Appendix 2: Supplementary tables [posted as supplied by author]

Table A Characteristics of 2,907 Multicenter Osteoarthritis Study (MOST) participants aged 50 to 79 y. Figures are medians (interquartile range) for continuous variable and numbers (percentage) for categorical variables

Variables[*]	High-risk cohort (N=1,942)	Knee osteoarthritis cohort (N=965)	P value
Median (IQR) age (years)	62 (55-68)	63 (56-70)	<0.001
Age group (years):			
<55	483 (25)	187 (19)	
55-64	722 (37)	343 (36)	<0.001
>64	737 (38)	435 (45)	
Men	813 (42)	348 (36)	0.003
Ethnicity:			
White or Caucasian	1662 (86)	765 (79)	
Black or African-American	251 (13)	190 (20)	<0.001
Other, missing	29 (1)	10 (1)	
Education level:			
Less than high school graduate	61 (3)	63 (7)	
High school graduate	440 (23)	277 (29)	
Some college	514 (26)	261 (27)	
College graduate	398 (20)	166 (17)	<0.001
Some graduate school	161 (8)	69 (7)	
Graduate degree	368 (19)	129 (13)	
Missing	0 (0)	0 (0)	
BMI	29.1 (26.1-32.4)	31.7 (27.9-36.5)	<0.001
Missing	0 (0)	1 (0)	
Modified Charlson comorbidity index:			
0	1396 (72)	597 (62)	
1	320 (16)	216 (22)	
2	151 (8)	94 (10)	<0.001
3	48 (2)	33 (3)	
4 or higher	27 (1)	25 (3)	
Missing	0 (0)	0 (0)	
Kellgren-Lawrence grade:			
0	951 (49)	0 (0)	
1	448 (23)	0 (0)	
2	283 (15)	253 (26)	<0.001
3	179 (9)	431 (45)	
4	64 (3)	275 (28)	
Missing	17 (1)	6 (1)	
Prior knee injury at baseline:			
Yes	1252 (64)	570 (59)	0.008
No	684 (35)	388 (40)	
Missing	6 (0)	7 (1)	
Prior knee surgery at baseline:			
Yes	1647 (85)	661 (68)	<0.001
No	290 (15)	301 (31)	
Missing	5 (0)	3 (0)	
Use of pain medication for osteoarthritis:			

Yes	1071 (55)	706 (73)	<0.001
No	871 (45)	259 (27)	
Missing	0 (0)	0 (0)	
SF-12* score			
Physical component summary (PCS)	51.4 (41.0-56.3)	39.4 (32.0-48.8)	<0.001
Mental component summary (MCS)	56.5 (51.2-59.3)	56.7 (48.8-60.5)	0.10
Missing	164 (8)	97 (10)	
SF-6D* utility index	0.86 (0.74-0.92)	0.80 (0.66-0.86)	<0.001
Missing	0 (0)	2 (0)	
WOMAC total score	10.3 (3.0-23.8)	34.4 (23.9-47.0)	<0.001
Missing	8 (0)	14 (1)	

BMI=body mass index; WOMAC=Western Ontario and McMaster Universities arthritis index.
*Range of scales: SF-6D, 0-1 scale (higher scores indicate better health); SF-12, 0-100 scale (higher scores indicate less severe symptoms); WOMAC, 0-100 scale (higher scores indicate more severe symptoms).

Table B Hazard ratios for total knee replacement (TKR) in Osteoarthritis Initiative (OAI, N=4,498) and Multicenter Osteoarthritis Study (MOST, N=2,907)

Predictors	Hazard ratio (95% CI)		P for Δ OAI *v* MOST
	OAI	MOST	
Male	0.68 (0.57 to 0.88)	0.63 (0.44 to 0.90)	0.66
Black or African-American	0.45 (0.32 to 0.63)	0.44 (0.24 to 0.66)	0.92
Knee osteoarthritis at baseline	1.62 (1.31 to 2.19)	1.69 (1.04 to 3.00)	0.88
Prior knee injury at baseline	0.73 (0.61 to 0.96)	0.79 (0.53 to 1.07)	0.69
Prior knee surgery at baseline	1.45 (1.14 to 1.84)	1.17 (0.82 to 1.62)	0.26
Ln(WOMAC pain score + 1)	1.76 (1.36 to 1.83)	2.16 (1.61 to 3.26)	0.25
Kellgren-Lawrence grade	2.57 (2.17 to 2.79)	2.87 (2.31 to 3.68)	0.32

