MULTICENTER OSTEOARTHRITIS STUDY

LONGITUDINAL KNEE RADIOGRAPH ASSESSMENTS & OUTCOMES

DATASET DESCRIPTION AND READING PROTOCOL

MARCH 2023

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This document contains information about the reading protocols for longitudinal x-ray assessments of features of osteoarthritis from knee x-rays from two periods in MOST:

(a) The baseline through 84-month visits of MOST from the original cohort of 3026 participants
(b) The 144-month and 168-month visits for both original cohort and a newly recruited cohort (total 4551 participants).

The document splits into 5 main parts

1. Description of the variables for knee x-rays readings/outcomes and their naming convention in this dataset along with definitions of Radiographic OA (ROA) of the knee used by MOST and how to utilize the pre-calculated variables of incidence and progression of ROA provided in these datasets
2. Details of the reading protocols and variables for scoring of Kellgren and Lawrence grades and other individual radiographic features (IRFs) of knee osteoarthritis from the baseline to 84-months in the MOSTV01235XRAY dataset
3. Details of the reading protocols and variables for scoring of Kellgren and Lawrence grades and other individual radiographic features (IRFs) of knee osteoarthritis from the 144-month and 168-month visits in the dataset MOSTV79XRAY_OUTCOMES
4. Description of the measurement of limb alignment and hip-knee-ankle angle (HKA) performed from long-limb radiographs.
5. An appendix describing the adjudication procedure for assessing knee OA x-ray outcomes using multiple readers.

1. Variables and definitions of radiographic OA and worsening

1.1 Visit Numbers in MOST

Visits at which x-ray readings were performed are numbers as in the table below

Visit Prefix	Follow-up contact	X-rays acquired
V0	Baseline	Knee x-rays and full limb x-rays
V1	15-months	Knee x-rays (subset of selected ppts)
V2	30-months	Knee x-rays
V3	60-months	Knee x-rays and full limb x-rays
V5	84-months	Knee x-rays
V7	144-months+	Knee x-rays and full limb x-rays*
V9	168-months+	Knee x-rays
+ only new cohort, and eligible original cohort had knee x-rays acquired at V7/V9 * full limb x-rays were only acquired in the original cohort at V0 and V3 and in the new cohort at V7		

1.2 Variable Naming Conventions

For each set of readings, the Variable Guides (VariableGuide_V01235xray.pdf and VariableGuide_V79XRAY_OUTCOMES.pdf) are a complete lists of all variables in each dataset, their SAS variable names, descriptive variable labels, and attributes. If you are unfamiliar with the data, it may be useful to begin by reviewing the matching annotated data collection forms (RadiographAnnotatedForms_V01235xray.pdf and RadiographAnnotatedForms_V79XRAY.pdf) to look for variables of interest.

The datasets contain three types of variables related to readings of bilateral PA view radiographs and Left/Right lateral views:

1. Raw radiograph reading from a specific visit: for example, V0XRKL: Right knee KLG at the baseline visit from PA view; V7XRKLPF: Right knee KLG of PF joint at the 144m visit from Right Lateral view.
2. Calculated TF/PF/WK OA status and change variables between any two time points.
3. Calculated Incidence KLG status and change in JSN between Baseline (enrollment) and 168m (or last available clinic visit with x-ray).

The following calculated variables were included in the radiographic assessment dataset:

- Derived status of a knee or person meeting the criteria for a specific measure: for example, V7XRTFROA: Right knee tibiofemoral radiographic OA at 144m.
- Change score between two visits for a specific measure: for example, V79XRKL_C: Right knee KLG change from 144m to 168m.
- Derived indicator of a knee meeting the criteria for a specific outcome measure: for example JSN progression: V79XRTFJSL_P: Right knee joint space narrowing progression from 144m to 168m.

Variables are prefixed VnXs and VnLXs indicating the visit (Vn), knee x-ray view (VnX for PA view or VnLX for lateral view) and side (VnXR/VnLXR for Right or VnXL/VnLXL for left). For example, in the prefix V7XR, V7 = 144m visit, XR = Right side parameter from PA view.

The following suffixes are used to identify derived indicator variables:

- _C: Change score between two visits (between any pair of visits).
- _P: Joint space narrowing progression status (from baseline to follow-up visits or between any pair of visits).
- k (lower case): Person level indicator of which knee meets the criteria for a specific measure

Variables associated with a specific visit have the root of their name preceded by the visit number, and variables related to a change between two visits are prefixed by the visit combination over which calculated. The suffix of a variable indicates a calculated variable (eg: related to change, progression, incidence, or which view (PA, lateral or both) the variable relates to).

A special prefix V99E is used to indicate an outcome derived from baseline (enrollment in the study) and last known follow up contact point.

The table below illustrates this:

Prefixes	Visit/Side	Suffix
Variables that are visit specific or related to a change between a pair of visits		
VnXR, VnXL	Visit n right/left knee	
VnmXR, VnmXL	Right/left knee change from Vn to VmBL	_C
VnmXR, XnmXL	Right/left knee progression determined by change from Vn to Vm	_P
VnX	Which knee at Vn	k (lower case)
Baseline to 84-month (V0-V5) outcomes		
V99ER, V99EL	Right/left knee Incident KLG=2 and KLG=2N from V0	
V99ER, V99EL	Right/left knee Change in JSN from V0, PA view	
V99ER, V99EL	Right/left knee Change in JSN from V0, Lateral view	_Lat
V99ER, V99EL	Right left knee Change in JSN from V0, PA or Lateral view	_any
Baseline to 168-month (V0-V9) outcomes		
V99E_R, V99E_L	Right/left knee Incident KLG=2 and KLG=2N from V0	
V99E_R, V99E_L	Right/left knee Change in JSN from V0, PA view	
V99E_R, V99E_L	Right/left knee Change in JSN from V0, Lateral view	_Lat
V99E_R, V99E_L	Right left knee Change in JSN from V0, PA or Lateral view	_any

1.3 Variables assessed from Bilateral PA View Knee Radiographs:

- Tibio-Femoral KLG (see Kellgren and Lawrence[1]) scored in whole grades, 0 to 4. Scores correspond to tibiofemoral osteoarthritis (TFOA) status, as follows:

TF KLG Score	Tibio-Femoral OA Status
KLG = 0 KLG = 1	No TFOA
KLG=1.9*	Definite TFOA but with OARSI JSN score of 0 (see pages 11-13 for more information)
KLG = 2	Definite TFOA with OARSI JSN score > 0
KLG=3	Severe TFOA (usually with OARSI JSN > 1)
KLG = 4	End stage TFOA (usually OARSI JSN score =3)

* Non-standard; see below.

Special missing values were used to code a knee replacement, poor quality x-ray meaning no reading was possible or that one of both of the PA and lateral views was not acquired, or that a knee was excluded from analysis for reasons such as rheumatoid arthritis, osteonecrosis, missing patella, for example.

The non-standard value of 1.9 (described as KLG=2N), represents a knee that has developed a definite osteophyte, but has no JSN assessed on the PA view (TF JSN from the lateral view was not taken into account). For the original cohort this was only allowed at follow-up visits (and not at baseline V0). For the new cohort recruited at V7 this value was allowed at 144m V7 as well as at their follow-up at 168m (V9).

Change variables were defined differently in the two datasets, related definite ROA with no JSN - KLG=1.9 (2N):

In the V0-V5 readings, the change from KLG=1 to KLG=1.9 (2N) is represented in change variables as a “within-grade” change, and represents a weaker definition of incident radiographic OA than transition from KLG<=1 to KLG>=2.

In the V7-V9 readings, the change from KLG=1 to KLG=1.9 (2N) is represented in change variables as a “full grade” change, and represents a less strict definition of incident radiographic OA than transition from KLG<=1 to KLG>=2.

Progression of ROA was also defined slightly differently in the two datasets:

In the V0-V5 readings, knees with KL=1.9 (ROA=No) were not counted as eligible for progression.

