

TABLE E-1 Population Characteristics of the Michigan Site Study of Women's Health Across the Nation (SWAN) Cohort and Participation Information for Follow-up Visit 11 When Knees Were Evaluated with Magnetic Resonance Imaging

	Overall	African-American	Caucasian
No. (%) of participants at baseline (1996-1997)	543	325 (60)	218 (40)
No. deceased at follow-up visit 11	18	11	7
No. (%) available for site-specific follow-up visit 11	442 (81)	266 (82)	176 (81)
No. (%) of available participants who completed the site-specific follow-up visit-11 protocol	419 (95)	253 (95)	166 (94)
No. (%) who completed follow-up visit-11 protocol including knee MRI	363 (82)	226 (85)	137 (78)
No. (%) who completed follow-up visit-11 protocol but not knee MRI	29 (6)	15 (5)	14 (8)
No. (%) who completed brief interview protocol	27 (6)	12 (5)	15 (9)

TABLE E-2 Right Knee Pain (in the Last Month at the Time of Follow-up Visit 11) or Any Knee Injury (in the Last Year at the Time of Follow-up Visit 11) Associated with the Three-Level Kellgren-Lawrence Score and Magnetic Resonance Imaging Features*

	Right Knee Pain in Last Month	Knee Injury in Last Year
	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Kellgren-Lawrence score		
0, 1	Reference category	Reference category
2	1.64 (0.94, 2.86)	3.66 (0.70, 19.21)
3, 4	11.27 (6.23, 20.41) [†]	5.86 (1.16, 29.65) [‡]
Cartilage		
Medial femoral condyle		
No cartilage defect	Reference category	Reference category
Cartilage defect ≤99%	1.55 (0.82, 2.93)	2.06 (0.25, 16.99)
Cartilage defect 100%	6.31 (2.80, 14.26) [†]	2.94 (0.26, 33.31)
Medial tibial plateau		
No cartilage defect	Reference category	Reference category
Cartilage defect ≤99%	1.76 (1.06, 2.94) [‡]	2.51 (0.52, 11.99)
Cartilage defect 100%	9.19 (3.68, 22.97) [†]	–
Lateral femoral condyle		
No cartilage defect	Reference category	Reference category
Cartilage defect ≤99%	1.20 (0.73, 1.96)	1.62 (0.32, 8.17)
Cartilage defect 100%	19.77 (4.29, 91.20) [†]	7.87 (1.03, 60.03) [‡]
Lateral tibial plateau		
No cartilage defect	Reference category	Reference category
Cartilage defect ≤99%	1.67 (1.05, 2.65) [‡]	3.65 (0.70, 19.08)
Cartilage defect 100%	13.46 (3.72, 48.71) [†]	21.43 (3.30, 138.96) [†]
Medial patella		
No cartilage defect	Reference category	Reference category
Cartilage defect ≤99%	1.21 (0.64, 2.28)	1.75 (0.21, 14.51)
Cartilage defect 100%	2.15 (1.01, 4.59) [‡]	1.90 (0.17, 21.54)
Lateral patella		
No cartilage defect	Reference category	Reference category
Cartilage defect ≤99%	2.36 (1.44, 3.89) [†]	1.36 (0.32, 5.78)
Cartilage defect 100%	2.82 (1.33, 5.95) [†]	2.54 (0.41, 15.77)
Osteophyte		
Medial compartment		
No osteophytes	Reference category	Reference category
Osteophyte ≤5 mm	2.54 (1.48, 4.35) [†]	5.55 (0.64, 48.06)
Osteophyte >5 mm	7.65 (4.00, 14.63) [†]	9.81 (1.07, 89.47) [‡]
Lateral compartment		
No osteophytes	Reference category	Reference category
Osteophyte ≤5 mm	2.43 (1.42, 4.16) [†]	1.40 (0.23, 8.51)
Osteophyte >5 mm	6.58 (3.42, 12.67) [†]	5.98 (1.13, 31.67) [‡]