Table C Missing data in outcomes of 1,327 Osteoarthritis Initiative (OAI) participants with knee osteoarthritis

Visit	SF-12	WOMAC	KOOS quality of life	Osteoarthritis pain medication
Baseline	21 (2%)	1 (0%)	0 (0%)	1 (0%)
Month 12	147 (11%)	79 (6%)	79 (6%)	79 (6%)
Month 24	210 (16%)	143 (11%)	143 (11%)	146 (11%)
Month 36	238 (18%)	171 (13%)	172 (13%)	170 (13%)
Month 48	227 (17%)	171 (13%)	169 (13%)	168 (13%)
Month 60	-	251 (19%)	250 (19%)	252 (19%)
Month 72	328 (25%)	291 (22%)	291 (22%)	292 (22%)
Month 84	-	296 (22%)	294 (22%)	293 (22%)
Month 96	377 (28%)	268 (20%)	266 (20%)	343 (26%)

Data on number with missing values (%) is given for 1,327 OAI participants with knee osteoarthritis at baseline, who were repeatedly followed up until 96 months. Deaths were counted as missing, since these were taking into account in the decision model through joint modelling of longitudinal outcomes such as SF-12 scores and use of pain medication and mortality.

Table D Changes in number of missed work days following total knee replacement (TKR) in three models*. Figures are effect estimates with 95% uncertainty intervals based on refitting all modeling steps in 500 bootstrap datasets given for 819 employed Osteoarthritis Initiative (OAI) participants with knee osteoarthritis at baseline who were repeatedly followed up until 96 months

Outcome	Model 1: unadjusted	Model 2: adjusted for baseline covariables	Model 3: adjusted for baseline and time-varying covariables
Odds ratio for having non-zero missed work days in last 3 months			
All measurements	1.90 (1.11 to 2.58)	1.92 (1.05 to 2.79)	2.29 (1.10 to 3.92)
Treating first measurement after TKR as missing	1.43 (0.67 to 2.13)	1.37 (0.62 to 2.01)	1.41 (0.57 to 2.42)
Δ in number of missed work days in last 3 months			
All measurements	2.09 (0.65 to 3.61)	2.38 (0.77 to 4.77)	2.92 (0.75 to 7.25)
Treating first measurement after TKR as missing	0.68 (-0.35 to 1.97)	0.49 (-0.41 to 1.72)	0.46 (-0.45 to 1.96)

Model 1 (unadjusted model) consisted of GEEs including only TKR, visit, and baseline number of missed work days as covariables. Model 2 (multivariable adjustment): GEEs extended with SF-12 MCS, SF-12 PCS, age, male, African-American ethnicity, income, education, history of knee injury, history of knee surgery, body-mass index, Charlson comorbidity index, use of osteoarthritis pain medication, self-reported diagnosis of knee osteoarthritis, Kellgren-Lawrence grade, WOMAC total, KOOS quality of life, and number of hours worked per week, all measured at baseline. Model 3: Multivariable adjusted GEEs were weighted for time-varying propensities of undergoing TKR. Changes (Δ) in number of missed work days in last 3 months were calculated by the recycle prediction method.

