

Triggers for acute flare in adults with, or at risk of, knee osteoarthritis: a web-based case-crossover study in community-dwelling adults

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Supplementary Data

Questionnaires

Q1. Example of question framing for the 21 putative activity-related, psychosocial and environmental triggers in the Scheduled questionnaire and Event-Driven questionnaire.

Figures

S1. Flowchart of participants recruited into study.

S2. Flowchart of participants recruited into study via general practice route.

S3. Mean pain scores from flare initiation over 10 days by flare duration.

Tables

S1. Reasons for exclusion: Scheduled questionnaires.

S2. Reasons for exclusion: Event-Driven flare questionnaires.

S3. Reasons for exclusion: Daily questionnaires during a flare.

S4. Gender, age and deprivation scores between non-responders, exclusions and responders for general practice register participants.

S5. Gender, age and deprivation scores between non-responders, exclusions and responders for community advertisement participants.

S6. Participant and knee pain characteristics of sample, percentage of missing data.

S7. Healthcare use for knee pain and general health at Baseline.

S8. Normal physical activities reported at Baseline.

S9. Associations between potential trigger exposure the day before, 2 days before and 3 days before flare onset (N=376 participants).

S10. Descriptive characteristics of participants for flare time course and consequences analysis.

S11. Knee flare characteristics in resolved flares (N=459).

S12. Pain scores, medication use and levels of bothersomeness at start and end of flare (N=119 flares).

S13. Associations between participant characteristics and time to flare resolution.

S14. Incidence rate of flares estimated from Poisson regression model with robust standard errors.

Table S15. Comparison of baseline characteristics across ineligible and eligible participants for each primary and secondary objective analysis.

Questionnaire Q1. Example of question framing for the 21 putative activity-related, psychosocial and environmental triggers in the Scheduled questionnaire and Event-Driven questionnaire.

PHYSICAL ACTIVITIES

1. For the below days, how much of the following activities did you do?
(Please select one box for each day, for each activity)

	Today / day of flare	Day before	2 days earlier	3 days earlier
a. Walking outside without a rest	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>

	Today / day of flare	Day before	2 days earlier	3 days earlier
b. Standing for long periods without a rest	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>

	Today / day of flare	Day before	2 days earlier	3 days earlier
c. Sitting for long periods without a break	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>

	Today / day of flare	Day before	2 days earlier	3 days earlier
d. Moderate-to-vigorous physical activity (this may include activities that make you breathe harder than normal)	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>

	Today / day of flare	Day before	2 days earlier	3 days earlier
e. Going up and down stairs	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>

	Today / day of flare	Day before	2 days earlier	3 days earlier
f. Driving	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>

	Today / day of flare	Day before	2 days earlier	3 days earlier
g. Squatting or kneeling	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>

	Today / day of flare	Day before	2 days earlier	3 days earlier
h. Lifting or moving heavy objects	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>

	Today / day of flare	Day before	2 days earlier	3 days earlier
i. Going up and down ladders	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>	Not at all <input type="checkbox"/> A little <input type="checkbox"/> A lot <input type="checkbox"/>

SLIPS, TRIPS, SPRAINS AND STRAINS

1. For the below days....*(Please select one box for each day)*

	Today / day of flare	Day before	2 days earlier	3 days earlier
a. Did you have a slip, trip or fall?	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>

	Today / day of flare	Day before	2 days earlier	3 days earlier
b. Did you have an episode where your knee buckled or gave way?	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>

HEALTH AND HEALTHCARE USE

1. For the below days....*(Please select one box for each day)*

	Today / day of flare	Day before	2 days earlier	3 days earlier
a. Did you reduce or miss taking some of your planned medication?	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>

	Today / day of flare	Day before	2 days earlier	3 days earlier
b. Did you take (extra) pain medication because you knew you would be busier than usual that day?	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>

	Today / day of flare	Day before	2 days earlier	3 days earlier
c. Did you have a cough or cold or other minor infection?	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>

STRESS AND OTHER THINGS

1. For the below days... *(Please select one box for each day)*

	Today / day of flare	Day before	2 days earlier	3 days earlier
a. Did anything happen at work that most people would consider stressful?	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>

	Today / day of flare	Day before	2 days earlier	3 days earlier
b. Did anything happen at home that most people would consider stressful?	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>

	Today / day of flare	Day before	2 days earlier	3 days earlier
c. Did anything happen to a close friend or relative that turned out to be stressful for you?	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>

	Today / day of flare	Day before	2 days earlier	3 days earlier
d. Did you feel low in mood or depressed?	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>

	Today / day of flare	Day before	2 days earlier	3 days earlier
e. Did you feel angry, irritable or hostile?	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>

	Today / day of flare	Day before	2 days earlier	3 days earlier
f. Did you wake up having had a poor night's sleep?	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>

	Today / day of flare	Day before	2 days earlier	3 days earlier
g. Did the weather feel generally cold and damp	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>	No <input type="checkbox"/> Yes <input type="checkbox"/>