Meniscal abnormalities		
Medial compartment		
Normal, no tear	Reference category	Reference category
Intrasubstance meniscal abnormality	1.69 (0.82, 3.47)	2.10 (0.25, 17.38)
Nondisplaced or displaced meniscal tear	4.75 (2.20, 10.23)†	1.27 (0.11, 14.30)
Lateral compartment		
Normal, no tear	Reference category	Reference category
Intrasubstance meniscal abnormality	1.85 (1.05, 3.25)‡	1.20 (0.22, 6.68)
Nondisplaced or displaced meniscal tear	4.45 (2.28, 8.67)†	3.34 (0.60, 18.77)
Bone marrow edema§		
Medial femoral condyle		
Normal, no BME	Reference category	Reference category
Small BME (<1 cm)	5.61 (2.64, 11.94)†	1.01 (0.12, 8.21)
Large or very large BME (≥1 cm)	4.29 (1.00, 18.32)‡	–
Medial tibial plateau		
Normal, no BME	Reference category	Reference category
Small BME (<1 cm)	2.23 (1.20, 4.14)‡	1.61 (0.33, 7.84)
Large or very large BME (≥1 cm)	7.28 (1.44, 36.76)‡	–
Lateral femoral condyle		
Normal, no BME	Reference category	Reference category
Small BME (<1 cm)	3.43 (1.36, 8.64)†	1.91 (0.23, 15.84)
Large or very large BME (≥1 cm)	4.57 (0.82, 25.34)	–
Lateral tibial plateau		
Normal, no BME	Reference category	Reference category
Small BME (<1 cm)	3.04 (1.56, 5.94)†	4.16 (1.00, 17.34)
Large or very large BME (≥1 cm)	14.93 (1.77, 125.8)‡	8.56 (0.89, 82.48)
Medial patella		
Normal, no BME	Reference category	Reference category
Small BME (<1 cm)	1.18 (0.73, 1.91)	0.28 (0.03, 2.20)
Large or very large BME (≥1 cm)	–	–
Lateral patella		
Normal, no BME	Reference category	Reference category
Small BME (<1 cm)	1.75 (1.06, 2.90)‡	0.79 (0.16, 3.80)
Large or very large BME (≥1 cm)	1.59 (0.26, 9.71)	–
Baker cyst		
Normal, no Baker cyst	Reference category	Reference category
Small Baker cyst	1.39 (0.86, 2.26)	8.68 (1.77, 42.52)†
Large Baker cyst	1.14 (0.41, 3.17)	7.00 (0.60, 81.15)
Effusion		
Normal, physiological fluid	Reference category	Reference category
Small effusion (≤10 mm)	1.32 (0.79, 2.21)	–
Moderate or large effusion (>10 mm)	6.44 (2.72, 15.25)†	–
Synovitis		
Normal, no synovitis	Reference category	Reference category

Mild synovitis	3.19 (1.81, 5.61)†	2.23 (0.54, 9.15)
Moderate to marked synovitis	4.35 (1.87, 10.13)†	1.85 (0.21, 16.04)

*Anterior cruciate ligament, medial collateral ligament, lateral collateral ligament, and subchondral cysts are not included in table because they were not significantly associated with knee pain or knee injury. All models are unadjusted. †p < 0.01. ‡p < 0.05. §BME = bone marrow edema.

Michigan SWAN
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KNEE MRI DATA COLLECTION FORM

SWAN ID: _____ **MRN:** _____

DATE OF MRI: ____/____/____ **HOSPITAL:** UM SJMHS

KNEE: RIGHT LEFT **RADIOLOGIST:** _____

DATE OF MRI READ: ____/____/____ **TIME OF MRI READ:** ____ : ____ AM/PM

Site	Cartilage						BME						
	0	1	2	3	4	5	0	0.5	1	1.5	2	2.5	3
Med. Fem. Condyle	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Med. Tib. Plateau	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Lat. Fem. Condyle	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Lat. Tib. Plateau	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Trochlea	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Medial Patella	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Lateral Patella	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Associated findings:

	Osteophyte							Subchondral Cyst			Meniscal Abnormalities			
	0	0.5	1	1.5	2	2.5	3	0	1	2	0	1	2	3
Medial Comp.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Lateral Comp.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
PF Comp.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				

	Meniscal Extrusion			
	0	1	2	Measurement
Medial Comp.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	mm
Lateral Comp.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	mm

General findings:

	0	1	2		0	1	2			0	1	2	3
Effusion	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	ACL	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	MCL	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Bakers cyst	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	PCL	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	LCL	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Synovitis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>										