In the V7-V9 readings, the transition from KL=1 (ROA=No) to KL=1.9 (ROA=Yes) is now marked as incidence ROA (full grade KL worsening) and knees with KL=1.9 (ROA=Yes) are eligible for progression. Transition from KL=1.9 to KL=2 is marked as progression ROA (within grade KL worsening).

See pages 11-13 for more information on these two definitions of incident radiographic OA used, and see Appendix A for a definition of how KLG 2N (1.9) was scored during these readings.

Grade changes and reliability of the scoring method are described by Felson et al[2].

- Individual Radiographic Features (IRFs) of tibio-femoral OA, such as osteophytes and JSN in specific anatomic locations, based on published atlases[3].

  Non-integer grades for medial and lateral compartment tibio-femoral joint space narrowing (TF JSN) variables at a follow-up visit represent the same OARSI grade as at the previous visit, but differ by a fraction of an integer to denote definite progression within an OARSI grade. This means that non-integer grades (e.g.,: x.2, x.4, x.5, x.7 and x.9) are used, and indicate whether JSN has narrowed, but by less than a whole OARSI grade. An example of this would be a knee scored JSN=2.2 at 84m, JSN=2.4 at 144m follow-up, and JSN=3 at 168m follow-up. This would indicate that the knee has an OARSI JSN grade=2 at 84m and 144m visits, JSN grade=3 at 168m visit, but that the readers had agreed that narrowing had occurred between 84m and 144m but it does not amount to the next level. There was then also narrowing between 144m and 168m, and that the 168m visit OARSI grade was 3. For more detail about the method see Felson *et al*[2].

  Non-integer grades for JSN variables at the baseline visit are used to indicate a special situation where the readers consider that the baseline score is very close to the next highest JSN grade (e.g.,: V0XLJSM=2.5 means that the baseline visit left knee medial joint space is very close to zero and could be considered “bone-on-bone” and it usually represents a situation where a later timepoint has VxXLJSM=3 indicating no medial joint space width and a JSN grade of 3). Users might want to treat knees with a baseline grade of JSN=2.5 as a special case of knees that are very close to end-stage.

1.4 Variables assessed from Lateral View Knee Radiographs:

Presence of patella-femoral (PF ROA) was scored slightly differently in the baseline through 84-month visit readings and in the 144-month/168-month readings (see section 1.10 for further discussion of this)

V0-V5:

- PF ROA was considered present if either of these conditions were met for IRFs scored in the PF joint::
  - any osteophytes >=2
  - JSN>=1 plus any osteophyte, sclerosis or cyst >=1

V7-V9:

- PF ROA was considered present if KLPF not in (0,1)
- Patello-Femoral KL grade (KLPF) was scored, similarly to TF KL grade (KL), in whole grades, 0 to 4. Scores correspond to patella-femoral osteoarthritis (PFOA) status, as follows:

PF KLG Score	Patello-Femoral OA Status
KLPF = 0 KLPF = 1	No PFOA
KLPF=1.9*	Definite PFOA but with PF JSN score of 0 (see pages 11-13 for more information)
KLPF = 2	Definite PFOA with PF JSN score > 0

KLPF=3	Severe PFOA (usually with PF JSN > 1)
KLPF = 4	End stage PFOA (usually OARSI JSN score =3)

* Non-standard; see below.

Special values (6, 8 and 9) and special missing values (.P=not expected, .M=missing) were used to code a knee replacement, poor quality x-ray meaning no reading was possible or that one of both of the PA and lateral views was not acquired, or that a knee was excluded from analysis for reasons such as rheumatoid arthritis, osteonecrosis, missing patella, etc noted by the reader for example.

As with TF KLG scores, the non-standard value of 1.9 (described as KLG=2N), represents a knee that has developed a definite osteophyte, but has no JSN. The change from KLG=1 to KLG=1.9 (2N) is represented in change variables as a "within-grade" change, and represents a less strict definition of incident radiographic OA than transition from KLG<=1 to KLG>=2. See pages 11-13 for more information on these two definitions of incident radiographic OA used, and see Appendix A for a definition of how KLG 2N (1.9) was scored during these readings.

Individual Radiographic Features (IRFs) of patella-femoral OA, such as osteophytes, sclerosis, cysts and JSN in specific anatomic locations, based on published atlases[3]. At V0-V5, these IRFs were used to define presence of radiographic OA in the patella-femoral joint, but except for patella-femoral JSN grades, these IRFs are not released.

As with TF JSN scores, non-integer grades for patella-femoral joint space narrowing (PF JSN) variables at a follow-up visit represent the same OARSI grade as at the previous visit, but differ by a fraction of an integer to denote definite progression within an OARSI grade.

> **IMPORTANT NOTE:** For both TF JSN and PF JSN scores, non-integer grades SHOULD NOT be used as equivalent to specific fractional amount of JSN (i.e., 2.2 to 2.4 does not represent two tenths of a grade change) but rather indicate only a perception of a qualitative increase in JSN within the same OARSI grade compare to another time point.

1.5 Calculated Variables for OA status and change

Radiographic tibiofemoral (TF), patellofemoral (PF), and whole knee (WK) OA status were defined for each knee at each visit if the corresponding features were read.

Slightly different definitions were used for V0-V5 readings and for V7-V9 readings:
V0-V5:

- Radiographic TF OA Status (Variable names: VnXsTFROA)
  - 0: No, KL grade 0-1 or 1.9 (special value)
  - 1: Yes, KL grade 2-4

- Radiographic PF OA Status (Variable names: VnXsPFROA)
  - 0: No
  - 1: Yes= Any osteophyte >=2 - or - JSN >= 1 plus any osteophyte, sclerosis, or cyst >= 1 in the PF joint

NOTE: although osteophyte, sclerosis and cyst scores recorded and were used to define PF ROA status at V0-V5, the individual IRFs are not released in these datasets

V7-V9:

- Radiographic TF OA Status (Variable names: VnXsTFROA)
  - 0: No, TF KL grade 0 or 1
  - 1: Yes, TF KL grade 1.9, 2, 3 or 4

- Radiographic PF OA Status (Variable names: VnXsPFROA)
  - 0: No, PF KL grade 0 or 1
  - 1: Yes, PF KL grade 1.9, 2, 3 or 4

Once TF and PF OA status is defined a "whole knee" (WK) radiographic status is defined:

- Radiographic WK OA Status (Variable names: VnXsWKROA) (See Felson et al. [4])
  - 0: No, neither TF nor PF radiographic OA (see above definitions)
  - 1: Yes, either TF or PF radiographic OA (see above definitions)

The presence of radiographic TF OA, PF OA, and WK OA was determined for right and left knees of each participant at each visit (when x-ray was obtained and read).

- Knees with radiographic TF OA (Variable names: VnXTFROAk)
  - 0: None
  - 1: Right
  - 2: Left
  - 3: Both

- Knees with radiographic PF OA (Variable names: VnXPFROAk)
  - 0: None
  - 1: Right
  - 2: Left
  - 3: Both

- Knees with radiographic whole knee OA (Variable names: VnXWKROAk)
  - 0: None
  - 1: Right
  - 2: Left
  - 3: Both

The MOSTV01235XRAY dataset contains additional symptomatic (Sx) OA status defined for each knee at each visit if the whole knee OA status was known at the visit or any prior visit, and the knee pain symptoms questionnaires (telephone and clinic interview) had no missing values. Symptomatic OA is derived from the variables VnXsWKROA (see above) and frequent knee pain (FKP) variables VnR_FKP / VnL_FKP (right and left) in the clinical datasets (VnENROLL).