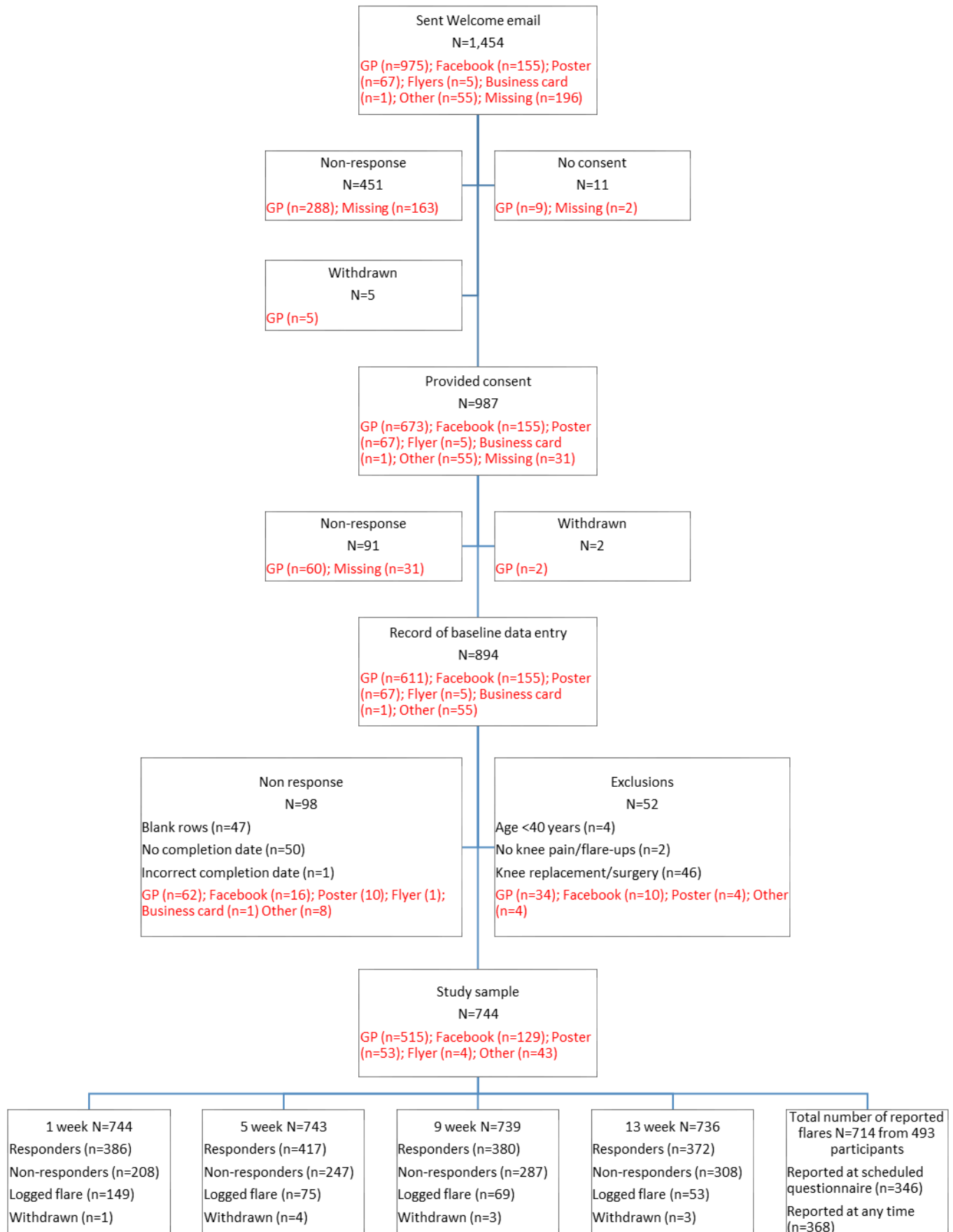


Figure S1. Flowchart of participants recruited into study.

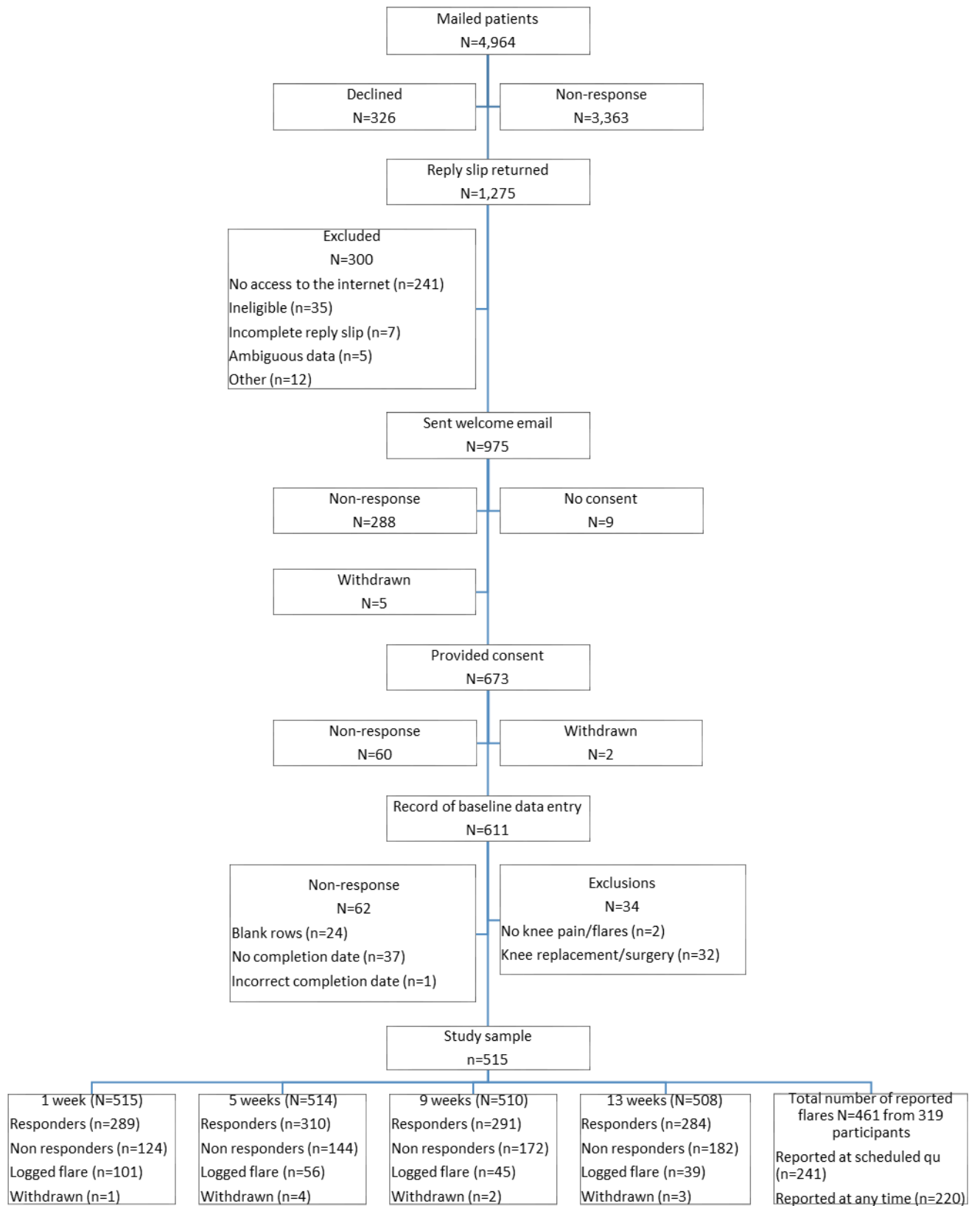


Figure S2. Flowchart of participants recruited into study via general practice route.

