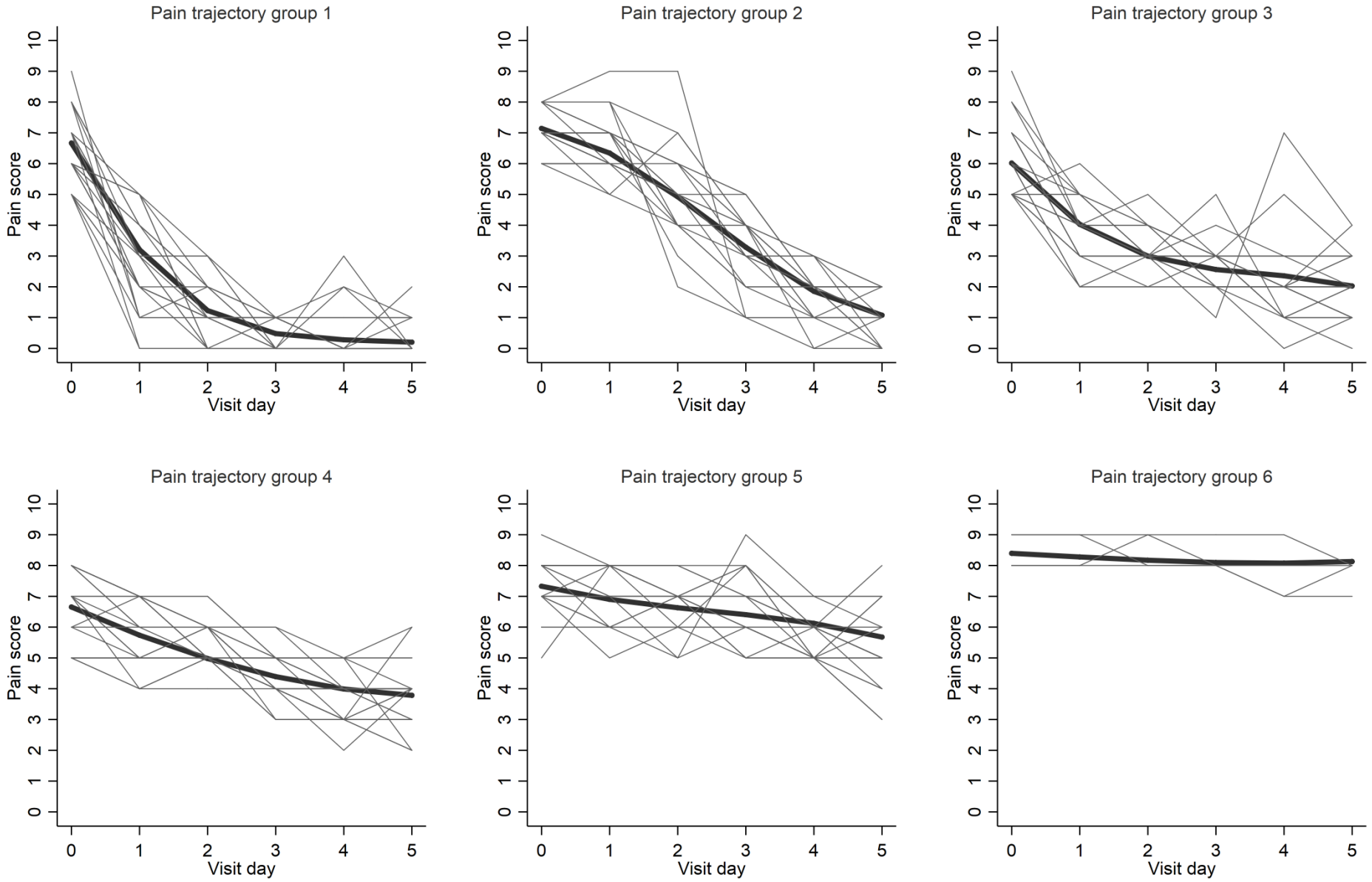
NSAID, Nonsteroidal anti-inflammatory drug; WOMAC, Western Ontario & McMaster Osteoarthritis Index.
For empty cells with no cases estimates could not be derived.