- Symptomatic OA status (Variable names: VnXsSxOA)
  - 0: No, whole knee radiographic OA was not present (see above definition) - or – knee pain questionnaires had no missing values and the answers were any combination other than Yes/Yes*
  - 1: Yes, whole knee radiographic OA was present and knee pain questionnaire answers were Yes/Yes* at both time points

  * Yes/Yes means that at both time points (telephone and clinic interview), the participant consistently reported knee pain, aching, and stiffness on most days in the past 30 days.

- Knees with symptomatic OA status (Variable names: VnXSxOAk)
    0: None
    1: Right
    2: Left
    3: Both

  Note: Symptomatic OA status at each visit is based on radiograph whole knee OA and frequent symptoms status at the indicated visit. Frequent symptom status can change over time, so a knee with symptomatic OA at baseline may not be classified as having symptomatic OA at follow-up if the participant no longer reports frequent symptoms in that knee. Investigators[5] have noted this pain fluctuation pattern in longitudinal studies of knee OA. MOST recruited and enrolled study participants with knee symptoms, so the prevalence of symptomatic OA was higher than in the general population.

  Note: The latest dataset (MOSTV79XRAY_OUTCOMES) does not contain Sx OA indicators. Investigators are encouraged to define and calculate Sx OA based on their own definition of symptoms.

Five-level JSN change variables between two visits were calculated for the medial TF compartment, lateral TF compartment, TF joint, and PF joint for each knee if the corresponding compartments or joint had JSN score < 3 in the corresponding compartment or joint at the earlier visit. It is not required that radiographic OA be present at baseline.

- Change of medial TF JSN (Variable names: VnmXsTFJSM_C) *Note: If JSN change was different on PA view and lateral view in the medial compartment, change in medial TF JSN was classified based on the view with the greatest change (even though medial/lateral JSN scores from the lateral view are not released).*
    1: decrease
    2: no change
    3: within grade increase
    4: full grade increase
    5: more than full grade increase

- Change of lateral TF JSN (Variable names: VnmXsTFJSL_C) *Note: If JSN change was different on PA view and lateral view in the lateral compartment, change in lateral TF JSN was classified based on the view with the greatest change (even though medial/lateral JSN scores from the lateral view are not released).*
    1: decrease
    2: no change
    3: within grade increase
    4: full grade increase
    5: more than full grade increase

- Change of TF JSN in either medial or lateral compartments (Variable names: VnmXsTFJS_C) *Note: If JSN change was different in compartments. TF JSN was classified based on the compartment with the greatest change.*
    1: decrease
    2: no change
    3: within grade increase
    4: full grade increase
    5: more than full grade increase

- Change of PF JSN (Variable names: VnmXsPFJS_C)
    - 1: decrease
    - 2: no change
    - 3: within grade increase
    - 4: full grade increase
    - 5: more than full grade increase

Four-level KL grade change variables between two visits were defined in TF joint for each knee if the knee had KLG < 4 in the corresponding joint at the earlier visit.

- Change of KLG (Variable names: VnmXsKL_C)
    - 2: no change
    - 3: within grade increase
    - 4: full grade increase
    - 5: more than full grade increase

    Note: Value of 3 (within grade increase) was assigned to change between KL grade=1 and special situation of KL grade=1.9 or 2N or between KL grade=2N and KL grade=2

Two-level JSN progression variables between baseline and each follow-up visit were calculated for the medial TF compartment, the lateral TF compartment, the TF joint, the PF joint, and the whole knee for each knee if the knee had radiographic OA but did not reach the end stage in the corresponding joint at the baseline visit.

- Progression of medial TF JSN (Variable names: V0nXsTFJSM_P)
    - 0: decrease or no change
    - 1: any increase, including within grade increase

- Progression of lateral TF JSN (Variable names: V0nXsTFJSL_ P)
    - 0: decrease or no change
    - 1: any increase, including within grade increase

- Progression of TF JSN (Variable names: V0nXsTFJS_ P)
    - 0: decrease or no change
    - 1: any increase, including within grade increase

- Progression of PF JSN (Variable names: V0nXsPFJS_ P)
    - 0: decrease or no change
    - 1: any increase, including within grade increase

- Progression of whole knee JSN (Variable names: V0nXsWKJS_ P)
    - 0: decrease or no change
    - 1: any increase, including within grade increase

NOTE: Those indicator variables were not included in the dataset MOSTV79XRAY_OUTCOMES as there were only 2 timepoints and progression (_P) would simply correspond to change (_C) and initial V7 value. Users are encouraged to use cross tabs (for example, V7XRTFJSM * V79XRTFJSM_C to identify knees eligible for progression and progressed).

1.6 Calculated Variables for Incident Radiographic OA and Progression since enrollment

Typically, incident radiographic OA at a specific visit is the development of structural changes scored as KLG >=2 at a follow-up visit, where the earlier visits were scored KLG 0 or 1.

Following this standard, incident radiographic knee OA occurred when a knee with a KLG of 0-1 became a grade 2 or higher at a subsequent visit.

In addition, the readers classified the incident KLG 2 radiographic OA as resulting from either:

a) new or enlarging definite osteophyte with normal joint space (described as KLG of 2N, represented by a value 1.9 in the variables VnXsKL),

or

b) the new combination of a definite osteophyte and joint space narrowing in a knee that did not have this combination at previous visits (denoted by a new KLG of 2).

The reason for doing this is related to the different definitions of each KLG that have been used over the years, where KLG=2 in particular was sometimes defined as an unimpaired joint space, and other times defined having joint space narrowing[6].

Definition (a) is a weaker definition of incident ROA and definition (b) is a stronger definition. In this dataset, knees which are KLG 0-1 at early visits, but which become KLG=2 at a later visit represent knees which meet either of these two definitions.

1.7 Radiographic Outcomes from baseline to 84-months

For analyses which might want to separate out knees which meet each of these two separate definitions, we recommend use of the MOSTOUTCOMES or MOSTV99OUTCOMES datasets which contains separate variables (V99ELXKL2N or V99E_LXKL2N for left knee, V99ERXKL2N or V99E_RXKL2N for right knee) that can used to identify knees with incident ROA which meets either definition (a) or (b) and separate variables (V99ELXKL2 or V99E_LXKL2 for left knee, V99ERXKL2 or V99E_RXKL2 for right knee) which identifies knees which only meet the stronger definition (b) of incident ROA. See the documentation for the MOSTOUTCOMES and MOSTV99OUTCOMES datasets for further information about these variables.

We define progression of ROA as a worsening of JSN score (including within-grade worsening) in a knee which has radiographic OA at the initial time point of the analysis. As well as variables V99EL/RXKL2N , V99E_L/RXKL2N , V99EL/RXKL2 and V99E_L/RXKL2 which indicate prevalence, incidence of radiographic OA from the baseline visit, the MOSTOUTCOMES and MOSTV99OUTCOMES datasets also contain variables for indicating cumulative worsening of joint space from baseline (eg: V99EL/RXJSNM or V99E_L/RXJSNM for medial tibio-femoral joint space, V99EL/RXJSNL or V99E_L/RXJSNL for lateral tibio-femoral joint space). Documentation for the MOSTOUTCOMES and MOSTV99OUTCOMES datasets provides further information about these variables.

IMPORTANT NOTES:

- In analyses using only V0-V5 data which exist only for the original cohort (N=3026), use only the MOSTOUTCOMES and MOSTV01235XRAY datasets.
- In analyses using only V7-V9 data, which exist for the original and new cohorts (n=2669), use only the MOSTV79XRAY_OUTCOMES dataset.

- In analyses at long term knee x-ray outcomes from the original cohort between enrollment (V0) and last known visit up to (V9), use the V99E_RX/ V99E_LX variables from MOSTV99OUTCOMES dataset, which includes all participants ever enrolled in the study (N=4551).
- Occasionally the previously indicated ROA status for original cohort participants (variables V99ERX/ V99ELX included in the MOSTOUTCOMES) would not correspond updated ROA status variables V99E_RX/ V99E_LX included in MOSTV99OUTCOMES– because new images collected at 144m or 168m allowed readers to re-assess the previous evaluation.
- if KR or end stage OA was determined at the previous visit and image was obtained (e.g. to confirm the KR), the reading was not required to be completed and therefore was not included in the MOSTV01235XRAY or MOSTV79XRAY_OUTCOMES datasets – but record is always included in the OUTCOMES and V99OUTCOMES datasets with KR indicator and last completed x-ray reading visit indicator.