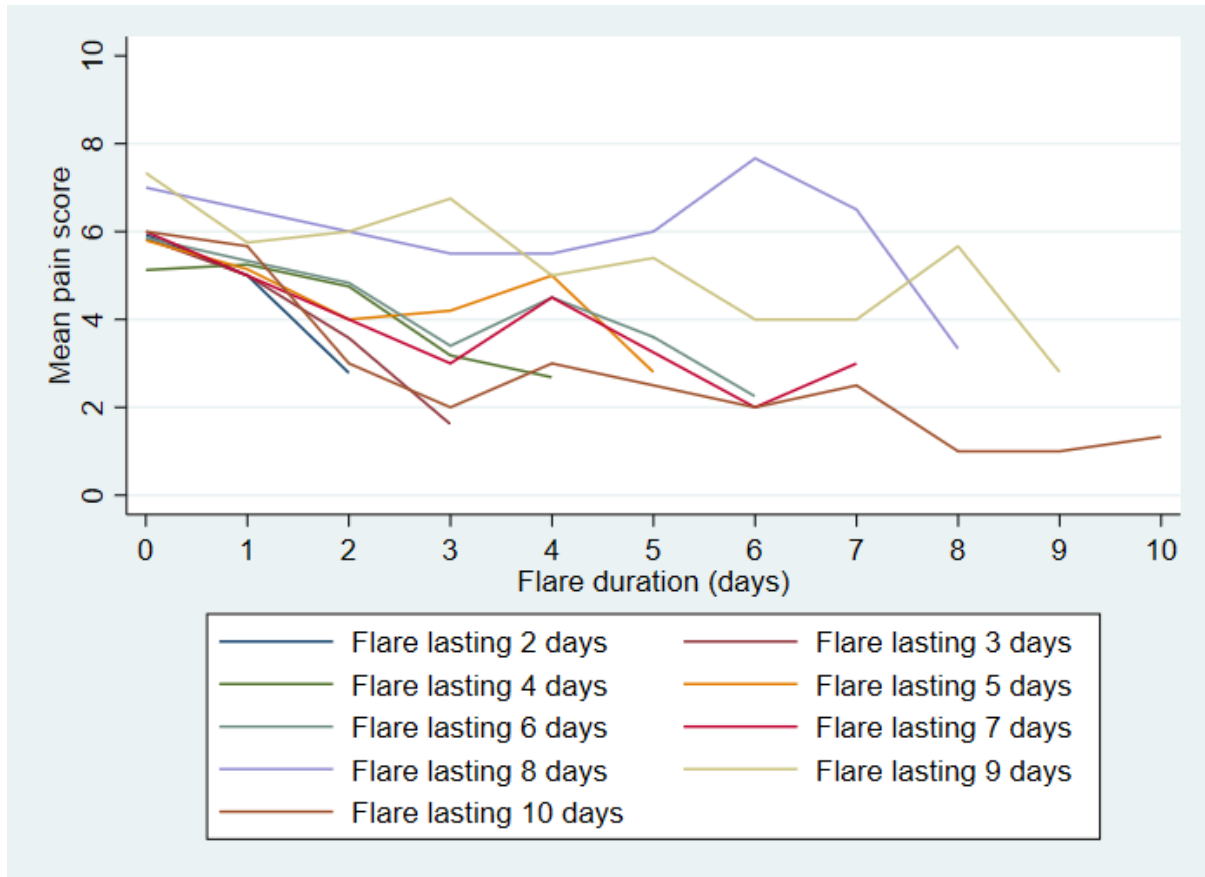


Figure S3. Mean pain scores from flare initiation over 10 days by flare duration.

Table S1. Reasons for exclusion: Scheduled questionnaires.

Reasons for exclusion	1 week N=669	5 week N=598	9 week N=539	13 week N=512
No Baseline questionnaire*	42	35	34	30
Duplicate entry*	1	6	0	2
No completion date	22	20	15	11
Questionnaire not completed within 7 days	0	0	0	0
Completed after study end date*	0	0	0	17
Reported flare (completed flare Event-Driven questionnaire)	197 (158)	113 (81)	107 (71)	77 (56)
Reported flare within 3 days of completing Questionnaire	10	5	2	0
Completed questionnaire within 3 days after flare ended	11	2	1	3
Eligible questionnaires	386	417	380	372

*Exclusions based on system errors. All other exclusions participant-led.

Table S2. Reasons for exclusion: Event-Driven flare questionnaires.

Reasons for exclusion	N=885
No Baseline questionnaire*	77
Duplicate entry*	0
No completion date	27
Questionnaire not completed within 7 days	1
Completed after study end date*	4
Participant did not indicate when flare started	5
Subsequent flare reported within 3 days of previously reported flare	4
Flare duration less than 24 hours, if known	49
Start date of flare \leq 3 days of end date of previous flare, if known	4
Eligible questionnaires for trigger and frequency of acute flares objectives	714
No Daily flare questionnaire	128
Eligible questionnaires with daily flare questionnaire for estimating time course and consequences objective	586

*Exclusions based on system errors. All other exclusions participant-led.