Comments: _____

<u>Cartilage.</u> Note: Ulceration is defined as a visible irregularity in the normal contour of the subchondral cortex. BME or subchondral sclerosis alone is not considered ulceration.	0	Normal
	1	Internal signal alteration only
	2	Defect <50%
	3	Defect 50%-99%
	4	100% defect, no bone ulceration
<u>BME.</u> Note: Measured perpendicular to adjacent articular surface.	5	100% defect, with bone ulceration
	0	Normal
	1	Small (largest diameter <1 cm)
	2	Large (largest diameter 1.01 – 2.0 cm)
	3	Very large (largest diameter >2.0 cm)
<u>Osteophyte.</u> Note: Osteophytes are defined as any abnormal bone growth arising from the margin of the involved compartment.	0	No osteophyte
	1	Osteophyte <5 mm
	2	Osteophyte >5 mm to ≤10 mm
	3	Osteophyte >10 mm
<u>Subchondral Cyst.</u> Note: Subchondral cysts are defined as discrete, marginated circular or oval areas of hyperintensity on FSE PD FS images in a subchondral location. Cysts have sharp, smoothly circumscribed margins, typically with a hyperintensity similar to synovial fluid.	0	Normal
	1	Small (<1 cm)
	2	Large (>1 cm)
Meniscal Abnormalities	0	Normal
	1	Intrasubstance (Crues Grades 1 and 2) meniscal abnormality only
	2	Non-displaced tear (extending to meniscal surface, Crues Grade 3)
	3	Displaced or macerated tears
Meniscal Extrusion	0	None
	1	<5 mm
	2	>5 mm
<u>Effusion.</u> Note: Effusion is significantly greater than expected physiologic amounts of synovial fluid in the lateral or medial	0	Normal, physiologic fluid
	1	Small (<10 mm)
	2	Moderate/large (>10 mm)

patellar recesses.		
<u>Bakers Cyst.</u> Note: Record meniscal cysts, ganglion cysts, and other non-specific periarticular cysts in the comments section.	0	Normal
	1	Small
	2	Large
<u>Synovitis.</u> Note: Defined as abnormally increased linear striations within the intrapatellar fat pad and irregular thickening at the margin of the fat pad with the articular cartilage. Low signal on short TE images, and intermediate to high signal on FSE PD FS images.	0	Normal
	1	Mild synovitis
	2	Moderate to marked synovitis
ACL, PCL	0	Normal
	1	Significant increased edema within or surrounding the ligament, with normal course and at least some intact fibers present
	2	Complete tear, acute or chronic
MCL, LCL	0	Normal ligament with minimal-to-none adjacent edema
	1	Significant periligamentous edema, ligament intact; high signal surrounding ligament with normal signal within it
	2	High signal surrounding and within the ligament – Partial tear
	3	Complete tear

PF = patellofemoral, ACL = anterior cruciate ligament, PCL = posterior cruciate ligament, MCL = medial collateral ligament, LCL = lateral collateral ligament, BME = bone marrow edema; FSE PD FS = fast spin echo, proton density, with fat saturation; and TE = echo time.

Appendix E-2: Description of magnetic resonance imaging (MRI) sequences protocol and MRI feature reading and scoring procedures for Michigan Study of Women's Health Across the Nation.

Knees were imaged at the time of follow-up visit 11 (which occurred during 2007 to 2008) with use of a 3.0-T MR scanner (Philips, Best, The Netherlands) equipped with a commercial knee surface coil or a 1.5-T MR scanner (General Electric Medical Systems, Milwaukee, Wisconsin). Specific sequences included sagittal, coronal, and axial fast spin echo (FSE) proton density (PD) with fat saturation (FS) sequences (repetition time [TR] 4000 msec, echo time [TE] 15 msec, 4-mm thickness), sagittal spin echo (SE) PD (TR 1000 msec, TE 14 msec, 3 mm thickness), and sagittal three-dimensional spoiled gradient echo (SPGR) with FS (TR 38 msec, TE 6.9 msec, flip angle (FA) 45°, 2-mm effective thickness). The field of view (FOV) was optimized between 12 and 14 cm. As the purpose of the study was to assess multiple knee joint structures, the FSE PD FS sequences were chosen to enable tissue contrast between articular cartilage, bone, and fluid while still maintaining a high signal to noise ratio (S/N) for evaluation of periarticular soft tissues¹⁻⁴. Since FSE PD FS sequences are considered suboptimal for meniscal evaluation, the additional sagittal SE short TE sequence contributed to optimal global joint assessment. The SPGR FS images were included for additional assessment of articular cartilage⁵.

MR images of each knee were interpreted in 2007-2008 by two musculoskeletal radiologists utilizing the score sheet (with definitions) attached in Appendix 1. To ensure reproducibility, there was an initial calibration session to generate comparable scored values (n = 20). A rigorous quality-control program was maintained such that 60% of MR images were double-read with agreement (kappa statistic) in excess of 90%. Scoring discrepancies were resolved by consensus. The radiologists were blinded to radiographic and clinical findings. Eleven alert letters were generated to address potentially important incidental findings.