1.8 Using variables for radiographic status and outcomes

For analyses that might want to separate out knees which meet each of these two separate definitions, this dataset contains separate variables (V99E_L/RXKL2N for left/right knee) that can used to identify knees with incident ROA which meets either definition (a) or (b) and separate variable (V99E_L/RXKL2 for left/right knee) which identifies knees which only meet the stronger definition (b) of incident ROA.

These variables indicate the following situations:

- whether there was a follow-up x-ray on which to determine incidence of ROA
- whether the knee had prevalent ROA (KLG=2 or KLG=2N) at baseline
- whether the knee was KLG 0-1 at baseline and had no incident ROA at last follow-up visit
- whether a knee had incident ROA and at which visit it occurred

Example:
Table 5. New Cohort TF ROA incidence KLG=2 vs incidence KLG=2N – Left knee

Table of V99E_LXKL2 by V99E_LXKL2n					
Controlling for COHORT=N					
V99E_LXKL2(Left knee BL-168M Summary incident KL >= 2 TF joint)	V99E_LXKL2n(Left knee BL-168M Summary incident KL >= 2N TF joint)				
	0: No follow-up knee x-rays or KL data	1: KL>=2N at BL	2: KL0-1 at BL, follow-up x-rays but no incident KL2N or KL2	8: KL0-1 at BL, incident KL2N or KL2 at 168 mo	Total
0: No follow-up knee x-rays or KL data	207	6 (1)	0	0	213
1: KL>=2 at BL	0	157	0	0	157
2: KL0-1 at BL, follow-up x-rays but no incident KL>=2	0	35 (2)	1040	22 (3)	1097
8: KL0-1 at BL, incident KL>=2 at 168 mo	0	8 (4)	0	47	55
Total	207	206	1040	69	1522

Footnote for Table 5:

(1) 6 knees were scored as KLG=2N at enrollment and did not have follow up visit
(2) 35 knees were scored as KLG=2N and continue to be KLG=2N at follow up
(3) 22 knees scored as KLG=0 or 1, developed incidence KLG=2N at follow up
(4) 8 knees scored as KLG=2N and developed incidence KLG=2 at follow up

Please note that variables V99E_LXLVSQD and V99E_RXLVSQD indicate the latest visit at which the knee had central x-ray readings performed. It is important to take the value of this variable into consideration when determining incidence of ROA. For example, for a knee with no ROA at baseline, if the latest visit with a central x-ray reading is the 144-month visit, then the radiographic OA status of that knee at the 168-month visit is unknown and depending on the type of analysis being performed, that knee might not be eligible for an analysis of incident radiographic OA.

Although this dataset does contain information about knee replacements in the x-ray readings, please be aware that it is possible that the latest visit with x-ray readings is NOT the latest visit (or contact point) at which the participant contributed the meaningful information to the study. This could be data from a knee replacement survey done after visit indicated by V99E_L/RXLVSQD visit indicator variable. The dataset MOSTV99OUTCOMES (information between V0 and V9) contains the most recent and comprehensive information separately as KR index point and knee status prior to the knee surgery.

Example:
Table 6. New cohort x-ray incidence KLG=2 vs last SQ readings– Left knee.

Table of V99E_LXKL2 by V99E_LXLVSQD				
Controlling for COHORT=N				
V99E_LXKL2(Left knee BL-168M Summary incident KL >= 2 TF joint)	V99E_LXLVSQD(Left knee, last visit with central reading follow-up knee x-ray SQ (KL or JSN) data)			
	0: No follow-up knee x-ray or SQ (KL or JSN) data	7: Last SQ data at 144 mo visit	9: Last SQ data at 168 mo visit	Total
.E:Excluded	3	0	0	3
0: No follow-up knee x-rays or KL data	0	213	0	213
1: KL>=2 at BL	0	26	131	157
2: KL0-1 at BL, follow-up x-rays but no incident KL>=2	0	0	1097	1097
8: KL0-1 at BL, incident KL>=2 at 168 mo	0	0	55	55
Total	3	239	1283	1525

In addition to the incidence, worsening of JSN scores (including within-grade worsening) in a knee which has JSN score<3 at the initial time point of the analysis from enrollment to the last available x-ray were calculated. The following list identifies the JSN progression/worsening variables and which knee compartment is involved and which x-ray view was being used:

From bilateral PA view knee radiograph:
V99E_L/RXJSNM – left/right knee medial tibio-femoral compartment JSN progression
V99E_L/RXJSNL – left/right knee lateral tibio-femoral compartment JSN progression

From left/right knee lateral view radiograph:
V99E_L/RXJSNM_Lat – left/right knee medial tibio-femoral compartment JSN progression
V99E_L/RXJSNL_Lat – left/right knee lateral tibio-femoral compartment JSN progression

The following 4 summary variables indicate whether narrowing was seen on either the PA view or the lateral view:
V99E_L/RXJSNM_any – left/right knee medial tibio-femoral compartment JSN progression
V99E_L/RXJSNL_any – left/right knee lateral tibio-femoral compartment JSN progression

The values taken by these variables are used to indicate the following situations:

- x-ray was not read for JSN
- there were no follow-up visit x-rays or readings
- the knee was JSN=3 at baseline and could therefore not worsen at later timepoints
- the knee was JSN <3 at baseline and within-grade worsening occurred
- the knee was JSN<3 at baseline and a full grade (or more) of worsening occurred

Consult the variable guide (VariableGuide_V79XRAY_OUTCOMES.pdf) and distributions document (Distributions_ V79XRAY_OUTCOMES.pdf) for this dataset for the descriptive labels

and values used for each of these variables and situations. When analyzing JSN progression/worsening status, the variables V99E_LXLVSQD and V99E_RXLVSQD (which indicate the latest visit at which the knee had central x-ray readings performed) should be considered.

All x-ray related outcome variables (prefixes: V99E_L and V99E_R) are also included in the dataset MOSTV99OUTCOMES for convenience of users who decided to use all image assessments that have ever been collected in MOST from enrollment to 168m. Consult the variable guide (VariableGuide_V99OUTCOMES.pdf) and distributions (Distributions_ V99OUTCOMES.pdf) and the documentation for the MOSTV99OUTCOMES dataset for further information.

Similar variables prefixed V99EL/V99ER exist based on V0-V5 x-ray readings for the entire original cohort (N=3026). Consult the variable guide (VariableGuide_OUTCOMES.pdf) and distributions document (Distributions_OUTCOMES.pdf) and the documentation for the MOSTOUTCOMES dataset for further information.

1.9 Comparing Patello-Femoral OA definitions

As described previously (page 6), at 144-month and 168-month visits, the definition of patella-femoral OA was based on Kellgren and Lawrence scores, but at earlier MOST visits, it was based on a combination of different IRFs (see page 6 and reference #4) because Kellgren and Lawrence scoring wasn't performed prior to the 144-month visit.

For Original Cohort participants with 144-month and/or 168-month visit x-rays, this means that there will be some with discrepancies in PF OA status depending on which definition is used. The following cross-tabulations show good agreement between the definitions when applied at the 144-month visit:

Table 7. Comparison of two PF ROA definitions.