Table S3. Reasons for exclusion: Daily questionnaires during a flare.

Reasons for deleted entries	N=10708
No Baseline questionnaire*	639
No completion date	157
Questionnaire not completed on the same day	3,375
Completed after study end date*	788
Flare questionnaire not completed*	16
Flare duration less than 24 hours	358
Start date of flare \leq 3 days of end date of previous flare	12
Completed on same day as flare questionnaire*	1
Questionnaires completed after flare resolution reported once	898
Eligible questionnaires for estimating time course and consequences objective	4464

*Exclusions based on system errors. All other exclusions participant-led.

Table S4. Gender, age and deprivation scores between non-responders, exclusions and responders for general practice register participants.

Characteristics of general practice register participants	Mailed participants (N=4964)	Non-responders, Refusals*, withdrawn (N=4115)	Exclusions (N=334)	Eligible (N=941)	Completed baseline (N=515)	Completed ≥1 scheduled questionnaire (N=426)	Completed ≥1 flare questionnaire (N=319)
Gender							
Male	2081 (42)	1722 (42)	125 (37)	425 (45)	234 (45)	190 (45)	127 (40)
Female	2883 (58)	2393 (58)	209 (63)	516 (55)	281 (55)	236 (55)	192 (60)
Age (years); mean (SD)	63.6 (12.6)	62.9 (12.7)	73.0 (11.4)	63.6 (10.6)	63.1 (10.1)	63.4 (9.9)	63.12 (10)
<55	1348 (27)	1204 (29)	26 (8)	207 (22)	118 (23)	91 (21)	75 (24)
55-64	1304 (26)	1094 (27)	46 (14)	286 (30)	164 (32)	140 (33)	102 (32)
65+	2311 (47)	1816 (44)	262 (78)	448 (48)	233 (45)	195 (46)	142 (45)
Males, age; mean (SD)	62.7 (12.3)	61.7 (12.3)	72.9 (11.4)	65.04 (11)	64.87 (10)	65.4 (9.7)	65.5 (10.3)
<55	593 (29)	544 (32)	10 (8)	78 (18)	39 (17)	28 (15)	20 (16)
55-64	591 (28)	500 (29)	18 (14)	125 (29)	73 (31)	61 (32)	36 (28)
65+	897 (43)	678 (39)	97 (78)	222 (52)	122 (52)	101 (53)	71 (56)
Females, age; mean (SD)	64.2 (12.8)	63.7 (12.9)	73.1 (11.4)	62.4 (10.4)	61.7 (9.9)	61.8 (9.9)	61.6 (10.1)
<55	755 (26)	660 (28)	16 (8)	129 (25)	79 (28)	63 (27)	55 (29)
55-64	713 (25)	594 (25)	28 (13)	161 (31)	91 (32)	79 (34)	66 (34)
65+	1414 (49)	1138 (48)	165 (79)	226 (44)	111 (40)	94 (40)	71 (37)
IMD							
Most deprived	817 (17)	724 (18)	41 (12)	108 (12)	52 (10)	39 (9)	38 (12)
2 nd most deprived	1200 (24)	1026 (25)	72 (22)	188 (20)	102 (20)	84 (20)	67 (21)
Mid-deprived	1203 (24)	986 (24)	98 (29)	233 (25)	119 (23)	102 (24)	68 (21)
2 nd least deprived	1149 (23)	929 (23)	76 (23)	257 (27)	144 (28)	114 (27)	90 (28)
Least deprived	591 (12)	448 (11)	46 (14)	154 (16)	97 (19)	87 (20)	56 (18)

*Refusals include those who declined or did not provide consent.

SD, Standard Deviation; IMD, Index of Multiple Deprivation.

Table S5. Gender, age and deprivation scores between non-responders, exclusions and responders for community advertisement participants.

Characteristics of community advertisement participants	Mailed participants	Non-responders, Refusals, withdrawn	Exclusions (N=18)	Eligible	Completed baseline (N=229)	Completed ≥1 scheduled questionnaire (N=165)	Completed ≥1 flare questionnaire (N=174)
Gender							
Male	-	-	11 (61)	-	59 (26)	40 (24)	43 (25)
Female	-	-	7 (39)	-	170 (74)	125 (76)	131 (75)
Age (years); mean (SD)	-	-	58.6 (15.2)	-	59.7 (10.2)	59.8 (10.1)	59.2 (9.9)
<55	-	-	5 (29)	-	67 (31)	50 (32)	54 (32)
55-64	-	-	4 (24)	-	83 (38)	55 (35)	66 (39)
65+	-	-	8 (47)	-	66 (31)	52 (33)	48 (29)
Males, age; mean (SD)	-	-	56.0 (18.0)	-	59.0 (10.7)	60.30 (11)	58.1 (10.1)
<55	-	-	4 (40)	-	20 (36)	13 (35)	16 (39)
55-64	-	-	0	-	17 (31)	9 (24)	13 (32)
65+	-	-	6 (60)	-	18 (33)	15 (41)	12 (29)
Females, age; mean (SD)	-	-	62.3 (10.3)	-	59.9 (10.1)	59.6 (9.8)	59.6 (9.8)
<55	-	-	1 (14)	-	47 (29)	37 (31)	38 (30)
55-64	-	-	4 (57)	-	66 (41)	46 (38)	53 (42)
65+	-	-	2 (29)	-	48 (30)	37 (31)	36 (28)
IMD							
Most deprived	-	-	5 (28)	-	47 (21)	35 (21)	35 (20)
2 nd most deprived	-	-	6 (33)	-	35 (15)	19 (12)	27 (16)
Mid-deprived	-	-	1 (6)	-	55 (24)	39 (24)	45 (26)
2 nd least deprived	-	-	3 (17)	-	47 (21)	35 (21)	33 (19)
Least deprived	-	-	3 (17)	-	45 (20)	37 (22)	34 (20)

SD, Standard Deviation; IMD, Index of Multiple Deprivation; -, not applicable.