Supplementary Table 6 Differences in outcomes by trajectory group, expressed as relative risk ratios from multinomial logistic regression, all participants

	Group 1 □	Group 2 ○	Group 3 ◇	Group 4 ●	Group 5 ◆	Group 6 ■	
N	41	38	98	143	104	25	**Likelihood ratio test**
End course 1 WOMAC pain score (0-50)	0.54 (0.46, 0.63)	0.73 (0.67, 0.80)	0.82 (0.78, 0.87)	Reference	1.10 (1.07, 1.14)	1.45 (1.30, 1.63)	χ^2=457.14, p=<0.001
End course 1 WOMAC stiffness score (0-20)	0.43 (0.34, 0.53)	0.65 (0.56, 0.75)	0.74 (0.68, 0.81)	Reference	1.17 (1.09, 1.25)	1.92 (1.57, 2.35)	χ^2=330.99, p=<0.001
End course 1 WOMAC function score (0-170)	0.84 (0.80, 0.88)	0.92 (0.90, 0.95)	0.95 (0.93, 0.96)	Reference	1.02 (1.01, 1.03)	1.07 (1.05, 1.09)	χ^2=387.89, p=<0.001
Flare fully controlled/Under control by the end of course 1	38 (5.13, 287)	36 (4.7, 266)	2.28 (1.32, 3.93)	Reference	0.34 (0.19, 0.58)	-	χ^2=163.34, p=<0.001
Beginning second course of NSAIDs	0.06 (0.01, 0.45)	-	0.58 (0.31, 1.07)	Reference	2.40 (1.42, 4.07)	5.11 (2.05, 12.8)	χ^2=87.67, p=<0.001
100% compliant with treatment course 1	0.60 (0.20, 1.84)	-	0.73 (0.30, 1.80)	Reference	0.88 (0.35, 2.21)	-	χ^2=12.01, p=0.03

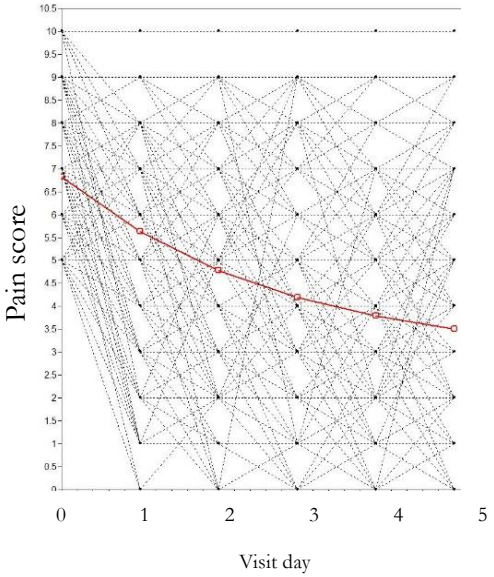
NSAIDs, Nonsteroidal anti-inflammatory drugs; WOMAC Western Ontario & McMaster Osteoarthritis Index.
For empty cells with no cases estimates could not be derived.

Supplementary Figure 1 Plots of estimated means of the final model and the observed individual trajectories, by pain trajectory group, all participants

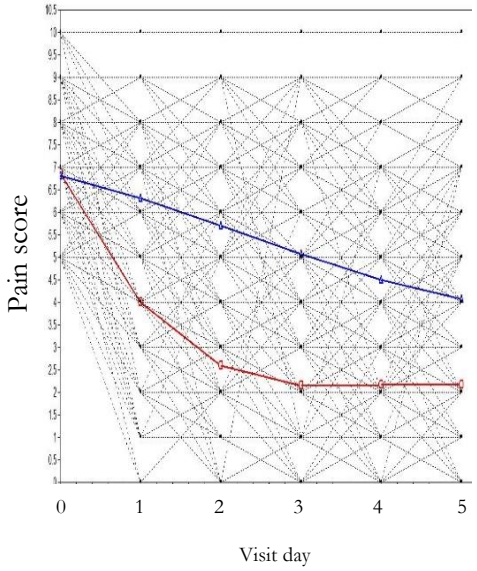


Supplementary Figure 2 Trajectory plots of the constrained GMM model with varying numbers of groups (i.e. with the variance of the cubic and quadratic terms constrained to 0)