Original Cohort						
Left knee				**Right knee**		
Kellgren & Lawrence Definition of PF OA	IRF based definition of PF OA			Kellgren & Lawrence Definition of PF OA	IRF based definition of PF OA	
	No	Yes			No	Yes
No	649	0		No	598	1
Yes	24	209		Yes	26	229
Kappa 0.928 (0.899 – 0.956)				Kappa 0.922 (0.894 – 0.951)		
New Cohort						
Left knee				**Right knee**		
Kellgren & Lawrence Definition of PF OA	IRF based definition of PF OA			Kellgren & Lawrence Definition of PF OA	IRF based definition of PF OA	
	No	Yes			No	Yes
No	1431	4		No	1408	0
Yes	4	83		Yes	5	109
Kappa 0.951 (0.918 – 0.985)				Kappa 0.976 (0.955 – 0.997)		
Overall Kappa coeff 0.938 (0.916 – 0.959)				Overall Kappa coeff 0.957 (0.940 – 0.974)		

Worsening of JSN PF score (including within-grade worsening) in a knee which has JSN score<3 at the initial time point of the analysis is included - variables from lateral view radiograph:

V99E_L/RXJSPF_Lat – left/right knee summary PF JSN progression

2. Methods specific to Baseline (V0) thru 84-month (V5) visit knee x-ray readings

Overview

Dataset: MOSTV01235XRAY
Observations: 3026 (1 record per study participant)
Annotated Forms: AnnotatedForms_V01235xray.pdf
Variable Guide: VariableGuide_V01235xray.pdf
Distributions: Distributions_V01235xray.pdf
Formats: FORMATS.SAS7BDAT (contains all the formats used for the dataset)

At present, data from baseline thru 84-month follow-up visit are released.

This dataset contains x-ray readings of Kellgren and Lawrence grades and OARSI joint space narrowing grades along with scores for other individual radiographic features (IRFs) such as osteophytes and sclerosis, along with variables for longitudinal changes between all possible paired combinations of visits from baseline (V0) to 84-month followup (V5).

There are also special variables for cumulative incidence of radiographic OA (ROA), and for progression of radiographic OA from the baseline visit. See page 11 of this document, give more information on the different definitions of incident ROA and progression of ROA that can be used. So for analyses involving incidence or progression of ROA, we recommend that the OUTCOMES dataset should be used.

Limb alignment measurements from baseline and 60-month visit full-limb radiographs are also in this dataset.

2.1 Introduction

MOST serial knee radiographs were read at the Boston University Clinical Epidemiology Research and Training Unit. The radiographs were read with visits grouped and temporal order known, from baseline to 15, 30, 60 and 84-month follow-up visits, by 2 readers for Kellgren-Lawrence grade (KLG) and Individual Radiographic Features (IRFs, see page 5). Knees without follow-up images were scored for baseline KLG only or baseline KLG and other features. The number of knees with various combinations of assessments is shown in the table below:

Assessments	Right Knee	Left Knee
Five x-ray Baseline to 15M, 30M,60M, and 84M Assessments	160	157
Quadruplet Baseline to 15M, 30M, and 60M Assessments	33	34
Quadruplet Baseline to 15M, 30M, and 84M Assessments	12	12
Quadruplet Baseline to 15M, 60M, and 84M Assessments	3	3
Quadruplet Baseline to 30M, 60M, and 84M Assessments	1508	1504
Triplet Baseline to 15M and 30M Assessments	58	53
Triplet Baseline to 15M and 60M Assessments	2	2
Triplet Baseline to 15M and 84M Assessments	1	1
Triplet Baseline to 30M and 60M Assessments	245	260
Triplet Baseline to 30M and 84M Assessments	79	82
Triplet Baseline to 60M and 84M Assessments	39	35
Paired Baseline to 15M Assessments	20	23

Assessments	Right Knee	Left Knee
Paired Baseline to 30M Assessments	472	461
Paired Baseline to 60M Assessments	23	26
Paired Baseline to 84M Assessments	15	17
Baseline KLG Only (Participants with baseline readings and no follow-up images)	209	210
Baseline KLG and Other Features (Subset of participants with baseline readings and no follow-up images)	98	89
No Assessments (baseline KR or other x-ray exclusion)	49	57
Total	**3026**	**3026**

At the baseline visit, MOST full limb radiographs were acquired in almost all participants. This dataset contains central measurements of frontal plane lower limb mechanical alignment using hip-knee-ankle (HKA) angle. The analysis of these images was performed by OAISYS Inc (Dr. Derek Cooke http://www.oaisysmedical.com) with support of staff at Queen's University, Kingston, Ontario.

2.2 Variables

The Variable Guide (VariableGuide_V01235xray.pdf) is a complete list of all variables in the dataset, their SAS variable names, descriptive variable labels, and attributes. If you are unfamiliar with the data, it may be useful to begin by reviewing the annotated data collection forms (AnnotatedForms_V01235xray.pdf) to look for variables of interest.

The dataset contains five types of variables, listed below. The first type is related to measurements of HKA from full limb radiographs and the remaining 4 types are related to readings of bilateral PA view radiographs:

- Measurements of HKA angle (in degrees) where neutral alignment is represented by 0 degrees with varus deviations negative and valgus deviations positive. (eg: V0XLHKA is left limb hip-knee-ankle angle) – see section 5 for more information.
- Raw radiograph reading from a specific visit (for example, V0XRKL: Right knee KLG at the baseline visit).
- Change score between two visits for a specific measure (for example, V02XRKL_C: Right knee KLG change from baseline to 30 months).
- Derived status of a knee or person meeting the criteria for a specific measure (for example, V0XRTFROA: Right knee tibiofemoral radiographic OA).
- Derived indicator of a knee meeting the criteria for a specific outcome measure (for example JSN progression: V02XRTFJSL_P: Right knee joint space narrowing progression from baseline to 30 months).

Section 1 gives more information about the naming convention for variables.

2.3 Missing Data

The dataset includes records for 3026 participants. Where expected data do not exist for a knee, special missing values are assigned to denote why the data were not acquired. The special missing values include:

.P	Not expected: Data missing because the exam was not done (appears only in follow-up data since all 3026 participants have a baseline exam).
.S	End stage OA: Data is missing because the maximum value was reached at the initial time point (used for change variables and progression status).
.X	X-ray not read: Baseline feature other than KLG was not read because only a single time point was available to be read.
.Z	Not determined: The value cannot be determined because the calculation is dependent on missing data (for example, if there is no tibiofemoral OA and patellofemoral radiographic OA was not read, whole knee OA cannot be determined).

2.4 Methods

Image Type:

Bilateral, weight-bearing fixed-flexion posteroranterior (PA) and lateral knee radiographs were acquired in MOST, along with Full Limb Radiographs. See the MOST Knee and Full-Limb Radiography (X-ray) Operations Manuals (available for Cycles 1-2 and Cycle 3 at https://agingresearchbiobank.nia.nih.gov/studies/most/documents/?f=Manual_of_Procedures)

Time Points:

Full Limb Radiographs:
Baseline and 60-month follow up visits.

Bilateral PA View Knee Radiographs and Lateral Knee Radiographs:
Baseline, 15-month follow-up (subset of cohort), 30-month, 60-month and 84-month follow-up visits.

Reading Methods:

Full Limb Radiographs:
For information about measurements taken from full limb radiographs, see section 5.

Bilateral PA View Knee Radiographs:
Two expert readers, blinded to subject's clinical data, assessed each participant's films. Baseline and follow-up films were scored while viewed simultaneously. Readers were not blinded to chronological order of the images. When readers disagreed on key features, or changes in key features, an adjudication procedure was followed (see Appendix A for more information).