Table E Lifetime cost effectiveness outcomes for different scenarios for determining which patients are eligible for undergoing total knee replacement (TKR) with 95% uncertainty intervals based on 500 bootstrap datasets for simulations of 965 Multicenter Osteoarthritis Study (MOST) participants with knee osteoarthritis

TKR scenarios ranked according to increasing costs	Lifetime TKR likelihood (%)	Costs ($)	QALYs	Incremental costs[*]	Incremental QALYs[*]	ICER ($/QALY)[*]	% most cost effective by $100K/QALY threshold	% most cost effective by $200K/QALY threshold
No TKR	0.0	8361 (7446 to 9510)	10.771 (10.143 to 11.536)	-	-	-	46.6	15.4
TKR if SF-12 PCS <20	1.8 (1.0 to 2.8)	8,721 (7768 to 9866)	10.775 (10.145 to 11.540)	360 (201 to 552)	0.004 (0.000 to 0.008)	101 364	8.6	3.0
TKR if SF-12 PCS <25	6.6 (4.9 to 8.7)	9862 (8799 to 11161)	10.785 (10.150 to 11.555)	1141 (831 to 1525)	0.010 (-0.001 to 0.023)	109 024	12.2	5.2
TKR if SF-12 PCS <30	14.6 (12.0 to 17.5)	11 774 (10 446 to 13 330)	10.801 (10.168 to 11.574)	1913 (1468 to 2385)	0.015 (-0.001 to 0.034)	123 827	11.0	7.6
TKR if SF-12 PCS <35	24.9 (21.4 to 28.6)	14 332 (12 742 to 16 083)	10.818 (10.189 to 11.589)	2557 (2064 to 3174)	0.018 (-0.002 to 0.037)	144 974	15.2	18.8
TKR if SF-12 PCS <40	34.9 (30.7 to 39.3)	16 835 (15 103 to 18 747)	10.831 (10.192 to 11.606)	2503 (2003 to 3077)	0.012 (-0.004 to 0.028)	206 091	5.0	23.8
TKR if SF-12 PCS <45	43.2 (38.4 to 48.0)	18 840 (16 900 to 21 009)	10.837 (10.194 to 11.614)	2005 (1566 to 2456)	0.006 (-0.008 to 0.019)	335 638	0.6	10.8
TKR if SF-12 PCS <50	51.8 (46.5 to 57.2)	20 932 (18 887 to 23 361)	10.839 (10.189 to 11.617)	2092 (1646 to 2614)	0.002 (-0.016 to 0.019)	1 037 105	0.6	6.4
TKR if SF-12 PCS <55	58.7 (53.0 to 64.5)	22 680 (20 408 to 25 361)	10.837 (10.187 to 11.619)	1747 (1319 to 2232)	-0.002 (-0.018 to 0.015)	Absolute dominance	0.0	1.6
Current TKR practice	61.5 (55.7 to 67.3)	23 441 (21 138 to 26 131)	10.834 (10.186 to 11.618)	2509 (1963 to 3100)	-0.005 (-0.033 to 0.022)	Absolute dominance	0.2	7.4

ICER=incremental cost effectiveness ratio; PCS=physical component summary.

*Calculated by comparison with the preceding undominated scenario.

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Table F Lifetime cost effectiveness outcomes for different scenarios for determining which patients are eligible for undergoing total knee replacement (TKR) with 95% uncertainty intervals based on 500 bootstrap datasets for simulations of 1327 participants from the Osteoarthritis Initiative (OAI) with knee osteoarthritis at baseline using EQ-5D scores used as utility values