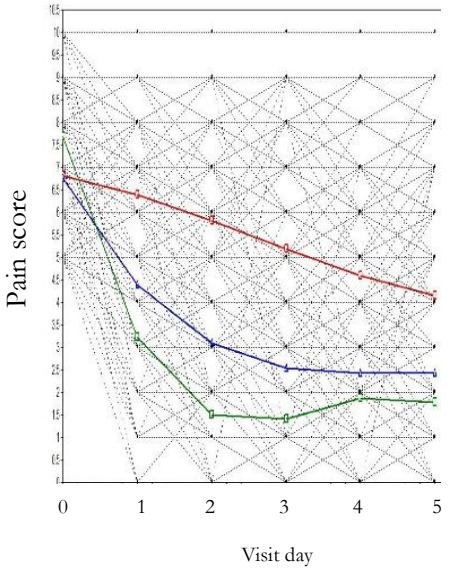
1-group model



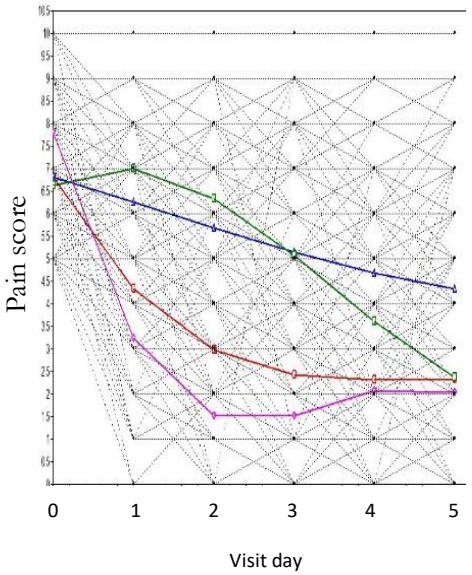
2-group model



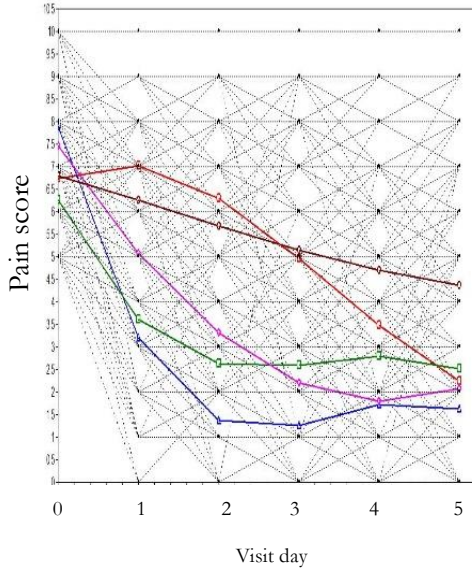
3-group model



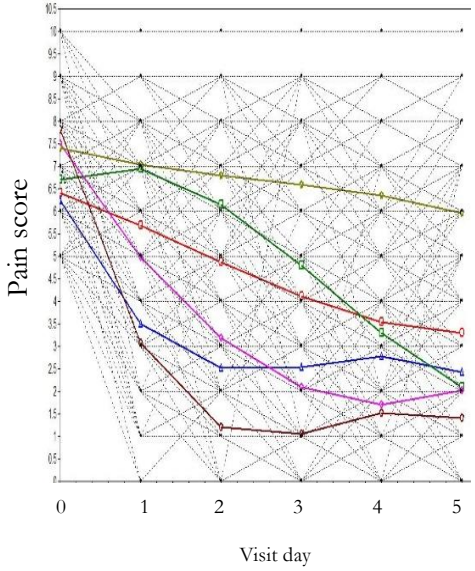
4-group model



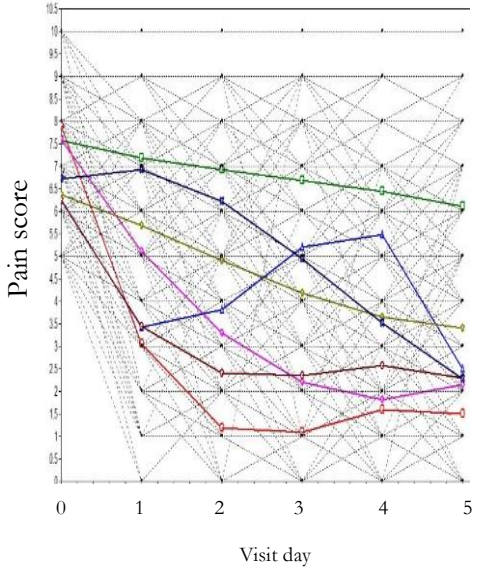