3. Methods Specific to 144-month (V7) to 168-month (V9) visit knee x-ray readings

All MOST participants with knee x-rays acquired at either 144- or 168-month follow-up visits have now been read and this is a complete and final dataset of x-ray readings. This dataset contains x-ray readings of Kellgren and Lawrence grades and OARSI joint space narrowing (JSN) grades along with scores for other individual radiographic features (IRFs) such as osteophytes. It also contains derived variables for OA status (prevalence, incidence and progression); changes between 144m and 168m (variables prefixes V79); and outcomes: incidence KL2/KL2N for TF and PF joint and changes in JSN from baseline (enrollment) visit to last available x-ray (variables prefixed V99E_)

> **IMPORTANT NOTE**: Kellgren and Lawrence grades (KLG) for TFROA and PFROA used in this dataset (MOSTV79XRAY_OUTCOMES) for all timepoint/visits include a special value of '1.9' (labelled KLG=2N), which is definite radiographic OA (knee meets criteria for KLG=2) but where the OARSI JSN scores are 0 (JSM and JSL on PA view for TF joint and JSN for PF joint). The KLG value '2' at all timepoints is used for knees with definite radiographic OA (KLG=2) but where the OARSI JSN score is > 0. Calculated outcome variables for incident radiographic OA classify knees that are KLG 0-1 at baseline (enrollment) as incident KLG 2N at follow-up timepoints with a KLG score of '1.9 or higher', and as incident KLG 2 at follow-up timepoints with a KLG score of '2 or higher'. Note: enrollment or baseline visit is V0 for Original Cohort and V7 (144m) for New Cohort.
>
> This scoring is slightly different compared to previous MOST x-ray OUTCOMES dataset for the original cohort, where the KLG value of 1.9 was not used at baseline (V0). A KLG value of '2' at baseline was used for knees with definite radiographic OA (met the criteria for KLG=2) whether or not JSN was present. Baseline KLG values of 2 (with or without JSN) remained KLG=2 at subsequent timepoints if there was no increase in KLG score. For knees that were KLG 0-1 at baseline (V0), incident OA was categorized separately for KLG 2N and KLG 2 in the same way as in the MOSTV79XRAY_OUTCOMES dataset.
>
> (See pages 7, 11-13 and Appendix A for more information on the above.)

3.1 Introduction

MOST serial knee radiographs are read at the Boston University Clinical Epidemiology Research and Training Unit. The radiographs were read with visits grouped and temporal order known, from 144-month to 168-month follow-up visits, by two readers for Kellgren-Lawrence grade (KLG) and Individual Radiographic Features (IRFs) (see Annotated Forms).

During readings for Original Cohort participants, the images from two closest previous visits (from baseline to 15-, 30-, 60- and 84-month follow-up visits) were always provided to readers, along with KLG/JSN and other IRFs from those visits for the readers to review and revise. If needed and requested, all previous visits and scores were provided to readers to review and revise.

The majority of participants from both cohorts had both 144-month and 168-month knee x-rays available for reading, but images were read even if only one new visit knee x-ray was available. The number of knees with various combinations of assessments by cohort is shown in the tables below:

Table 1. Original Cohort – 144m x-ray acquired, 168m visit missed.

Original Cohort Assessments (single 144m image)	Participants	Adjudicated records
Baseline – 144m	1	
Baseline – 30m – 144m	8	
Baseline – 84m – 144m	1	
30m – 60m – 144m	18	
30m – 84m – 144m	10	
60m – 84m – 144m	162	
Total	**200**	**0* (none)**

*single 144m images were not adjudicated according to the x-ray reading protocol.

Table 2. Original Cohort – 144m visit missed, 168m x-ray acquired.

Original Cohort Assessments (single 168m image)	Participants	Adjudicated records
Baseline – 168m	2	
Baseline – 15m – 168m	1	
Baseline – 30m – 168m	8	
Baseline – 60m – 168m	1	
Baseline – 84m – 168m	1	
15m - 30m – 168m	1	
30m – 60m – 168m	15	
30m – 84m – 168m	6	
60m – 84m – 168m	89	
Total	**124**	**6 (4.8%)**

Table 3. Original Cohort – 144m/168m paired x-ray acquired.

Original Cohort Assessments: 144m/168m paired	Participants	Adjudicated records
Baseline – 144m – 168m	2	
Baseline – 30m – 144m – 168m	4	
Baseline – 84m – 144m – 168m	5	
30m – 60m – 144m – 168m	27	
30m – 84m – 144m – 168m	29	
60m – 84m – 144m – 168m	753	
Total	**820**	**515 (62.8%)**

Table 4. New Cohort 144m only or 144m/168m paired x-ray acquired;

New Cohort Assessments	Participants	Adjudicated records
144m	238	0* (none)
144m – 168m	1287	**415 (32.2%)**
Total	**1525**	

*single 144m images were not adjudicated according to the x-ray reading protocol.

IMPORTANT NOTE: Merge with caution datasets: MOSTV01235XRAY, MOSTOUTCOMES and MOSTV79XRAY_OUTCOMES. Reading parameters, x-ray status and outcomes have been updated for many original cohort participants who completed either 144m or 168m visit with x-ray images obtained.
The outcome variables of MOSTV79XRAY_OUTCOMES dataset provides all prevalence and incidence on KL grade and JSN changes since enrollment visit for all participants who completed 144m (V7) and/or 168m (V9) with knee x-ray images obtained (N=2669).
The outcome variables of MOSTV99OUTCOMES dataset provides all prevalence/incidence on KL grade and JSN changes since enrollment visit for all participants ever enrolled in the study (N=4551).

IMPORTANT NOTE: Note that knee replacements and x-ray exclusion criteria (RA, amputation, missing patella, osteonecrosis, etc.) reported in the x-ray reading dataset is not a comprehensive accounting – it is marked only for the knees in which an x-ray was acquired and exclusion noted for the first time. Use the dataset MOSTV99OUTCOMES for comprehensive and adjudicated KR information and x-ray exclusions.

IMPORTANT NOTE: One participant completed the 144-month clinic visit with x-rays (no MRI due to equipment issues) but then returned for an MRI on the right knee but left knee was reported replaced between 144-month x-ray and MRI visit. Therefore, this participant will have a left knee x-ray reading at 144-months and also a left knee replacement reported at 144-months.

3.2 Variables

The Variable Guide (VariableGuide_V79XRAY_OUTCOMES.pdf) is a complete list of all variables in the dataset, their SAS variable names, descriptive variable labels, and attributes. If you are unfamiliar with the data, it may be useful to begin by reviewing the annotated data collection forms (RadiographAnnotatedForms_V79XRAY.pdf) to look for variables of interest.

The dataset contains three types of variables related to readings of bilateral PA view radiographs and Left/Right lateral views:

4. Raw radiograph reading from a specific visit: for example, V7XRKL: Right knee KLG at the 144m visit from PA view; V7XRKLPF: Right knee KLG of PF joint at the 144m visit from Right Lateral view.
5. Calculated TF/PF/WK OA status and change variables between 144m and 168m.
6. Calculated Incidence KLG status and change in JSN between Baseline (enrollment) and 168m (or last available clinic visit with x-ray).

The following calculated variables were included in the radiographic assessment dataset:

- Derived status of a knee or person meeting the criteria for a specific measure: for example, V7XRTFROA: Right knee tibiofemoral radiographic OA at 144m.
- Change score between two visits for a specific measure: for example, V79XRKL_C: Right knee KLG change from 144m to 168m.
- Derived indicator of a knee meeting the criteria for a specific outcome measure: for example JSN progression: V79XRTFJSL_P: Right knee joint space narrowing progression from 144m to 168m.

Section 1 of this document describes the naming conventions for variables.

3.3 Missing Data

All MOST participants with knee x-rays acquired at either 144- or 168-month follow-up visits have now been read and this is a complete and final dataset of their x-ray readings. Where expected data do not exist for a knee, special missing values are assigned to denote why the data were not acquired. The special missing values include:

.P or '.'	Not expected: Data missing because the x-ray exam was not done.
.S	End stage OA: Data is missing because the maximum value was reached at the initial time point (used for change variables and progression status).
.X	X-ray not read: Baseline feature other than KLG was not read because only a single time point was available to be read.
.Z	Not determined: The value cannot be determined because the calculation is dependent on missing data (for example, if there is no tibiofemoral OA and patellofemoral radiographic OA was not read, whole knee OA cannot be determined).