Table S6. Participant and knee pain characteristics of sample, percentage of missing data.

Characteristic	Baseline responders (n=744)
Participant characteristic	
Age (years)	13 (2)
Gender	0
Current employment	7 (1)
Body mass index (kg/m ²)	84 (11)
Family history of total/partial knee replacement	35 (5)
Knee pain characteristic*	
Time since onset	22 (3)
Knee pain pattern in the last year	14 (2)
Pain experience over last 6 months	8 (1)
Pain, aching, stiffness in last month	6 (1)
Worse pain last week (0-10 NRS)	3 (<1)
Least pain last week (0-10 NRS)	2 (<1)
Average pain (0-10 NRS)	8 (1)
Pain right now (0-10 NRS)	3 (<1)
Bothersomeness last 24 hours	7 (1)
KOOS Physical Function (0-100)	35 (5)
KOOS Quality of Life (0-100)	0
Flare at present	8 (1)
Varus-valgus malalignment	15 (2)
Foot rotation	11 (2)
Previous knee injury	4 (1)

*The index knee was selected based on the knee with highest ‘average pain’ score on a 0-10 numerical rating scale. If scores were equal, then the knee with the highest ‘worst pain in the last week’ followed by the highest ‘current pain’, followed by random selection were selected. If left, or right knee score was missing, the available knee score was included.

NRS, Numerical Rating Scale; KOOS, Knee injury and Osteoarthritis Outcome Score.

Table S7. Healthcare use for knee pain and general health at Baseline.

Characteristic	Baseline responders (n=744)
Medication use for knee pain, last week	
Paracetamol	294 (40)
NSAIDs	125 (17)
Opioids	49 (7)
Herbal	56 (8)
Topical	6 (1)
None of the above	211 (28)
Missing	3 (<1)
Healthcare professional consultation for knee pain, last 12 months	
General Practitioner	505 (68)
Practice/District Nurse	20 (3)
Physiotherapist	236 (32)
Surgeon	80 (11)
Rheumatologist	18 (2)
Acupuncturist	22 (3)
Occupational Therapist	13 (2)
None of the above	180 (24)
Missing	3 (<1)
Previous knee surgery, ever	201 (27)
Missing	33 (4)
Corticosteroid injection last 3 months	58 (8)
Missing	0 (0)
On TKR waiting list	16 (2)
Missing	4 (1)
Perceived general health	
Excellent	82 (11)
Very good	301 (41)
Good	245 (33)
Fair	99 (13)
Poor	16 (2)
Missing	1 (<1)
Physical activity	
Active	172 (23)
Moderately active	123 (17)
Moderately inactive	106 (14)
Inactive	274 (37)
Missing	69 (9)

NSAIDs, Nonsteroidal Anti-inflammatory Drugs; TKR, Total Knee Replacement.

Table S8. Normal physical activities reported at Baseline.

Characteristic	Baseline responders (n=744)
Normal physical activities on a normal day	
Walking outside without a rest	
Not at all	63 (9)
A little	436 (59)
A lot	235 (32)
Missing	10 (1)
Standing for long periods without rest	
Not at all	200 (27)
A little	382 (51)
A lot	149 (20)
Missing	13 (2)
Sitting for long periods without break	
Not at all	113 (15)
A little	399 (54)
A lot	215 (29)
Missing	17 (2)
Moderate-to-vigorous physical activity	
Not at all	196 (26)
A little	427 (57)
A lot	106 (14)
Missing	15 (2)
Going up/down stairs	
Not at all	77 (10)
A little	375 (50)
A lot	289 (39)
Missing	3 (<1)
Driving	
Not at all	106 (14)
A little	444 (60)
A lot	187 (25)
Missing	7 (1)
Squatting or kneeling	
Not at all	358 (48)
A little	334 (45)
A lot	42 (6)
Missing	10 (1)
Lifting or moving heavy objects	
Not at all	344 (46)
A little	354 (48)
A lot	38 (5)
Missing	8 (1)
Going up and down ladders	
Not at all	604 (81)
A little	115 (16)
A lot	16 (2)
Missing	9 (1)

Table S9. Associations between potential trigger exposure the day before, 2 days before and 3 days before flare onset (N=376 participants).