TKR scenarios ranked according to increasing costs	Costs ($)	QALYs	Incremental costs[*]	Incremental QALYs[*]	ICER ($/QALY)[*]	% most cost effective by $100K/QALY threshold	% most cost effective by $200K/QALY threshold
No TKR	7939 (7162 to 8793)	12.718 (12.129 to 13.322)	-	-	-	36.4	9.2
TKR if SF-12 PCS <20	8181 (7390 to 9041)	12.721 (12.136 to 13.327)	242 (114 to 399)	0.003 (0.000 to 0.007)	83 107	11.6	1.6
TKR if SF-12 PCS <25	8489 (7633 to 9431)	12.724 (12.139 to 13.330)	307 (175 to 486)	0.003 (0.000 to 0.007)	97 313	14.2	4.4
TKR if SF-12 PCS <30	9159 (8298 to 10 118)	12.730 (12.146 to 13.339)	671 (424 to 943)	0.006 (0.001 to 0.013)	111 552	17.4	8.6
TKR if SF-12 PCS <35	10 194 (9164 to 11 287)	12.738 (12.155 to 13.347)	1035 (732 to 1396)	0.008 (0.001 to 0.016)	135 336	13.6	10.8
TKR if SF-12 PCS <40	11 649 (10 386 to 12 795)	12.747 (12.165 to 13.359)	1455 (1055 to 1895)	0.009 (0.001 to 0.018)	168 172	4.4	29.4
TKR if SF-12 PCS <45	13 193 (11 734 to 14 684)	12.753 (12.172 to 13.366)	1544 (1161 to 2007)	0.006 (-0.002 to 0.014)	241 614	1.6	16.6
TKR if SF-12 PCS <50	15 022 (13 384 to 16 590)	12.758 (12.176 to 13.368)	1829 (1349 to 2305)	0.005 (-0.006 to 0.014)	387 768	0.6	10.0
TKR if SF-12 PCS <55	16 483 (14 782 to 18 361)	12.759 (12.174 to 13.363)	1461 (1046 to 1960)	0.001 (-0.009 to 0.011)	1 370 901	0.0	2.0
Current TKR practice	17 168 (15 307 to 19 124)	12.758 (12.170 to 13.352)	685 (402 to 985)	-0.001 (-0.009 to 0.005)	Absolute dominance	0.2	7.4

ICER=incremental cost effectiveness ratio; PCS=physical component summary.

*Calculated by comparison with the preceding undominated scenario.

Table G Lifetime cost effectiveness outcomes for different scenarios for determining which patients are eligible for undergoing total knee replacement (TKR) with 95% uncertainty intervals based on 500 bootstrap datasets for simulations of 1327 participants from the Osteoarthritis Initiative (OAI) with knee osteoarthritis at baseline increasing TKR rates by 30%

TKR scenarios ranked according to increasing costs	Lifetime TKR likelihood (%)	Costs ($)	QALYs	Incremental costs[*]	Incremental QALYs[*]	ICER ($/QALY)[*]	% most cost effective by $100K/QALY threshold	% most cost effective by $200K/QALY threshold
No TKR	0.0	7954 (7183 to 8857)	11.151 (10.636 to 11.685)	-	-	-	40.4	13.2
TKR if SF-12 PCS <20	1.3 (0.7 to 2.1)	8232 (7433 to 9144)	11.154 (10.642 to 11.689)	278 (127 to 463)	0.003 (0.000 to 0.008)	86 375	15.4	5.2
TKR if SF-12 PCS <25	2.9 (2.0 to 4.1)	8576 (7743 to 9534)	11.157 (10.649 to 11.692)	343 (188 to 514)	0.003 (0.000 to 0.007)	108 652	12.6	4.2
TKR if SF-12 PCS <30	6.3 (4.6 to 8.0)	9331 (8440 to 10 339)	11.163 (10.657 to 11.697)	755 (508 to 1047)	0.006 (0.000 to 0.014)	123 037	16.8	13.0
TKR if SF-12 PCS <35	11.4 (9.3 to 13.6)	10 522 (9510 to 11 648)	11.171 (10.666 to 11.708)	1191 (852 to 1573)	0.007 (-0.001 to 0.017)	158 889	9.8	18.0
TKR if SF-12 PCS <40	18.5 (15.5 to 21.7)	12 206 (11 113 to 13 562)	11.179 (10.666 to 11.716)	1684 (1296 to 2199)	0.008 (-0.003 to 0.019)	216 190	3.4	23.2
TKR if SF-12 PCS <45	26.3 (22.6 to 30.2)	13 980 (12 579 to 15 503)	11.183 (10.669 to 11.719)	1774 (1338 to 2289)	0.005 (-0.007 to 0.016)	373 214	0.8	10.2
TKR if SF-12 PCS <50	35.5 (30.6 to 40.0)	16 147 (14 541 to 18 086)	11.186 (10.675 to 11.717)	2167 (1653 to 2763)	0.002 (-0.014 to 0.019)	1 041 142	0.8	4.2
TKR if SF-12 PCS <55	42.5 (37.3 to 47.6)	17 878 (16 110 to 19 849)	11.184 (10.674 to 11.718)	1732 (1292 to 2243)	-0.002 (-0.018 to 0.013)	Absolute dominance	0.0	1.8
Current TKR practice	45.7 (40.2 to 51.2)	18 733 (16 898 to 20 906)	11.181 (10.670 to 11.719)	2586 (2012 to 3330)	-0.005 (-0.032 to 0.021)	Absolute dominance	0.0	7.0