3.4 Methods

Image Type:

Bilateral, weight-bearing fixed-flexion posteroanterior (PA) and lateral knee radiographs were acquired and read in MOST. See the MOST Knee and Full-Limb Radiography (X-ray) Operations Manuals (available for Cycles 1-2 and Cycle 3 at https://agingresearchbiobank.nia.nih.gov/studies/most/documents/?f=Manual_of_Procedures)

Time Points:

Original Cohort:
Bilateral PA View Knee Radiographs and Lateral Knee Radiographs:

- Baseline, 15-month follow-up (subset of cohort), 30m, 60m and 84m follow-up visits.
- Unilateral or Bilateral PA View Knee Radiographs and Lateral Knee Radiographs for knees with previously scored KL grade of 1 to 2: 144m and 168m follow-up visit.

Note: According to the protocol, if the knee was reported as KR (knee replacement) or determined as x-ray exclusion or if knee KLG was scored 3 or 4 at any prior visit, it was not eligible for the radiograph image at 144m or 168m follow-up.

New Cohort:
Full Limb Radiographs at enrollment (144m visit).

Bilateral PA View Knee Radiographs and bilateral Lateral Knee Radiographs:

- 144-month (enrollment screen visit) and 168-month follow-up visits.

Reading Methods:

Bilateral PA View Knee Radiographs:
This section describes the reading methods for longitudinal semi-quantitative (SQ) assessments of the bilateral PA View Knee radiographs. Two expert readers, blinded to participant's clinical data, assessed each participant's films. For new cohort participants, V7 and V9 films were scored while viewed simultaneously. For original cohort participants, V0, V5 films were viewed showing existing readings and V7 and V9 films were displayed for paired readings with the

earlier visits (if V5 films were not obtained, the last visit prior to V5 was used). Readers were not blinded to chronological order of the images. When readers disagreed on key features, or changes in key features, an adjudication procedure was followed (see Appendix A for more information).

4. Measurements from Full Limb Radiographs

In general, frontal plane lower limb alignment is measured from standing bilateral radiographs of the lower limbs in their entirety, with knees fully extended (called 'full-limb' radiographs in MOST). Positional reliability is provided for by aligning the 'knee flexion plane' ahead. Frontal alignment may be defined as the angle between the mechanical axes of the femur and tibia. This angle has been termed the hip-knee-ankle (HKA) angle or the mechanical axis angle. The measurements in this dataset have been made from digital full-limb images using software programs (OAISYS Inc) to obtain the measurement of alignment. These publications give more details about the methods and measurement performance:

- *Cooke TD, et al. Frontal plane knee alignment: a call for standardized measurement. J Rheumatol. 2007; 34(9):1796-801. PMID: 17787049.*
- *Cooke TD, et al. Analysis of limb alignment in the pathogenesis of osteoarthritis: a comparison of Saudi Arabian and Canadian cases. Rheumatol Int. 2002; 22(4):160-4. PMID: 12172956*
- *Sled E, et al. Reliability of lower limb alignment measures using an established landmark-based method with a customized computer software program. Rheumatol Int. 2011: 31:71-7*

From the anatomical and functional perspective, the orientation of the femur and tibia at the knee is best described in terms of the bones' mechanical axes. The orientation of these axes reflects alignment in stance, which may be neutral, varus (bowlegged), or valgus (knock-kneed) (Figure 1).

The mechanical axis of the femur (FM) is located as a line from the center of the femoral head running distally to the mid-condylar point between the cruciate ligaments. In the case of the tibia, the mechanical axis (TM) is a line from the center of the tibial plateau (interspinous intercruciate midpoint) extending distally to the center of the tibial plafond. The angle between these two axes is the hip-knee-ankle (HKA) angle. In the neutrally-aligned limb the HKA angle approaches 180°. At this point FM and TM are co-linear, pass through the knee center, and are coincident with the load-bearing axis (LBA) which is the line of ground reaction force passing from the ankle to the hip (Figure 1B).

In *varus* the knee center is lateral to the LBA (Figure 1A), whereas in *valgus* the knee center is displaced medially (Figure 1C). As a convention the HKA is expressed as its angular deviation from 180° (i.e. HKA = 0° in neutral alignment). Varus deviations are negative and valgus ones are positive. The choice of varus as a negative value and valgus as positive is based on the general observations of a more serious problem of loading and damage in the varus knee.

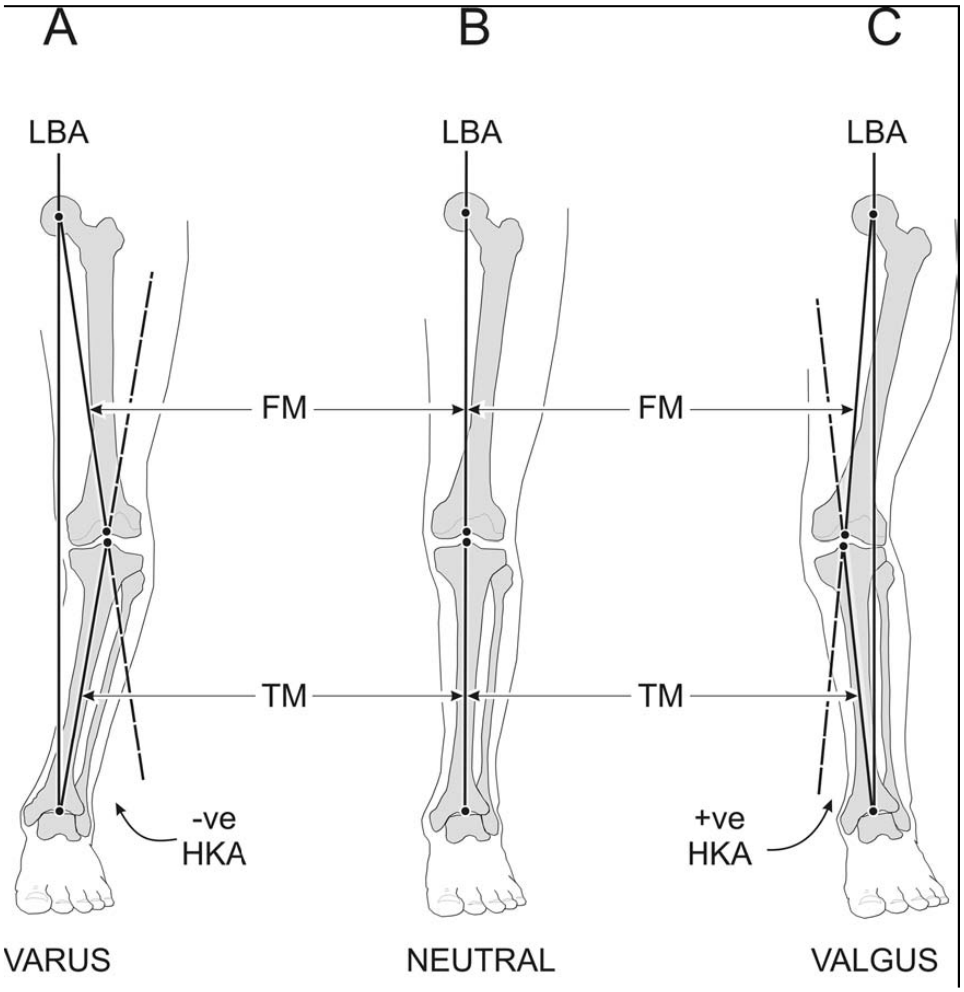

Figure 1. Common frontal plane lower limb alignment patterns. A. Varus alignment: knee center is lateral to the LBA (HKA is negative). B. Neutral alignment: knee center is located on the LBA (HKA = 0°); femoral and tibial mechanical axes are colinear. C. Valgus alignment: knee center is medial to the LBA (HKA is positive). LBA: load-bearing axis, HKA: hip-knee-ankle angle, FM: femoral mechanical axis, TM: tibial mechanical axis.