Potential trigger	Day before OR (95% CI)	2 days earlier OR (95% CI)	3 days earlier OR (95% CI)
<i>Physical activities</i>			
Walking outside without a rest			
Not at all	1	1	1
A little	1.30 (0.90, 1.86)	0.74 (0.51, 1.07)	0.65 (0.46, 0.93)
A lot	0.81 (0.53, 1.23)	0.66 (0.44, 0.99)	0.43 (0.28, 0.66)
Standing for long periods without a rest			
Not at all	1	1	1
A little	1.02 (0.77, 1.36)	0.91 (0.68, 1.22)	0.74 (0.56, 0.98)
A lot	1.16 (0.79, 1.70)	0.90 (0.60, 1.34)	0.66 (0.44, 0.98)
Sitting for long periods without a break			
Not at all	1	1	1
A little	0.76 (0.55, 1.06)	0.73 (0.53, 1.01)	0.61 (0.45, 0.84)
A lot	0.66 (0.44, 0.98)	0.57 (0.38, 0.85)	0.56 (0.38, 0.84)
Moderate-to-vigorous physical activity			
Not at all	1	1	1
A little	0.90 (0.68, 1.19)	0.79 (0.60, 1.06)	0.77 (0.58, 1.03)
A lot	0.84 (0.58, 1.23)	0.67 (0.46, 0.99)	0.71 (0.48, 1.04)
Going up and down stairs			
Not at all	1	1	1
A little	0.98 (0.61, 1.58)	0.83 (0.53, 1.28)	0.74 (0.48, 1.14)
A lot	1.00 (0.58, 1.72)	0.55 (0.33, 0.93)	0.43 (0.26, 0.72)
Driving			
Not at all	1	1	1
A little	1.15 (0.84, 1.58)	1.03 (0.73, 1.44)	0.96 (0.68, 1.35)
A lot	0.88 (0.55, 1.40)	0.88 (0.54, 1.43)	0.65 (0.41, 1.04)
Squatting or kneeling			
Not at all	1	1	1
A little	0.95 (0.70, 1.29)	1.13 (0.82, 1.56)	1.04 (0.75, 1.44)
A lot	1.57 (0.98, 2.51)	1.62 (0.97, 2.70)	1.16 (0.71, 1.89)
Lifting or moving heavy objects			
Not at all	1	1	1
A little	0.82 (0.61, 1.09)	0.95 (0.69, 1.30)	0.98 (0.71, 1.34)
A lot	1.51 (0.87, 2.63)	1.22 (0.68, 2.20)	0.90 (0.50, 1.64)
Going up and down ladders			
Not at all	1	1	1
A little	1.74 (1.06, 2.85)	1.54 (0.93, 2.54)	1.09 (0.63, 1.87)
A lot	2.96 (1.19, 7.34)	1.25 (0.46, 3.43)	1.31 (0.46, 3.68)
<i>Slips, trips, sprains, and strains</i>			
Slip, trip or fall			
No	1	1	1
Yes	0.62 (0.28, 1.34)	0.32 (0.12, 0.82)	0.63 (0.32, 1.25)
Episode of buckling or giving way			
No	1	1	1
Yes	1.35 (0.93, 1.98)	0.63 (0.41, 0.97)	0.66 (0.42, 1.06)
<i>Health and healthcare use</i>			
Reduce or miss medication			
No	1	1	1
Yes	0.55 (0.32, 0.94)	0.46 (0.26, 0.82)	0.56 (0.32, 0.97)
Take extra pain medication in anticipation of increased activity/busier			
No	1	1	1
Yes	1.08 (0.74, 1.58)	0.30 (0.18, 0.50)	0.32 (0.19, 0.53)
Cough, cold or other minor infection			
No	1	1	1
Yes	0.68 (0.49, 0.93)	0.71 (0.51, 0.98)	0.70 (0.50, 0.97)

Table S9. continued...

Potential trigger	Day before OR (95% CI)	2 days earlier OR (95% CI)	3 days earlier OR (95% CI)
<i>Stress and other things</i>			
Work-related stress			
No	1	1	1
Yes	0.98 (0.63, 1.53)	0.80 (0.50, 1.29)	0.82 (0.53, 1.29)
Home-related stress			
No	1	1	1
Yes	0.94 (0.66, 1.35)	0.76 (0.52, 1.09)	0.88 (0.62, 1.25)
Friend/family-related stress			
No	1	1	1
Yes	0.74 (0.49, 1.11)	0.70 (0.45, 1.08)	0.73 (0.49, 1.10)
Low mood/depression			
No	1	1	1
Yes	1.27 (0.93, 1.73)	0.75 (0.53, 1.05)	0.83 (0.60, 1.16)
Feeling angry, irritable or hostile			
No	1	1	1
Yes	1.09 (0.77, 1.56)	0.77 (0.52, 1.14)	1.06 (0.72, 1.55)
Poor night's sleep			
No	1	1	1
Yes	0.83 (0.64, 1.09)	0.58 (0.44, 0.76)	0.52 (0.39, 0.70)
Generally cold and damp weather			
No	1	1	1
Yes	1.06 (0.83, 1.37)	0.75 (0.59, 0.97)	0.76 (0.59, 0.98)

OR, odds ratio; CI, confidence interval.

Table S10. Descriptive characteristics of participants for flare time course and consequences analysis.

Descriptive characteristic	
Number of participants	314
Number of reported flares	459
Female	221 (70%)
Age (years); mean (SD)	61.1 (9.8)
Body mass index (kg/m ²); mean (SD)	29.1 (5.4)
Number of flares per participant	Median (IQR): 1 (1, 2) 68% (n=212) reported 1 flare 24% (n=74) reported 2 flares 5% (n=17) reported 3 flares 3% (n=8) reported 4 flares 1% (n=2) reported 5 flares <1% (n=1) reported 6 flares
Duration of flare (days)	Mean (SD): 7.4 (8.6) Median (IQR): 5 (3, 8) Range: 2 to 88
Reported flare ending on two consecutive days	257 (56%)

SD, Standard Deviation; IQR, Interquartile Range.

Table S11. Knee flare characteristics in resolved flares (N=459).

Responses from Event-Driven flare questionnaire	N (%)
When did flare start	
Today	119 (26)
Yesterday	156 (34)
2 days ago	67 (15)
3 days ago	30 (7)
4 or more days ago	87 (19)
Was flare unexpected	
No	133 (29)
Yes	326 (71)
Flare in which knee*	
Left knee only	159 (35)
Right knee only	205 (45)
Both knees	90 (30)
Average left knee pain in last 24 hours	4.1 (3)
Average right knee pain in last 24 hours	4.5 (3)
Knee pain in affected knee; mean (SD) ^a	6.2 (2)
Knee pain in unaffected knee; mean (SD) ^b	0.9 (2)
Pain increase ≥ 2 points from baseline in affected knee ^a	240 (45)
Pain increase ≥ 2 points from baseline in unaffected knee ^b	10 (4)
<i>Changes noticed since flare (more than usual)</i>	
Limping	268 (58)
Swelling	151 (33)
Stiffness	294 (64)
Everyday activities more difficult/impossible to do	262 (57)
Sleep disturbance	222 (48)

SD, Standard Deviation. *Percentages may not add up to 100 due to missing data. ^aSome participants reported flares occurring in both knees therefore the total number of affected knees for analysis was 544. ^bAnalysis was based on 294 unaffected knees.

Table S12. Pain scores, medication use and levels of bothersomeness at start and end of flare (N=119 flares).