5-group model



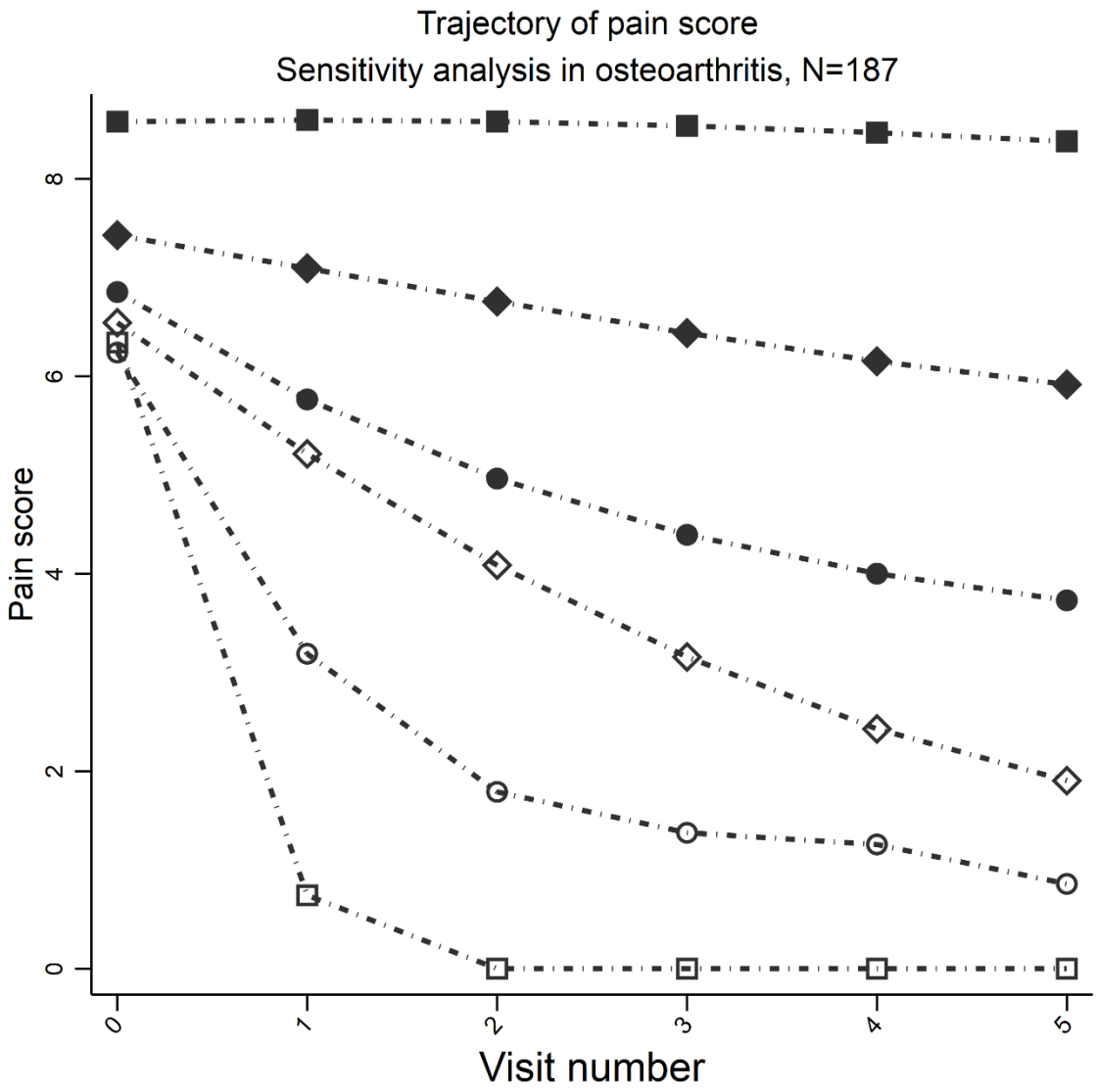
6-group model



7-group model



Supplementary Figure 3 Pain score by group-based trajectory membership, diagnosed osteoarthritis only (n=187)



On the x-axis, 0 = baseline (no medication), and day one is first treatment day.