ICER=incremental cost effectiveness ratio; PCS=physical component summary.

*Calculated by comparison with the preceding undominated scenario.

Table H Lifetime cost effectiveness outcomes for different scenarios for determining which patients are eligible for undergoing total knee replacement (TKR) with 95% uncertainty intervals based on 500 bootstrap datasets for simulations of 1327 participants from the Osteoarthritis Initiative (OAI) with knee osteoarthritis at baseline applying a standardised mortality ratio (SMR) of 1.55 (95%CI 1.41-1.70)

TKR scenarios ranked according to increasing costs	Lifetime TKR likelihood (%)	Costs ($)	QALYs	Incremental costs[*]	Incremental QALYs[*]	ICER ($/QALY)[*]	% most cost effective by $100K/QALY threshold	% most cost effective by $200K/QALY threshold
No TKR	0.0	7213 (6502 to 8048)	10.141 (9.601 to 10.716)	-	-	-	47.8	15.8
TKR if SF-12 PCS <20	1.0 (0.5 to 1.7)	7431 (6662 to 8291)	10.143 (9.603 to 10.717)	218 (96 to 388)	0.002 (0.000 to 0.005)	98 447	16.6	5.8
TKR if SF-12 PCS <25	2.2 (1.4 to 3.2)	7693 (6907 to 8613)	10.145 (9.606 to 10.719)	262 (132 to 421)	0.002 (0.000 to 0.006)	119 560	13.8	4.4
TKR if SF-12 PCS <30	4.8 (3.5 to 6.3)	8291 (7446 to 9233)	10.149 (9.612 to 10.721)	598 (385 to 882)	0.004 (0.000 to 0.010)	137 608	12.4	13.8
TKR if SF-12 PCS <35	8.8 (7.1 to 10.9)	9222 (8286 to 10 260)	10.155 (9.620 to 10.724)	931 (627 to 1275)	0.005 (-0.001 to 0.012)	179 684	7.6	20.8
TKR if SF-12 PCS <40	14.5 (11.9 to 17.1)	10 553 (9487 to 11 770)	10.160 (9.625 to 10.732)	1330 (950 to 1780)	0.006 (-0.002 to 0.013)	239 043	1.2	23.0
TKR if SF-12 PCS <45	20.6 (17.4 to 23.9)	11 952 (10 625 to 13 359)	10.163 (9.630 to 10.735)	1400 (1051 to 1816)	0.003 (-0.005 to 0.012)	415 889	0.4	7.2
TKR if SF-12 PCS <50	27.8 (23.9 to 32.0)	13 654 (12 208 to 15 366)	10.165 (9.635 to 10.733)	1702 (1270 to 2181)	0.001 (-0.010 to 0.013)	1 157 318	0.2	2.6
TKR if SF-12 PCS <55	33.3 (29.1 to 38.0)	14 999 (13 376 to 17 003)	10.164 (9.637 to 10.724)	1345 (975 to 1817)	-0.001 (-0.013 to 0.010)	Absolute dominance	0.0	0.8
Current TKR practice	35.8 (31.3 to 40.5)	15 660 (13 994 to 17 687)	10.161 (9.637 to 10.723)	2007 (1494 to 2595)	-0.004 (-0.022 to 0.015)	Absolute dominance	0.0	5.8

ICER=incremental cost effectiveness ratio; PCS=physical component summary.

*Calculated by comparison with the preceding undominated scenario.