Characteristic	Start of flare	End of flare
Pain score of affected knee	Median (IQR): 6 (4, 8)	Median (IQR): 2 (1, 4)
Bothersomeness		
Not at all	1 (1)	22 (18)
Mildly	15 (13)	70 (59)
Moderately	49 (41)	20 (17)
Severely	27 (23)	4 (3)
Totally	6 (5)	0 (0)
Missing	21 (18)	3 (3)
Medication use		
No	22 (18)	62 (52)
Less than usual	3 (3)	19 (16)
Same as usual	31 (26)	33 (28)
More than usual	23 (19)	5 (4)
Missing	40 (34)	0 (0)

SD, Standard Deviation; IQR, Interquartile Range. Analysis performed in participants who reported their flare on the day it started.

Table S13. Associations between participant characteristics and time to flare resolution.

	Unadjusted time ratio (95% CI)
Age (years)	1.00 (0.99, 1.00)
Gender	
Male	1
Female	0.95 (0.84, 1.10)
Duration of symptoms	
<1 year ago	1
1-4 years ago	0.97 (0.84, 1.11)
5-9 years ago	0.83 (0.71, 0.98)
≥10 years ago	0.89 (0.77, 1.04)

CI, Confidence Interval.

Table S14. Incidence rate of flares estimated from Poisson regression model with robust standard errors.

Participant characteristics	Descriptive statistics N (%)	Unadjusted incidence rate ratios of flares (95% CI)
Age (years); mean (SD)	62.9 (10.1)	0.98 (0.97, 0.99)
Gender		
Male	184 (39)	1
Female	292 (61)	1.85 (1.43, 2.39)
Knee injury		
No knee injury	188 (40)	1
Injury in either or both knees	278 (60)	0.97 (0.77, 1.22)
Most severe knee pain trajectory (Left or Right)		
Single episode	23 (5)	0.27 (0.06, 1.11)
Few episodes	167 (35)	1
Few severe episodes and some pain	176 (37)	1.70 (1.29, 2.23)
Severe episodes and up and down pain	95 (20)	2.04 (1.54, 2.70)
Severe pain all the time	15 (3)	2.06 (1.17, 3.63)
Knee surgery		
No knee surgery	335 (73)	1
Surgery on either or both knees	125 (27)	1.10 (0.87, 1.39)
Index of multiple deprivation		
Least deprived	110 (23)	1
2 nd least deprived	126 (27)	0.85 (0.61, 1.19)
Mid-deprived	111 (23)	1.06 (0.76, 1.47)
2 nd most deprived	81 (17)	1.18 (0.84, 1.64)
Most deprived	48 (10)	1.31 (0.91, 1.90)

CI, Confidence Interval; SD, Standard Deviation.

Table S15. Comparison of baseline characteristics across ineligible and eligible participants for each primary and secondary objective analysis.

Characteristic	Primary analysis: ineligible n=368	Primary analysis: eligible n=376	Secondary analysis 1: ineligible n=430	Secondary analysis 1: eligible n=314	Secondary analysis 2: ineligible n=268	Secondary analysis 2: eligible n=476
Age (years); mean (SD)	62.4 (10.4)	61.8 (10.1)	62.9 (10.5)	61.1 (9.8)	60.6 (10.4)	62.9 (10.1)
Female	197 (53.5)	254 (67.6)	230 (53.5)	221 (70.4)	159 (59.3)	292 (61.3)
Current employment						
Employed/Self-employed	164 (44.8)	161 (43.4)	181 (42.4)	144 (46.5)	133 (49.8)	192 (40.9)
Retired	156 (42.6)	162 (43.7)	193 (45.2)	125 (40.3)	91 (34.1)	227 (48.3)
Looking after home or family	18 (4.9)	22 (5.9)	20 (4.7)	20 (6.5)	13 (4.9)	27 (5.7)
Unable to work (sick/disabled)	19 (5.2)	12 (3.2)	19 (4.4)	12 (3.9)	23 (8.6)	8 (1.7)
Unemployed/voluntary work	2 (0.5)	0 (0.0)	2 (0.5)	0 (0.0)	1 (0.4)	1 (0.2)
Full, part-time student	6 (1.6)	7 (1.9)	9 (2.1)	4 (1.3)	4 (1.5)	9 (1.9)
None of the above	0 (0.0)	2 (0.5)	1 (0.2)	1 (0.3)	0 (0.0)	2 (0.4)
BMI (kg/m ²); mean (SD)	28.9 (5.4)	29.5 (5.9)	29.3 (5.9)	29.1 (5.4)	30.4 (5.7)	28.5 (5.5)
Family history of total/partial knee replacement	51 (13.9)	61 (16.2)	65 (15.1)	47 (15.0)	40 (14.9)	72 (15.1)
<i>Knee characteristic*</i>						
Time since onset of pain						
<1 year ago	56 (15.5)	63 (17.0)	60 (14.2)	59 (19.0)	42 (15.8)	77 (16.5)
1 to 4 years ago	143 (39.6)	126 (34.0)	159 (37.7)	110 (35.5)	110 (41.5)	159 (34.0)
5 to 9 years ago	62 (17.2)	70 (18.9)	78 (18.5)	54 (17.4)	43 (16.2)	89 (19.1)
≥10 years ago	94 (26.0)	108 (29.1)	118 (28.0)	84 (27.1)	69 (26.0)	133 (28.5)
Knee pain pattern in the last year						
Single episode	26 (7.2)	10 (2.7)	28 (6.6)	8 (2.6)	8 (3.0)	28 (6.0)
Few episodes	121 (33.7)	92 (24.8)	135 (32.0)	78 (25.3)	51 (19.4)	162 (34.7)
Few episodes and some pain	109 (30.4)	152 (41.0)	137 (32.5)	124 (40.3)	88 (33.5)	173 (37.0)
Severe episodes and up and down pain	79 (22.0)	99 (26.7)	94 (22.3)	84 (27.3)	88 (33.5)	90 (19.3)
Severe pain all the time	24 (6.7)	18 (4.9)	28 (6.6)	14 (4.5)	28 (10.6)	14 (3.0)

Table S15. Continued...