Group 1 (n=3) □

Group 2 (n=27) ○

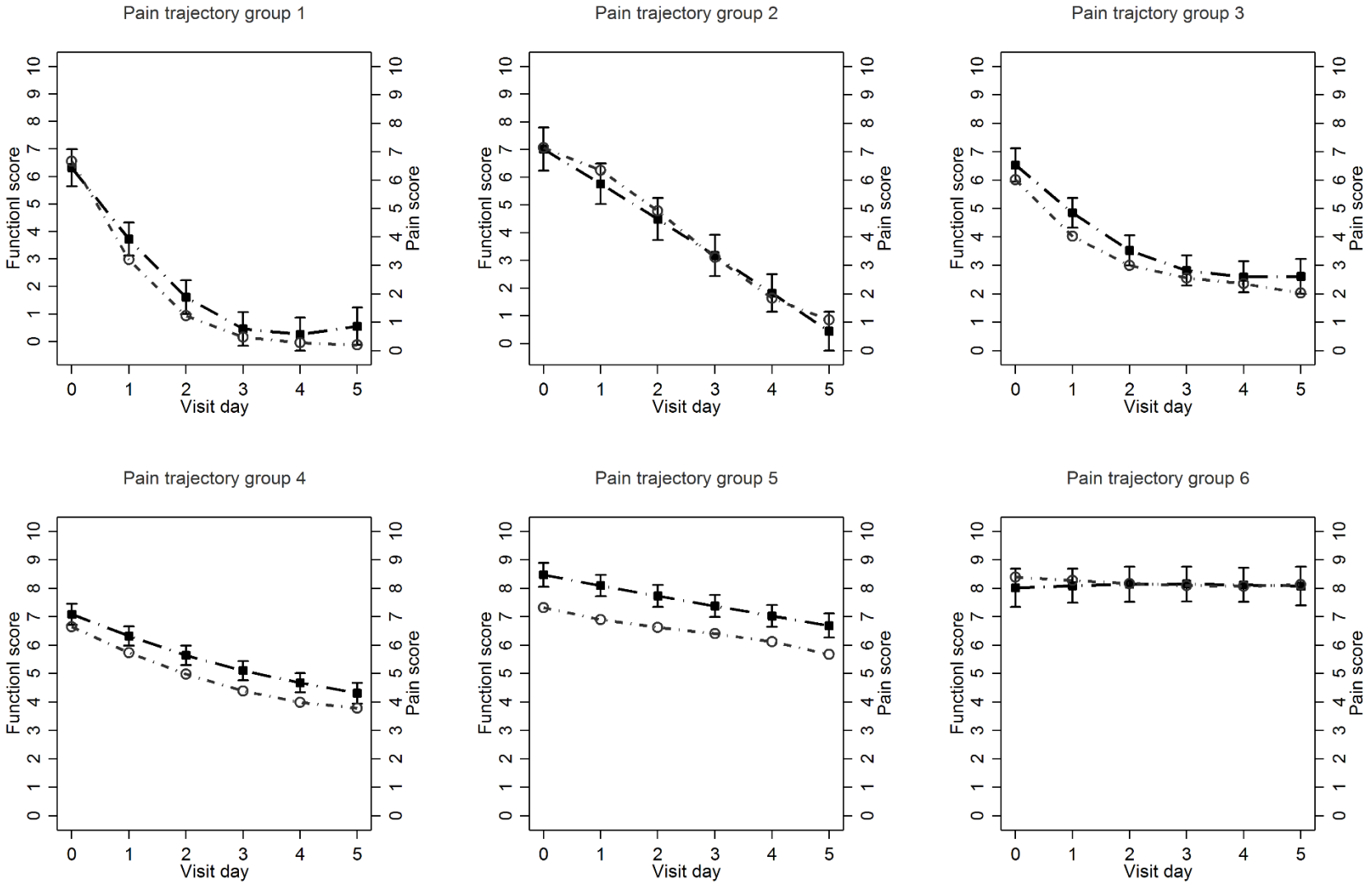
Group 3 (n=50) ◇

Group 4 (n=59) ●

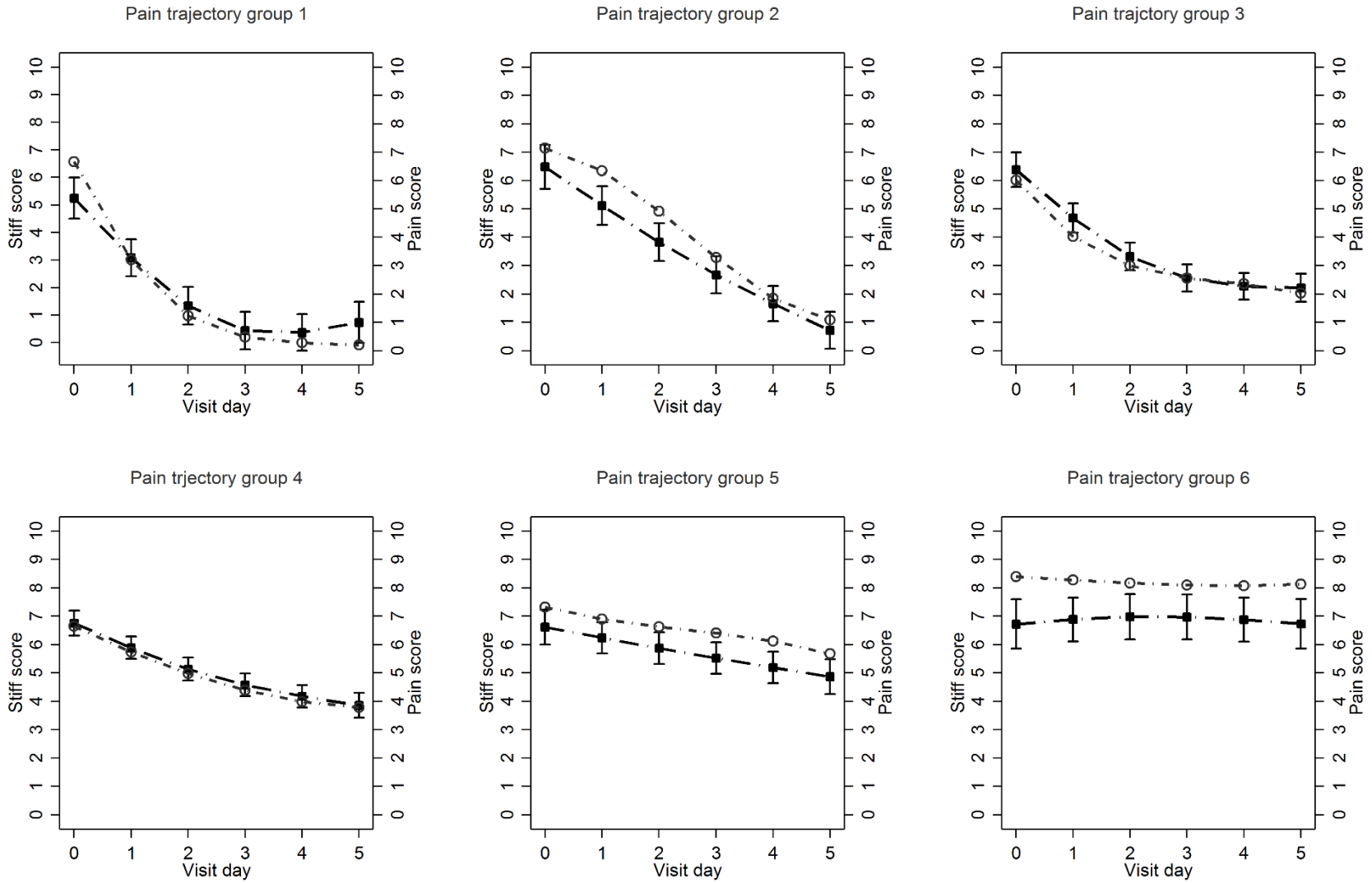
Group 5 (n=37) ◆

Group 6 (n=11) ■

Supplementary Figure 4 Pain interference with participant-nominated activity (■), by pain (○) trajectory group, all participants



Supplementary Figure 5 Stiffness (■), by pain (○) trajectory group**,** all participants



Supplementary Figure 6 Swelling (■), by pain (○) trajectory group, all participants