Cartilage defects: Each knee was evaluated for location, severity, and approximate size of cartilage defects in three compartments (medial femorotibial, lateral femorotibial, and patellofemoral) and seven specific surfaces (medial tibial, medial femoral, lateral tibial, lateral femoral, trochlea, medial patellar facet, and lateral patellar facet). Cartilage defects were scored for depth on the basis of the classification adopted by Drapé et al.⁶ and across multiple compartments with use of the Noyes arthroscopic system, adapted to MR imaging⁷. Cartilage was graded for each surface as Grade 0, indicating normal; Grade 1, internal signal alteration only; Grade 2, a defect of <50%; Grade 3, a defect of 50% to 99%; Grade 4, 100% defect with no bone ulceration; and Grade 5, 100% defect with bone ulceration. For Grade 5, ulceration was defined as a visible irregularity in the normal contour of the subchondral cortex. Bone marrow lesions or subchondral sclerosis alone was not considered ulceration.

Subchondral trabecular bone-marrow signal changes: Bone marrow lesions were defined as focal but noncircumscribed (see cysts, below) areas of abnormal high signal on FSE PD FS images, in a subchondral location. Bone marrow lesions were recorded by site and severity, measured perpendicular to the bone cortex in the following manner, and were graded, with Grade 0 indicating normal; Grade 1, the largest diameter was <1 cm; Grade 2, the largest diameter was 1.01 to 2.0 cm; and Grade 3, the largest diameter was >2.0 cm^{4,8}.

Osteophytes: Osteophytes were abnormal bone growths arising from the margin of the involved compartment. Tibial spine growths were considered as osteophytes in their respective compartments only if there were definite excrescences as opposed to mere “pointing” of the tibial spines. Osteophytes were graded in each compartment, with Grade 0 indicating no osteophyte; Grade 1, an osteophyte of ≤5 mm; Grade 2, an osteophyte of >5 to 10 mm; and Grade 3, an osteophyte of >10 mm⁹.

Subchondral cysts: Cysts were defined as discrete, margined circular or oval areas of hyperintensity on FSE PD FS images in a subchondral location¹⁰. Cysts had sharp, smoothly circumscribed margins, typically with a hyperintensity similar to synovial fluid. Cysts were graded by compartment, with Grade 0 indicating normal; Grade 1, ≤10 mm; and Grade 2, >10 mm.

Joint effusion: Effusions represent substantially greater than expected physiologic amounts of synovial fluid in the lateral or medial patellar recesses exceeding 10 mm in width¹¹. They were graded, with Grade 0 indicating physiologic fluid; Grade 1, a small effusion (≤10 mm); and Grade 2, a moderate and/or large effusion (>10 mm).

Synovitis: Synovitis was defined as abnormally increased linear or irregular striations within the infrapatellar (Hoffa) fat pad or joint recesses and irregular thickening at the margin of the fat pad with the articular cartilage^{12,13}. These changes consisted of low signal on SE short TE images and intermediate-to-high signal on FSE PD FS images. Synovitis was graded, with Grade 0 indicating normal; Grade 1, mild synovitis; and Grade 2, moderate-to-marked synovitis.

Synovial cysts: Cysts were fluid-filled collections arising from the joint, extending in the standard fashion (Baker cyst) between the semimembranosus tendon and the medial head of the gastrocnemius muscle, or in a less typical site, if confirmed to be in continuity with the joint¹¹. Meniscal cysts, ganglion cysts, and other nonspecific periarticular cysts were recorded but not included in the analysis. Cysts were graded on a semiquantitative scale, with Grade 0 indicating normal; Grade 1, small; and Grade 2, large.

Ligamentous abnormalities: Cruciate ligament abnormalities were graded, with Grade 0 indicating normal; Grade 1, increased edema within or surrounding a ligament with normal course and at least some intact fibers present; and Grade 2, a complete tear, acute or chronic. Collateral ligament abnormalities were graded, with Grade 0 indicating a normal ligament with minimal to no adjacent edema; Grade 1, periligamentous edema, with the ligament intact; Grade 2, a partial tear; and Grade 3, a complete tear.

Meniscal abnormalities: Intrameniscal abnormalities as well as frank tears incorporated a modification of the system of Crues et al.¹⁴⁻¹⁶: Grade 0 indicated normal; Grade 1, intrasubstance (Cruces Grades 1 and 2) meniscal abnormality only; Grade 2, nondisplaced tear (extending to meniscal surface, Cruces Grade 3); and Grade 3, displaced or macerated tear. Meniscal extrusion was measured on the coronal MR images from the outer edge of the tibia (not including osteophytes) to the outer edge of the meniscus.

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