5. References

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APPENDIX A: Knee X-ray Reading Discrepancy Adjudication

Overview

V0-V5: Films were read independently by two primary readers and discrepancies adjudicated in order to allow comparison of key findings that the senior reader may have missed and to ensure high quality data by reducing measurement error.

Pre-specified discrepancies between readers were adjudicated in a consensus session with films viewed simultaneously and a third reader participating. The values in this dataset are the final, adjudicated readings. When a variable was not adjudicated for discrepancies, the value in the dataset is from the senior reader.

Reader disagreements that were adjudicated were TF OA and PF OA status (Y/N) and its change in all knees, and progressive JSN (Y/N) in those knees with OA in the TF and/or PF joints at one or more time points.

V7-V9: Paired films were read independently by two primary readers (Reader #1: rheumatologist; Reader #2: senior reader/musculoskeletal radiologist). There were two stages of adjudication. First, the rheumatologist reader (Reader #1) was presented the x-rays for knees where Reader #1 scores disagreed with that of the senior reader (Reader #2), a musculoskeletal radiologist and Reader #1 was told Reader #2's scores. Reader #1 was asked whether he agreed with Reader #2 or whether he thought Reader #2, the senior reader was in error. If Reader #1 agreed, then Reader #2's, the senior reader's reading was used. For the group of films where Reader #1 did not agree, the films were shown again to Reader #2, the senior reader. Those films for which there was persistent disagreement were brought to the adjudication panel.

The adjudication panel resolved persistent disagreements in a consensus session with films viewed by both Reader #1 and Reader #2 and a third reader (Reader #3), another senior musculoskeletal radiologist.

The values in datasets are the final, adjudicated readings. When a variable was not adjudicated for discrepancies (these are listed below), the value in the dataset is from Reader #2, the senior reader.

Reader disagreements that were adjudicated were TF OA and PF OA status (Y/N) and its change in all knees, and progressive JSN (Y/N) in those knees with OA in the TF and/or PF joints at one or more time points. Adjudication rules for the key variables are listed below. For all of these variables, readings for only these variables were adjudicated only if the two readers did not agree on the variable.

X-rays for participants with single new visits (144-month only or 168-month only) were read by the senior reader (Reader #2) and then scores were reviewed by Reader #1. They did not go through the entire adjudication process.

PA and Lateral Radiographs

Knee OA status and its progression was classified into one of the following 4 groups in either the tibiofemoral or patellofemoral compartment for each of two consecutive visits (we note that the tibiofemoral JSN adjudication occurred when there was disagreement on either or both of

the PA and lateral views). Readings were adjudicated if the two readers did not agree on the following classifications:

1. No OA at either time point.
2. Incident OA (no OA at baseline, OA at follow-up).
3. Prevalent OA at the earlier visit, no progression in either KLG or JSN in the follow-up visit.
4. Knees without OA (KL grade <=1) but with JSN not equal to 0.

A knee was not adjudicated if:

- Both readers agreed there was 'No OA' longitudinally but one reader scored KLG progression while the other did not (e.g., KLG 0 → 1 by one reader vs. other reader scored knee as 1 → 1).

- Both readers agreed there was incident OA but the KLG at either visit differed by reader (e.g., reader one scored 1 → 2; reader two scored 1 → 3).

- Both readers agreed there was prevalent OA at the earlier visit but the KLG at either visit differed by reader as long as both agreed on the presence or absence of KLG progression (e.g., reader one scored 3 → 3; reader two scored 2 → 2).

Joint Space Narrowing (JSN)

Joint space narrowing was scored 0-3 based on the OARSI Radiographic Atlas. However, when follow-up film clearly showed worsening JSN Knee X-ray Reading compared to the film from the previous visit, but narrowing for both films was still within one OARSI grade, readers were permitted to use non-integer grades (e.g. 2 → 2.3). Progression was defined as present when there was an increase in score by >0. Progression status was classified into one of the following two groups for consecutive visits, and readings were adjudicated if the two readers did not agree on the classification:

- JSN progression in either the medial and/or lateral compartments in the follow-up visit.

- JSN progression in the follow-up visit but in different compartments (e.g. one reader scored progression in the medial compartment whereas other reader scored it in the lateral).

Lateral Radiographs

TF and/or PF JSN Progression

Change of TF JSN and/or PF JSN was classified into one of the following two groups for consecutive visits and the knee was adjudicated if the two readers did not agree on the classification:

- TF JSN progression in the follow-up visit.
- PF JSN progression in the follow-up visit.

A knee was not adjudicated if:

- One reader scored TF JSN and/or PF JSN but the other reader did not, as long as neither read progression in JSN.
- The two readers agreed on progression but differed on the amount of progression.

PF Osteoarthritis

Knee Patellofemoral OA status and its progression (based on PF JSN scores) was classified into one of the following 3 groups for each two consecutive visits, and the readings adjudicated if Reader #1 and Reader #2 did not agree on the classification:

1. No OA at either time point.
2. Incident OA (no OA at baseline, OA at follow-up).
3. Prevalent OA at the earlier visit, no progression in PF KLG and/or PF JSN in the follow-up visit.

For V0-V5 readings, PF OA status was judged as simply present/absent. For the V7-V9 readings PF KLG scores were used.

Adjudication sessions were held approximately every two months. These sessions were attended by both primary readers and a third reader. All adjudicated readings were arrived at by consensus of readers and the adjudicated score was recorded on the senior reader's scoring sheet. After consensus was reached, the dataset was updated. When readers' data are in agreement, both are archived and the dataset of the senior reader used in analysis.

The following features were not adjudicated: cysts, osteophytes, sclerosis, chondrocalcinosis.

For these features, readings from Reader #2, the senior reader's readings were used. However, to make the data consistent after adjudication, some of the scores for these variables especially osteophytes were changed during adjudication, e.g., if KLG and/or progression was changed during adjudication, osteophyte scores were often modified to be consistent with the adjudicated score. For example, if the adjudicated score was KLG 2 and the senior reader had '0' for all osteophytes, then this was reevaluated by the readers to create logical consistency of all the feature scores.

Guidance for Analysts

Guidance for Analysts for the 2N or Kellgren and Lawrence Score of 1.9

A 2N or 1.9 Kellgren and Lawrence score is applied to a compartment (tibiofemoral or patellofemoral) in a knee where there are osteophytes but no JSN. The JSN score for that compartment must be 0 and there must be at least one grade 2 osteophyte (a moderate to large osteophytes) or at least three grade 1 osteophytes (multiple small osteophytes).

JSN Improvement

Occasionally we noticed unexpected "improvement" in JSN scoring – this could be attributed to different beam angle when reader was unsure how to compare two or three images for JSN change.

Guidance for Analysts on Consistent Scoring of Patellofemoral OA

In MOST, the radiographic diagnosis of patellofemoral OA changed at the 144m visit and thereafter. At the 144m visit, we began to apply Kellgren and Lawrence grading to the PF joint, in a similar way to applying it in the with the TF joint.

Previously, we generally followed the rule that the PF joint met criteria for OA if there was BOTH narrowing in that joint (a score of >0 for PF narrowing) and an osteophyte score in that joint of > 0. An osteophyte score > 1 with PF JSN=0 would also meet the criteria for OA (see page 9 for details on the previous calculations used for defining PF OA). There are 3 locations for osteophytes in the PF joint on the lateral view: superior patella, inferior patella and anterior femur. A PF joint would have Kellgren and Lawrence score >=2 if there was both JSN in the joint and an osteophyte >=1 in any of the 3 locations. We now use the special value PF KLG=1.9 (2N) for the situation where there are large enough osteophytes that the reader considered PF OA to have occurred, but where PF JSN=0.

If the analyst wants to create consistency in characterizing PF OA before the 144m visit, they can apply the rules above to PF joint scores of JSN and osteophytes at all exams.