Table I Lifetime cost effectiveness outcomes for different scenarios for determining which patients are eligible for undergoing total knee replacement (TKR) with 95% uncertainty intervals based on 500 bootstrap datasets for simulations of 1327 participants from the Osteoarthritis Initiative (OAI) with knee osteoarthritis at baseline including costs of lost workdays and informal caregiving

TKR scenarios ranked according to increasing costs	Costs ($)	QALYs	Incremental costs[*]	Incremental QALYs[*]	ICER ($/QALY)[*]	% most cost effective by $100K/QALY threshold	% most cost effective by $200K/QALY threshold
No TKR	7939 (7162 to 8793)	11,155 (10.634 to 11.686)	-	-	-	44.8	13.8
TKR if SF-12 PCS <20	8196 (7400 to 9070)	11,157 (10.636 to 11.692)	257 (117 to 430)	0.003 (0.000 to 0.007)	94 389	17.2	5.4
TKR if SF-12 PCS <25	8527 (7676 to 9490)	11,160 (10.639 to 11.698)	330 (183 to 538)	0.003 (0.000 to 0.007)	116 929	15.8	6.8
TKR if SF-12 PCS <30	9275 (8362 to 10 318)	11,166 (10.643 to 11.705)	748 (450 to 1098)	0.005 (0.000 to 0.012)	141 439	12.2	13.8
TKR if SF-12 PCS <35	10 412 (9263 to 11 660)	11,172 (10.654 to 11.709)	1137 (784 to 1544)	0.006 (0.000 to 0.014)	176 852	7.0	23.8
TKR if SF-12 PCS <40	12 052 (10 634 to 13 469)	11,179 (10.667 to 11.714)	1640 (1164 to 2187)	0.007 (-0.002 to 0.017)	245 281	2.0	18.0
TKR if SF-12 PCS <45	13 786 (12 126 to 15 508)	11,183 (10.672 to 11.718)	1734 (1281 to 2316)	0.004 (-0.006 to 0.014)	417 230	0.8	8.4
TKR if SF-12 PCS <50	15 877 (13 968 to 17 819)	11,184 (10.668 to 11.720)	2091 (1538 to 2730)	0.002 (-0.012 to 0.015)	1 268 824	0.2	3.2
TKR if SF-12 PCS <55	17 583 (15 393 to 19 977)	11,183 (10.665 to 11.710)	1706 (1207 to 2323)	-0.002 (-0.016 to 0.011)	Absolute dominance	0.0	1.2
Current TKR practice	18 406 (16 118 to 20 886)	11,180 (10.662 to 11.700)	2529 (1815 to 3408)	-0.004 (-0.027 to 0.017)	Absolute dominance	0.0	5.6

ICER=incremental cost effectiveness ratio; PCS=physical component summary.

*Calculated by comparison with the preceding undominated scenario.

Table J Incremental cost-effectiveness ratios based on N bootstrap datasets are given for simulations of 1,327 OAI participants with knee osteoarthritis at baseline

TKR scenarios ranked according to increasing costs	N=100	N=200	N=300	N=400	N=500
No TKR	-	-	-	-	-
TKR if SF-12 PCS <20	98 264	93 421	93 444	90 075	88 903
TKR if SF-12 PCS <25	116 026	113 718	114 579	111 004	108 773
TKR if SF-12 PCS <30	143 569	132 380	133 889	129 908	126 762
TKR if SF-12 PCS <35	174 551	167 473	170 324	163 908	160 974
TKR if SF-12 PCS <40	229 845	216 307	230 363	222 709	217 615
TKR if SF-12 PCS <45	373 802	359 416	394 892	381 429	371 439
TKR if SF-12 PCS <50	832 502	875 940	1 167 708	1 119 125	1 109 675
TKR if SF-12 PCS <55	Absolute dominance	Absolute dominance	Absolute dominance	Absolute dominance	Absolute dominance
Current TKR practice	Absolute dominance	Absolute dominance	Absolute dominance	Absolute dominance	Absolute dominance

PCS=physical component summary.