Characteristic	Primary analysis: ineligible n=368	Primary analysis: eligible n=376	Secondary analysis 1: ineligible n=430	Secondary analysis 1: eligible n=314	Secondary analysis 2: ineligible n=268	Secondary analysis 2: eligible n=476
Pain experience over last 6 months						
No knee pain	37 (10.2)	9 (2.4)	40 (9.4)	6 (1.9)	6 (2.3)	40 (8.5)
Pain is predictable	116 (32.0)	95 (25.4)	131 (30.9)	80 (25.6)	42 (15.9)	169 (35.8)
Predictable, becoming more unpredictable	136 (37.6)	188 (50.3)	169 (39.9)	155 (49.7)	130 (49.2)	194 (41.1)
Constant	73 (20.2)	82 (21.9)	84 (19.8)	71 (22.8)	86 (32.6)	69 (14.6)
Pain, aching, stiffness in last month						
No days	31 (8.5)	10 (2.7)	35 (8.2)	6 (1.9)	7 (2.6)	34 (7.2)
Few days	69 (18.9)	45 (12.1)	78 (18.3)	36 (11.6)	22 (8.3)	92 (19.5)
Some days	68 (18.6)	98 (26.3)	87 (20.4)	79 (25.4)	47 (17.7)	119 (25.2)
Most days	102 (27.9)	109 (29.2)	118 (27.6)	93 (29.9)	79 (29.8)	132 (27.9)
All days	95 (26.0)	111 (29.8)	109 (25.5)	97 (31.2)	110 (41.5)	96 (20.3)
Worse pain last week (0-10 NRS); mean (SD)	5.1 (2.9)	5.9 (2.5)	5.1 (2.8)	6.1 (2.5)	6.5 (2.4)	4.9 (2.7)
Least pain last week (0-10 NRS); mean (SD)	3.2 (3.0)	3.6 (2.7)	3.2 (2.9)	3.7 (2.9)	4.6 (2.9)	2.7 (2.6)
Average pain (0-10 NRS); mean (SD)	4.5 (2.6)	5.0 (2.2)	4.5 (2.5)	5.2 (2.2)	5.8 (2.3)	4.2 (2.3)
Pain right now (0-10 NRS); mean (SD)	3.1 (3.1)	3.6 (2.7)	3.1 (2.9)	3.7 (2.9)	4.6 (3.1)	2.6 (2.6)
Bothersomeness of knee pain in the last 24 hours						
Not at all	85 (23.2)	43 (11.6)	96 (22.5)	32 (10.3)	22 (8.3)	106 (22.4)
Mildly	83 (22.7)	92 (24.8)	101 (23.7)	74 (23.8)	39 (14.8)	136 (28.8)
Moderately	97 (26.5)	117 (31.5)	119 (27.9)	95 (30.5)	74 (28.0)	140 (29.6)
Severely	75 (20.5)	89 (24.0)	81 (19.0)	83 (26.7)	89 (33.7)	75 (15.9)
Totally	26 (7.1)	30 (8.1)	29 (6.8)	27 (8.7)	40 (15.2)	16 (3.4)
KOOS Physical Function (0-100); mean (SD)†	37.2 (19.9)	41.3 (16.3)	37.1 (19.3)	42.3 (16.3)	46.7 (19.6)	35.3 (16.2)
KOOS Quality of Life (0-100); mean (SD)‡	47.2 (24.9)	40.3 (22.0)	47.2 (24.5)	39.0 (21.8)	35.7 (23.5)	48.3 (22.7)

Table S15. Continued...

Characteristic	Primary analysis: ineligible n=368	Primary analysis: eligible n=376	Secondary analysis 1: ineligible n=430	Secondary analysis 1: eligible n=314	Secondary analysis 2: ineligible n=268	Secondary analysis 2: eligible n=476
Flare at present	125 (34.4)	129 (34.6)	134 (31.5)	120 (38.6)	151 (56.8)	103 (21.9)
Varus-valgus malalignment						
Very bow legged	3 (0.8)	4 (1.1)	4 (1.0)	3 (1.0)	4 (1.5)	3 (0.6)
Bow legged	39 (10.9)	38 (10.3)	52 (12.4)	25 (8.1)	27 (10.3)	50 (10.7)
Normal	286 (79.7)	272 (73.5)	331 (78.6)	227 (73.7)	201 (77.0)	357 (76.3)
Knock-knee	30 (8.4)	51 (13.8)	30 (7.1)	51 (16.6)	27 (10.3)	54 (11.5)
Very knock-knee	1 (0.3)	5 (1.4)	4 (1.0)	2 (0.6)	2 (0.8)	4 (0.9)
Foot rotation						
Very turned out	5 (1.4)	9 (2.4)	6 (1.4)	8 (2.6)	6 (2.3)	8 (1.7)
Turned out	98 (27.1)	92 (24.7)	114 (27.0)	76 (24.4)	73 (28.0)	117 (24.8)
Straight	231 (64.0)	236 (63.4)	272 (64.5)	195 (62.7)	151 (57.9)	316 (66.9)
Turned in	23 (6.4)	35 (9.4)	27 (6.4)	31 (10.0)	28 (10.7)	30 (6.4)
Very turned in	4 (1.1)	0 (0.0)	3 (0.7)	1 (0.3)	3 (1.1)	1 (0.2)
Previous knee injury	195 (53.4)	204 (54.4)	224 (52.5)	175 (55.9)	148 (55.4)	251 (53.1)

Figures are numbers (%) unless otherwise stated.

SD, Standard Deviation; BMI, Body Mass Index; NRS, Numerical Rating Scale; KOOS, knee injury and Osteoarthritis Outcome Score.

*The index knee was selected based on the knee with highest ‘average pain’ score on a 0-10 numerical rating scale. If scores were equal, then the knee with the highest ‘worst pain in the last week’ followed by the highest ‘current pain’, followed by random selection were selected. If left, or right knee score was missing, the available knee score was included.

†Higher scores indicate worse physical function.

‡Lower scores indicate worse quality of life.